THE CANCER LETTER

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Doctor's Allegation Of Drug Safety Problem Starts Controversy With Manufacturer

Last year, researchers at the H. Lee Moffitt Cancer Center & Research Institute in Tampa noted an increase in side effects experienced by patients receiving a high dose regimen of ifosfamide, carboplatin and etoposide (ICE).

They came up with a possible explanation: the hospital pharmacy substituted generic etoposide for the brand-name version of the drug.

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In Brief

Calabresi Named To President's Cancer Panel; Mays Leaves NCI Technology Office For IVAX

PAUL CALABRESI has been appointed to the President's Cancer Panel, the White House announced earlier this week. Calabresi, professor of medicine and chairman emeritus of the Dept. of Medicine at Brown Univ., replaces **Henry Pitot**, of the McArdle Laboratory at Univ. of Wisconsin. Members of the panel serve for a three-year term. The panel is responsible for "alerting the President to any delays or blockages in the rapid execution of the National Cancer Program," a White House statement said. Calabresi served as chairman of the National Cancer Advisory Board from 1991 to 1994, and last year chaired a committee that recommended measures to strengthen the National Cancer Program. He is co-chairman, with Michael Bishop, of the NCAB Working Group on the NCI Intramural Program. Other members of the President's Cancer Panel are **Harold Freeman**, of Harlem Hospital, and **Fran Visco**, president of the National Breast Cancer Coalition. . . . **TOM MAYS**, director of the NCI Office of Technology Development since 1990, has accepted a position at Miami-based IVAX Corp. Mays will be an intellectual property attorney with the firm, starting June 5. Samuel Broder, former NCI director, is scientific director at IVAX. "[Broder's] position would be a natural interface with me," Mays said to **The Cancer Letter**. "I certainly enjoyed working with him while he was at NCI, and I would enjoy working with him in another capacity." . . . **NORMAN ANDERSON** was appointed to the newly created position of NIH associate director for behavioral and social sciences research. Anderson is an associate professor in psychiatry and psychology at Duke Univ. Anderson will be responsible for directing trans-NIH behavioral and social sciences research, NIH Director Harold Varmus said. . . . **DIANE VAN OSTENBERG**, administrative director of the Grand Rapids Clinical Oncology Program, has become president of the Association

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Generic Maker Asks Scientist To Withdraw Abstract On Drug

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The Moffitt researchers stopped using the generic and notified the manufacturer of the problem. Also, they prepared to share the findings of their retrospective review with other scientists at the meeting of the International Society of Oncology Pharmacy Practice in Hamburg on May 3-6.

However, at that point, the maker of the generic, Gensia Inc., protested. In a letter to Moffitt, an official of the San Diego-based company raised detailed questions about the circumstances under which the ICE regimen was administered and challenged the assumption in the abstract that all the patients received the Gensia version of etoposide.

"Because of multiple concerns raised above... we believe that it would be appropriate to withdraw your abstract at the present time," said the letter dated Jan. 24 and signed by Daniel Pertschuk, associate director, clinical research, at Gensia Inc.

The branded version of etoposide, VePesid, is produced by Bristol-Myers Squibb Co. The generic etoposide believed to have been used at Moffitt was produced by Gensia Laboratories Ltd. of Irvine, CA, a subsidiary of Gensia Inc.

Pertschuk's letter served to bring into focus the question of how complete should the data be before they can be presented in a scientific forum. While the Moffitt researchers acknowledged that their findings were preliminary and, in essence, asked colleagues in other institutions to examine their experience with generic etoposide, the maker of the drug was demanding greater scientific certainty.

Also, Gensia's statement that the abstract should be withdrawn appeared to leave open the possibility of an "or else," said Gerald Elfenbein, director of the Division of Bone Marrow Transplantation at Moffitt.

"I've never had a company suggest to me that I withdraw a publication," Elfenbein said to **The Cancer Letter**. "A mere suggestion that I withdraw a publication is a thinly veiled threat."

Contacted by **The Cancer Letter**, the Gensia official who wrote the letter to Moffitt said that no threat was implied. The letter merely pointed out what the company believed to be the flaws in the abstract, Pertschuk said.

"As far as I am concerned, [the investigator] would be the first to agree that there were so many scientific flaws in [the abstract] that it doesn't qualify as what would be called a bona fide scientific study," Pertschuk said to **The Cancer Letter**.

The investigator disagrees. After receiving what he interpreted as a threat, Elfenbein withdrew the abstract. His reason: since Gensia was demanding a greater scientific certainty, he would do his best to provide it.

"We did not wish to get into a shouting match," Elfenbein said to **The Cancer Letter**. "We did not wish to refute their claims item for item. We did not wish to get into counter-proclamations."

The original abstract stated clearly that the data were preliminary.

"This retrospective review appears to suggest an association between the use of a generic product of etoposide and increased severity of enteritis, delayed neutrophil recovery, and longer hospitalization," the abstract said. "These preliminary data are suggestive and require confirmation from other institutions using etoposide in high doses."

Having withdrawn the abstract, Elfenbein said he has begun to compile follow-up data on patients receiving high-dose ICE. His original abstract compared side effects in patients before generic etoposide was introduced with side effects in patients after the generic was ordered by the pharmacy.

Now, Elfenbein has added a third group: patients treated after the generic was discontinued, he said.

"We are gathering new data that will make the scientific certainty even stronger," Elfenbein said.

The studies will not be prospectively designed controlled clinical trials since, as a consequence of Elfenbein's findings, the cancer center has resolved to discontinue the use of the generic in a high-dose setting, he said.

"I felt that I had obligations to fulfill, and I

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fulfilled my obligations to my patients, and to the government regulatory bodies," said Elfenbein, author of several studies of high-dose ICE. The most recent of these studies was published in the February issue of the Journal of Clinical Oncology.

Several observers contacted by **The Cancer Letter** said it is inappropriate for a drug company to suggest that a researcher withdraw a publication.

"This sort of behavior has the ultimate chilling effect on academic freedom," said Grace Monaco, director of legal and professional affairs of the Candlelighters Childhood Cancer Foundation and former member of the FDA Oncologic Drugs Advisory Committee. "Ultimately, this could adversely affect the opportunity for patients to receive curative care."

Robert Charrow, an attorney who handles academic freedom and scientific integrity cases, agreed.

"The bottom line is that the law on defamation is always evolving," said Charrow, of Crowell & Moring, a Washington firm. "Nonetheless, in the area of exchange of scientific ideas, information and data, scientists have a wide latitude.

"And I assume that no reputable company would make any effort to attempt to impede the free and open dissemination of useful data," Charrow said.

Generally, drug companies have the standing to review scientific publications when company-sponsored protocols as well as patent issues are involved, observers said.

"I don't see that in this case the company has any standing to call for withdrawal of the abstract, even if the Moffitt researchers were making an accusation about the company, which they weren't," Robert Young, president of Fox Chase Cancer Center and chairman of Bristol's oncology advisory board, said to **The Cancer Letter**.

Gensia official Pertschuk said his letter to Moffitt represented a scientific disagreement rather than an attempt to suppress data.

"I think what we are saying was put right in black and white," Pertschuk said to a reporter. "If you are trying to insinuate that we are trying to suppress scientific data, I think you are barking up the wrong tree. We would be very happy to do any kind of a reasonable study.

"Obviously, the [investigator] felt that scientifically there was an issue there. Obviously, we can't require him to withdraw [the abstract], so his decision to withdraw it was his own. If he felt real strongly that this was scientifically valid data that he wanted to stand up in public and make these statements, then he is certainly free to do it," Pertschuk said.

"We have no control over him. We don't have any relationship with him."

The following is a review of documents obtained by The Cancer Letter:

Moffitt researchers informed Gensia of their results in a letter dated Jan. 12, documents indicate.

The letter, addressed to Diane Beck, manager of professional services at Gensia Laboratories, provided an overview of the findings. The letter said data accrual and analyses were completed on 1/11/95.

"To the best of our knowledge, the pharmacy at our Institution began using generic etoposide in February [1994]," the letter said.

Also included was a copy of the abstract.

The abstract, reproduced verbatim, states:

"We have conducted a retrospective review to determine if the incidence or severity of toxicities related to high dose chemotherapy at our Institution has been associated with the change from VePesid brand etoposide to a generic product. Twenty-four consecutive patients received the generic product as a part of our ICE (ifosfamide [20.1 g/m^2] carboplatin [1.8 g/m^2] and etoposide [3 g/m^2] regimen prior to hematopoietic stem cell rescue (SCR). We compared neutrophil engraftment (day after SCR that absolute neutrophil count [ANC] reached 500/uL), the length of hospitalization after SCR, the severity of mucositis and enteritis, and the mortality of these patients with the 60 preceding consecutive patients treated with the same doses of ICE using VePesid. Mucositis and enteritis were graded according to a modification of the World Health Organization grading scale for toxicity. The results of that comparison are presented in the table below:

Product	Median day to ANC >500/uL (days)	Median day to discharge (days)	Median grade of mucositis	Median grade of enteritis	Mortality
VePesid (n=60)	17	24	3	2	3/60 (5%)
Generic (n=24)	17.5	24.5	3	3	4/24 (17%)
two tail p value	0.037[1]	0.032[1]	0.54[2]	.014[2]	0.54[3]

[1]log rank [2]Wilcoxan rank sum [3]Fisher's exact

"This retrospective review appears to suggest an association between the use of a generic product of etoposide and increased severity of enteritis, delayed neutrophil recovery, and longer hospitalization. These preliminary data are suggestive and require confirmation from other institutions using etoposide in high doses."

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On Jan. 26, Gensia officials wrote a letter to FDA in which the company informed the agency of the Moffitt report and stated that the company questioned the report's validity.

The letter, signed by Karen Church, divisional vice president, regulatory affairs and research quality assurance at Gensia Inc., stated:

"The entire validity of this report is questionable for the following reason: Gensia was informed by this site that the pharmacy has no record of which patients actually received Gensia's etoposide or VePesid and that the center assumed that all patients treated after February 1994 received the generic product. Gensia's records indicate that the hospital did not purchase etoposide from Gensia until mid-April, 1994. In addition, the Moffitt Cancer Center has informed us that they continued to receive VePesid after purchasing Gensia's product. Therefore, the conclusions reached in this retrospective review are based on unverifiable and inaccurate data...

"This report was also brought to our attention by Bristol-Myers Squibb," the letter stated. "[If] this abstract is intended to be used as advertising for VePesid, in order to compare the safety of VePesid with that of a generic etoposide, the study should have been conducted under an IND. To the best of our knowledge, that was not the case...

"This report DOES NOT QUALIFY as an increased frequency 15-day report... Gensia has received no spontaneous reports or other literature reports of gastrointestinal toxicities or death following the administration of Gensia etoposide, since its introduction to the marketplace."

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In another letter, addressed to Janelle Perkins, the lead author of the abstract and Elfenbein's associate at Moffitt, Gensia officials requested additional information and said that it would be "appropriate" that the abstract be withdrawn.

"There are a number of additional items which are germane to consideration of the abstract and as to which we would appreciate some clarification," the letter, dated Jan 24 and signed by Pertschuk, stated.

Pertschuk requested:

1."An assessment of comparability of the treatment groups with regard to their demographics, medical conditions, baseline blood counts, cancer type and stage...

2. ..."We would appreciate clarification as to whether the protocol standardized the treatment of the patients in terms of prophylactic antibiotics and use of bone marrow stimulating agents. These are critical issues since bone marrow stimulation could affect your endpoint 'median day to ANC of 500/uL' and antibiotic treatment could have affected both enteritis and the mortality endpoints.

3. ..."Was there any attempt to analyze the data with respect to exposure to other experimental or approved medications? You have also indicated that during the period in question the care of these patients was transferred to different nurses on another ward. We would like to know the exact timing of this change since it may have unintentionally biased the results.

4. "We also discussed the fact that enteritis score does not exist, as such, in the medical record, and that you had to modify the WHO scoring system. Was this endpoint clearly defined, in writing, prior to review of the charts, or did the definition change as the study progressed? What modification was made to the WHO criteria, and why?...

"Because of the multiple concerns raised above, especially the fact that a number of the patients in the generic treatment group in your abstract apparently received VePesid, we believe that it would be appropriate to withdraw your abstract as the present time. We would like to work with you in reviewing this matter and would be prepared to assist you in a review of the relevant data in your medical records and, if warranted, initiating a prospectively designed controlled clinical trial to unequivocally define the potential safety issues you have raised regarding the use of our generic product at high doses in this clinical setting."

In Brief

ACCC Elects New Officers

(Continued from page 1)

of Community Cancer Centers, a national organization of 478 hospital cancer programs. She succeeds Carl Kardinal. **John Feldmann**, medical director, Cancer Service, Mobile Infirmary Medical Center, was elected president-elect. **James Wade III**, director of medical oncology, Decatur Memorial Hospital, was elected secretary.

Breast Cancer Coalition Widens Its Advocacy Agenda

In a legislative agenda made public earlier this week, the National Breast Cancer Coalition said it intends to lobby against efforts in Congress to reduce funding for NIH.

By doing so, the group, which unites breast cancer patient activists throughout the US, becomes a powerful ally to the professional societies that lobby on behalf of federal funding for biomedical research.

NBCC said it also plans to draft legislation to protect the privacy and insurability of people who test positive for the presence of cancer genes.

Another goal for the group is to fight what it views as extreme regulatory reform of the Environmental Protection Agency and FDA.

Visco: "Message No Longer Fits On A Sign"

Since its inception four years ago, NBCC has emphasized increasing federal funding for breast cancer research. The coalition's involvement in issues that affect all cancer care and research represents a new phase in the group's work.

"We no longer have a message that can fit on one sign: More Money for Breast Cancer Research," NBCC President Fran Visco said at the annual NBCC Breast Cancer Advocacy conference in Washington. "Now our message is exceedingly complicated, exceedingly difficult."

The day following Visco's remarks, NBCC members put the new, broader agenda into action by visiting members of Congress.

"We have done a great deal in four years, so we should congratulate ourselves on that, and take a deep breath, because we have so much more to do," Visco said.

NBCC's Legislative Agenda

NBCC has decided to work to preserve funding for NIH, because budget reductions at the institutes also reduce funding for cancer research, Visco said at the conference.

"We are fighting the new Congress, which is considering cutbacks at NIH," she said. "We will not let them take money away from cancer research."

Joanne Howes, a principal in the Washington firm Bass and Howes Inc. and a lobbyist for NBCC, said Visco's statement did not reflect a dramatic shift in priorities. "We have been involved in many efforts to improve biomedical research funding overall, such as the Harkin-Hatfield amendment," Howes said to **The Cancer Letter**.

That amendment, introduced last year by Sens. Tom Harkin (D-IA) and Mark Hatfield (R-OR), proposed to fund medical research through a surcharge on health insurance premiums.

"We are totally committed to making the pie bigger," Howes said.

For FY96, the coalition is lobbying for an increase in NCI's funding of breast cancer research to a total of $485 million. The group also wants Congress to include $100 million in the Dept. of Defense budget to fund the US Army Breast Cancer Research Program for a third year.

NBCC is working with other organizations to try to stem the regulatory reform movement in Congress. The breast cancer advocates have been meeting with Citizens for Sensible Safeguards, a coalition of organizations that oppose the weakening of the authority of agencies including EPA and FDA.

"We have to deal with the regulatory reform movement on Capitol Hill, because that movement impacts breast cancer," Visco said. "Just when we are starting to get policymakers to turn their attention to breast cancer and possible environmental links, now is not the time to put handcuffs on EPA."

Similarly, efforts to weaken FDA's review of new drugs and devices are not acceptable to breast cancer advocates, Visco said. "We all know the drug approval process needs work, but we want to be sure we are part of the planning to change that process," she said.

Breast cancer activists lobbied in support of the Mammography Quality Standards Act, which FDA administers, Visco said. "We got it enacted. We cannot afford to see it stopped."

NBCC has held an educational session for members of Congress and their staffs on discrimination and privacy issues related to insurance coverage for women who test positive for breast cancer genes.

The coalition is working on model legislation that would protect such women from discriminatory insurance practices, Visco said. Presumably, the legislation would be applicable to all persons who test positive for cancer genes.

In addition, NBCC is working on several other issues that affect access to health services, Visco said. "True access involves health care reform, insurance reform, elimination of pre-existing conditions, insurance availability, increased access for everyone, coverage for clinical trials, coverage for

mammograms, access to clinical trials," she said.

"There are so many other issues we now have to deal with," Visco said to the advocates. "We have to learn so much, we have to be in so many places, and we have to do so many things.

"But remember what our mission is: To eradicate breast cancer.

"We have to continue to speak out," Visco said. "We have to continue to grow, to learn, to move, to come together, to yell, to scream, to bang the table, to speak—whatever is needed to eradicate this disease."

Four Years In Review

The coalition of breast cancer patients and activists has accomplished "incredible things" since its beginning four years ago, Visco said.

Visco said the group's accomplishments include: an increase of $400 million in federal funding for breast cancer research since 1991, the establishment of a peer-reviewed breast cancer research program funded by the Dept. of Defense, and the development of a National Action Plan on Breast Cancer, led jointly by the NBCC and the Dept. of Health and Human Services.

"Until the National Breast Cancer Coalition began, and until we came together and raised our voices, until we were determined to make a difference in this disease, very little happened," Visco said.

"We have made our mark," Visco said. "We cannot stop now. Because our agenda is more and more complicated.

"I truly believe that together we will reach the day when we are here celebrating the end of the breast cancer epidemic," she said.

NBCC is comprised of 350 member organizations and 31,000 individual members, Visco said.

Sondik: NCI Goal To Increase Minority Participation In Trials

NCI is committed to increasing the participation of minorities in clinical trials, the Institute's acting director said last week.

Edward Sondik, speaking at a symposium on minorities and cancer held in Washington last week, said cancer researchers have had only limited success in involving more minorities in their studies.

"We are having difficulties recruiting minorities to these trials," Sondik said. "We have tried mightily."

Improving that deficiency is part of the policy agenda of a new coalition, called The Intercultural Cancer Council, formed last week at the conference in Washington (**The Cancer Letter**, April 28).

Sondik's remarks were made at the final session of the conference.

"I wholeheartedly endorse the idea of this council," Sondik said. He said he would relay the concerns of the ICC to the new NCI director when one is appointed.

The conference was sponsored by Baylor College of Medicine, the Susan G. Komen Breast Cancer Foundation, M.D. Anderson Cancer Center, Howard Univ. Hospital, the American Cancer Society, and Kellogg Co.

Southwestern, M.D. Anderson, Form Cancer Center In Dallas

Two prominent Texas medical centers plan to create a new cancer care program in Dallas, the centers announced last week.

The UT Southwestern Medical Center at Dallas and M.D. Anderson Cancer Center in Houston have signed a letter of intent to create the new program, called the UT Southwestern/M.D. Anderson Cancer Center at Dallas.

The cancer center will be located at UT Southwestern and its affiliated hospitals, and will be jointly managed and staffed by representatives of both institutions, the centers said. UT Southwestern's Harold C. Simmons Comprehensive Cancer Center will be an integral part of the new venture, officials said.

"Building this integrated cancer treatment network achieves several goals shared by UT Southwestern and M.D. Anderson," Willis Maddrey, executive vice president for clinical affairs for UT Southwestern, said. The center will promote the development of a multidisciplinary approach to cancer treatment, he said.

"This arrangement will help both institutions develop close relationships with cancer physicians throughout North Texas," Maddrey said.

Expanding clinical services at UT Southwestern's outpatient facilities will enable both institutions to participate in a growing number of regional and national managed health care contracts, Maddrey said. "We think it is important for participants in managed care to have access to the finest cancer treatment possible, " Maddrey added.

Charles Balch, executive vice president for health affairs at M.D. Anderson, said collaboration between

two Univ. of Texas System institutions "bolsters the basic science expertise of both M.D. Anderson and UT Southwestern. We also will be able to develop additional joint clinical research protocols and foster important educational programs."

Kern Wildenthal, UT Southwestern president, said the two institutions are recognized for producing world-leading research and unsurpassed clinical care for cancer patients. "This joint venture strengthens both institutions and will help us deliver health care in a more cost-effective fashion," he said.

Charles LeMaistre, M.D. Anderson president, said, "M. D. Anderson has a global reputation for making rapid advances in cancer patient care through productive research. This consortium helps us fulfill our missions of patient care, research, education and cancer prevention."

The comprehensive cancer program developed by the consortium will be multidisciplinary and offer oncologic physician services, radiation therapy, medical oncology and surgery in both inpatient and outpatient settings. The center also will provide ancillary physician services such as pain management and psychiatry, support services and long-term follow-up care, including home health care and hospice services. Both adult and pediatric patients will be treated as part of this new venture.

Officials of the two institutions said they hope to conclude a complete agreement by the end of the year.

The agreement also specifies that both parties may participate in any cancer treatment venture either decides to establish or operate in North Texas. The letter of intent between the two medical centers anticipates that M.D. Anderson and UT Southwestern will join with other health care organizations in providing comprehensive cancer services in the Dallas/Fort Worth region.

Last December, M.D. Anderson and the Moncrief Radiation Center announced that the Moncrief Radiation Center was being given to M. D. Anderson Cancer Center Outreach Corporation. UT Southwestern now will become a participant in collaborative programs with the new M.D. Anderson Moncrief Cancer Center at Fort Worth and other joint ventures undertaken by M.D. Anderson and other health care providers in North Texas.

UT Southwestern currently offers clinical cancer services for children and adults through the Harold C. Simmons Comprehensive Cancer Center with facilities at the James W. Aston Ambulatory Care Center, Zale Lipshy University Hospital, St. Paul Medical Center, Children's Medical Center of Dallas, Parkland Memorial Hospital, and Dallas Department of the Veteran's Affairs Medical Center.

NCI Scientists Immunize A Healthy Donor For BMT

NCI scientists have successfully immunized a healthy donor for a bone marrow transplant against a rare blood cancer, then transferred that immunity to the marrow recipient, a cancer patient diagnosed with multiple myeloma.

The patient has been in remission for two years.

The unusual treatment approach is described in the April 21 issue of Lancet and was recently approved by FDA for phase I testing in up to 20 patients.

"To my knowledge, this is the first time that a normal donor has been immunized with a purified tumor protein and that immunity transferred to a recipient," said Larry Kwak, the study's principal author and a senior investigator at the NCI Biological Response Modifiers Program.

The vaccine protocol is similar in design to one used in another B-cell malignancy trial, which Kwak and his colleagues began last April. More than 20 patients are enrolled in that phase II study in which a treatment vaccine for newly diagnosed B-cell lymphoma is custom-made from a patient's own tumor.

However, in the new study, Kwak said, "all the maneuvers are done in a healthy sibling donor" whose tissue is matched to the recipient's human leukocyte antigens.

"The idea is that for reasons that are still unknown the immune systems of cancer patients are not activated to recognize cancer and get rid of it," Kwak said. "We are trying to elicit an immune response in a normal, healthy person who should be able to respond vigorously against the foreign tumor protein, and to transfer that immunity to the original cancer patient through a bone marrow transplant."

The first patient in whom this was tried is a 43-year-old woman whose case history is detailed in the Lancet article. The woman approached investigators at the BRMP in Frederick, MD, herself, after reading about the treatment's success in an animal model.

Because the woman's clinical status was quickly deteriorating, she needed a rapid medical intervention, Kwak said. Within three weeks, NCI investigators had created a prototype myeloma vaccine.

To produce a vaccine, Kwak and his colleagues purified the protein of interest—a receptor molecule

synthesized by her malignant plasma cells—to serve as the antigen for a vaccine. Because the receptor molecule (from the patient's plasma) is an immunoglobulin, it is "exquisitely specific for this type of tumor," Kwak said. "And since it is unique to a given plasma cell, any tumor derived from that malignant cell will have this marker."

In the next step, investigators chemically coupled the receptor molecule to a highly immunogenic carrier protein. Then, to provoke a vigorous immune response to the marked tumor cells, they added an adjuvant or immune system booster. The vaccine mixture was given to the donor, the patient's brother, in two separate inoculations. At the same time, the woman received chemotherapy before transplantation of the marrow to reduce her tumor burden.

The transplantation was performed at the Fred Hutchinson Cancer Research Center in Seattle.

Once the immunization was complete, investigators took lymphocytes from the donor and mixed them with the foreign tumor protein. The procedure was repeated in the woman before and after transplantation. By day 60, there was activation of her lymphocytes against her cancer protein, the investigators said.

RFP Available

RFP N01-CP-61001-21

Title: **Laboratory Support For Processing And Storage Of Biological Specimens From Persons At High Risk From Cancer**

Deadline: Approximately June 12

The NCI Epidemiology and Biostatistics Program is seeking a contractor to provide for the maintenance of the existing EBP inventory of biologic specimens and to receive, process and store new samples as they are collected. This is a 100% small business set-aside, SIC Code 8731 with a size standard of 500 employees.

The contractor shall provide the services described below, in accordance with contractor-developed, government-approved protocols: 1) separation and viable cryopreservation of blood mononuclear lymphocytes, 2) separation, aliquotting and storage of serum, plasma and/or urine as needed, 3) cryopreservation of bone marrow samples, 4) storage of tumor extracts, 5) cryopreservation of xhole tumor tissue, 6) cryopreservation of intact red blood cells 7) viable lines, 8) storage of DNA and other biological materials as specified by the NCI Project Officer, 9) extracting of DNA from biologic materials, 10) logging in, labelling and tracking of each vial of each sample employing an NCI developed computerized specimen tracking system, including all laboratory safeguards to insure the fidelity and purity of each sample, 11) maintenance of the previously-established repository currently containing 1 million biological specimens, and 12) allowance for an estimated increase of up to 25% of freezer storage space. The Contractor shall, for example, provide messenger service for pick-up of specimens or inter-laboratory communication from medical care facilities in the Washington, DC, area or at area transportation centers (i.e., Dulles, DC National and BWI Airports), be responsible for secording and monitoring shipping and receiving of specimens to minimize delay or loss, maintain a repository of biologic specimens which shall include frozen serum, plasma, urine, tumor tissue, tumor -issue extracts, whole red blood cells, separated and frozen white blood cells or fractions of white blood cell populations, bone marrow cells, body fluids, lymphoblastoid cell lines, DNA, stool specimens or smears on slides and other types of specimens as specified by NCI, provide and train primary and backup staff in the operation of a computerized record system for specimens which has been developed and furnished by NCI, prepare a variety of specimens for storage, utilize freezers equipped with a stylus recording system indicating consistency of temperature, maintain a central alarm indicating consistency of temperature, maintain a central alarm system monitored 24 hours a day, 365 days a year, keep clear records of all manipulations on all specimens and carefully document specimen type, volume, cell concentration, source, "crisis event," etc. for each sample, prepare specimens for shipment, supply shipping containers and make arrangements to send biologic specimens to collaborating investigators in an expeditious (e.g. overnight or same day) fashion, inventory, store and maintain a large repository of sera and cells used for immunogenetic tissue typing, be prepared to process up to 1100 mls of blood per day, four days per week, from lymphocyte harvesting (coded from as many as 60 donors per day), handle international shipments of biological specimens (blood components, urine, gastric juice and biopsy specimen) and clearance of these specimens through US and foreign customs, and submit monthly computerized and written reports, annual reports and a final report.

Contract will be a cost-reimbursement type for a 60-month period. The total estimated level-of-effort to be provided is 93,100 direct productive labor hours. Award is anticipated by March 1, 1996. The Contractor is expected to provide the facilities and all major equipment. Additional Government-furnished equipment, currently in use under the existing contract (NO1-CP-33060 with BTRL Contracts and Services Inc., dba Biotech Research Laboratory) will be provided.

Contracting Officer: Barbara Shadrick, RCB, Cancer Etiology Contracts Section, Executive Plaza South Rm 620, 6120 Executive Blvd. MSC 7224, Bethesda, MD 20892-7224, tel: 301/496-8611.