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Congress Urges CMS To Soften Proposal For Coverage Of ESAs In Oncology

By Paul Goldberg

House and Senate members representing the majority of both chambers urged CMS to tone down its draft National Coverage Decision on erythropoiesis stimulating agents in oncology.

The CMS mailbag this week included a sign-on letter from 224 House members, a letter signed by 46 Senators, as well as letters from individual legislators.

In a related barrage, the agency received over 1,850 comments about the NCD from patients, doctors and nurses, with over 97 percent of those comments criticizing the proposed decision, industry sources said.

CMS is expected to publish its final coverage decision by Aug. 12, and

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In the Cancer Centers:

Alabama Native Edward Partridge Appointed Director, UAB Comprehensive Cancer Center

EDWARD PARTRIDGE was named director of the University of Alabama at Birmingham Comprehensive Cancer Center. He has served as interim director for the past year.

"Ed has been instrumental in shaping the future of the center, ensuring that we remain one of the premiere cancer centers in the nation," said **Robert Rich**, senior vice president and dean of the UAB School of Medicine. "He is leading the effort as we prepare our renewal application [for the NCI cancer center grant]. We have been trying to convince Ed for nearly three years that he is the best person to lead our program. We finally have succeeded."

Partridge, a gynecological cancer specialist, has spent his entire career at UAB, starting with medical school. He joined the faculty in 1976 as an instructor. He became director of the Division of Gynecologic Oncology in 1990. In 1999, he was named to the Margaret Cameron Spain Chair in Obstetrics and Gynecology.

"As a native of Demopolis, Ala., I have for my entire life witnessed the health issues our state faces," Partridge said. "To positively impact the health care of Alabamians has been a principle that has guided my professional career. I look forward to helping our physicians, researchers, and all our health care providers as we strive to find improved ways to prevent, detect early, and treat cancer in the men and women we serve."

Partridge is the principal investigator for the Deep South Network

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Congress Weighs In As CMS Prepares Coverage Decision

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sources said the document has been completed and is going through internal debates and clearance.

The lobbying effort that produced the letters from Congress was carried out by US Oncology, Community Oncology Alliance, the University of Pittsburgh Medical Centers, the Society of Gynecologic Oncologists, and the sponsors of the two ESAs sold in the U.S., Amgen Inc., and Johnson & Johnson, sources said.

"The letters were drafted with the idea that it would raise issues that are appropriate to Congress," said Dan Cohen, senior vice president for government relations and public policy for US Oncology, a nationwide cancer care network that treats over 15 percent of all newly diagnosed cancers. "Congress isn't going to go in and start arguing hemoglobin levels of 9 g/dL, or 10, or 11. But they certainly can argue for evidence-based decisions that reflect 15 years of clinical experience. The impact on blood supply is a very legitimate concern for Congress as well."

The sign-on letter was first circulated by the House Cancer Care Working Group, a Congressional organization headed by Reps. Anna Eshoo (D-Calif.) and Mike Rogers (R-Mich.).

Later, Sens. Kent Conrad (D-N.D.) and Thad Cochran (R-Miss.) started to circulate a similar document in the Senate.As the letters made rounds on Capitol Hill, grassroots political networks of oncologists were being asked urged to contact their representatives.

"It's really a testament to the issue that you can get this many members of Congress to sign on to such a thing in such a short period of time," Cohen said. "I've been involved with challenging letters where you have to explain what's going on to people, and this we haven't had this problem. Members get it."

The Eshoo-Rogers letter included 224 signatures and was sent out July 18. Another House letter was sent by the Republican members of the House Ways & Means Committee's Health Subcommittee, including the ranking Republican Dave Camp of Michigan, Phil English (R-Penn.), Sam Johnson (R-Tex.), Jim Ramstead (R-Minn.), and Devin Nunes (R-Calif.)

The Conrad-Cochran letter included 46 signatures and was sent out July 17. Also, letters were sent by the Senate Finance Committee Chairman Max Baucus (D-Mont.), and Sens. Richard Burr (R-N.C.), Tom Coburn (R-Okla.), Dianne Feinstein (D-Calif.), Lindsey Graham (R-S.C.), Blanche Lincoln (D-Ark.), Richard Lugar (R-Ind.) Arlen Specter (R-Penn.), John Warner (R-Va.), and Ron Wyden (D-Ore.).

The House letter contains a strong endorsement of the safety of ESAs. "We understand that ESAs have been used without a single reported safety signal when used in accordance with clinical pathways that reflect mainstream practice," the document states. ESAs were approved based on their ability to reduce the need for blood transfusions, and their impact on survival and time to progression hasn't been studied at hemoglobin levels recommended on the label. Even the dose-response curve for these agents in oncology is unknown.

By signing these letters, members of Congress aren't committing to take any action, and the letters aren't expected to have any impact on the House and Senate committees' investigations of the safety of ESAs.

Coverage With Evidence Development

Some scientists believe that if CMS is interested in answering questions about ESAs, it should use the "coverage with evidence development" mechanism for these agents, much like it had done with PET scanning.

"Why are there such large differences in point of view regarding the appropriate indications for these drugs, particularly when you consider that they confer an added risk of adverse events, but potential benefits as well?" said Peter Bach, a pulmonologist and health systems researcher at Memorial Sloan-Kettering Cancer Center, who served as a policy advisor to the former

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CMS Administrator Mark McClellan.

"These drugs have been on the market for more than a decade and used in hundreds of thousands of patients. If the payers limit coverage and indications due to lack of evidence, then maybe we'll get some practical answers to some important questions. For instance, how should doctors dose these drugs to adhere to the warnings on the label to use the lowest doses possible and avoid raising hemoglobin too quickly? The best way to answer the questions, though, is not to end coverage, but to use coverage to foster a healthcare system that continually learns and shares knowledge. We just haven't figured out how to do that effectively for this class of drugs the way CMS has done for the PET scan."

In the process of finalizing the coverage decision, CMS asked the "stakeholders" to address 14 separate questions on ESAs. The questions were contained in a June 14 letter to "stakeholder" organizations. Two weeks later, on June 28, the stakeholders met with the agency officials at the CMS offices in Baltimore. The meeting was technically requested by J&J, but was also attended by Amgen, US Oncology, as well as the American Society of Clinical Oncology and the American Society of Hematology, sources said.

The two professional societies weren't involved in the Congressional letter-writing campaign, but had submitted comments on the draft decision. ASH had focused on preserving coverage for ESAs in the treatment of MDS. ASCO argues that the Medicare law prohibits "coverage limits that are more restrictive than the science- and evidence-based decisions of FDA regarding the usage of marketed drug or biologic products."

US Oncology appears to have been the only participants of the June 28 meeting to respond to CMS publicly and in writing.

The response lists the 14 questions posed by the agency and draws defensive lines around some ESA indications while surrendering others.

The network said it doesn't support coverage for the following indications:

—Any anemia due to folate deficiency, B-12 deficiency, iron deficiency, hemolysis, bleeding or bone marrow fibrosis.

—Myeloid cancers, provided that CMS reclassifies multiple myeloma as a lymphoid cancer rather than a myeloid cancer.

—Anemia associated with radiotherapy.

—Prophylactic use to prevent chemotherapy-induced anemia.

—Prophylactic use to reduce tumor hypoxia

—Anemia in patients with erythropoietiv-type resistance due to neutralizing antibodies.

—Anemia due to cancer treatment if patients have uncontrolled hypertension.

US Oncology said CMS shouldn't use Coverage with Evidence Development, because high quality evidence already exist to support coverage for:

—The treatment of MDS.

—Patients receiving anti-angiogenic drugs.

—Patients receiving monoclonal antibodies directed against epiderman growth factor receptor.

—Patients with thrombotic episodes related to malignancy.

—Patients with cancer undergoing chemotherapy.

The letter states that additional data are needed for anemia of cancer not related to cancer treatment. Specifically, the letter called for generation of evidence on non-chemo related anemia in B-cell malignancies in patients who have stable disease or are in remission and patients with metastatic prostate and breast cancer.

US Oncology said it would like to work with ASCO, ASH, and the sponsors to develop a research plan that would use the Medicare claims system for collection of data. The practice network argued that ESAs are safe when initiated at hemoglobin levels of under 11 g/dL and when stopped at 12. The CMS draft proposes starting ESAs when the hemoglobin level drops below 9 g/dL.

The letter states:

"It is of primary importance that the decision to use ESAs in CIA is a patient and physician case-by-case event. Patients with cancer have complicated clinical issues that require individually designed intervention. For example, a treatment decision for ESA use in the Rocky Mountains with patients living at high altitude will likely be substantially different than for a patient living at sea level.

"It is important to keep in mind that a decision by CMS to cover ESA use in patients on chemotherapy at Hgb level of <11 does not mean that all patients will get an ESA.

"Establishing an NCD that limits the use of ESAs in patients receiving chemotherapy is an inappropriate practice of medicine by CMS because it influences decisions patients and physicians make as to the appropriate type of chemotherapy administered. The CMS coverage policy for ESAs should not influence the decision as to the type and form of appropriate chemotherapy.

"At the stakeholder meeting on June 28th, the length

of time required for bone marrow recovery after the completion of chemotherapy was discussed. The bone marrow of approximately 95% of chemotherapy patients recovers in less than 90 days. Therefore, failure of the bone marrow to recover at 90 days post-chemotherapy completion is the most appropriate point in time for a physician to initiate a look for non-chemotherapy related causes of persistent anemia. CMS should cover ESA use during all phases of chemotherapy and for up to 90 days after final dose administration.

"Lastly, the Network requests that CMS clarify that coverage under this indication is available for all anemia-inducing anticancer agents including the newer oral products used for multiple myeloma and CML."

The USON letter is posted at www.legislink.com/site/MessageViewer?em_id=6941.0

The California Blues

The CMS action is likely to resonate through the industry, as insurers make their own coverage decisions. This process has already begun, as Blue Shield of California earlier this month enacted drug coverage criteria that largely mimicked the CMS draft decision.

In addition to restricting coverage, the California insurer declared J&J's Procrit to be "the preferred product" over Amgen's Aranesp. Efforts to discuss the new policy with the insurer were unsuccessful.

Though many insurers are aggressively limiting coverage for ESAs, they are also willing to wait for actions from CMS, FDA and the professional societies. Lee Newcomer, business leader for oncology services for UnitedHealthcare, said his company expects to realize substantial savings on the agents while saying in the mainstream of science.

"UnitedHealthcare is using the guidelines from ASCO and NCCN for its erythropoietin policies," said Lee Newcomer, business leader for oncology services for UnitedHealthcare. "We pay for therapy up to a hematocrit of 36, but deny claims for all oncology values exceeding that limit as suggested by the guidelines. Our initial pilot in New York, New Jersey, and Connecticut demonstrated a 35 percent reduction in ESA usage with that simple review.

"It is my belief that the other criteria are either impractical to administer or aren't supported by sufficient evidence and professional society concurrence," Newcomer said.

Overall, concerns from patients and changes in medical practice appear to have driven down the utilization of ESAs. According to Johnson & Johnson's quarterly results released earlier this month, U.S. sales of Procrit declined by 14 percent compared to second quarter of 2006.

"Procrit results have been impacted by a combination of a decline in the market versus the second quarter of 2006 and our competitors' anti-competitive contracting strategies," said Louise Mehrotra, J&J vice president, investor relations, at a teleconference July 17. Amgen's sales figures are expected in mid-August.

Dominic Caruso, J&J vice president of finance and chief financial officer, said the California action surprised the company. "We found it actually surprising that they came out with their conclusion prior to CMS concluding on the national coverage decision," he said at the conference. "Obviously, we are happy that they selected Procrit as the product to reimburse, but we were a little disappointed that they actually adopted some of the more stringent reimbursement guidelines that CMS had suggested."

FDA is believed to be reviewing the ESA label for the oncology indication, and the nephrology indication is expected to go to an advisory committee Sept. 11.

Appropriations:

House Approves 1.9% Increase For NIH, $72M More For NCI

By Kirsten Boyd Goldberg

The House July 19 approved a Labor-HHS-Education appropriations bill that would provide $29.649 billion for NIH, $750 million above the fiscal 2007 appropriation and $1.028 billion more than the administration's request.

The House bill would provide $4.87 billion for NCI, an increase of $72.743 million over FY07, and $88.268 million more than the President's FY08 budget request.

The bill passed on a vote of 276-140. President Bush has said he would veto the Labor-HHS legislation unless it is trimmed.

The House bill appears to provide a 2.6 percent increase to NIH, but it includes funding that is passed through to the Global AIDS Initiative. Without the AIDS funding, the increase is 1.9 percent.

The Senate spending bill for Labor-HHS is expected to go to the floor in September, and would provide a 2.8 percent increase for NIH, not including the AIDS funding.

In its report on the appropriations bill, the House Appropriations Committee said it "made difficult choices" to provide a $750 million increase for NIH. "The committee hopes to stop the funding rollercoaster

NIH has experienced during the past decade and provide a substantial and sustainable growth path for the future," the report said.

The funding level for NIH would provide 10,666 new and competing grants, an increase of 545 over fiscal year 2007, the report said. The number of total grants would rise to 39,003, and the two-year freeze in the inflationary adjustment of grants would be reversed, with an average two percent increase for new grants.

Funding would be provided for three programs to support young investigators, as well as a 2 percent average increase in research training stipends, the report said. The funding for young investigators includes:

—$91.5 million in the NIH Office of the Director for the Director's one-year Bridge awards for investigators who either are being considered for their first award renewal or have just missed the funding payline with no other sources of support.

—$31 million funded through all the institutes and centers for the Pathways to Independence program to provide new investigators with mentored grants that convert into independent research project grants.

—$40 million through the Common Fund for the New Innovator awards that provide first-time independent award funding for a five-year period based more on ideas than experimental data.

The committee also provided $27 million within the Common Fund for the Director's Pioneer Awards for high-risk research, as well as the administration's request for $95.3 million for radiological, nuclear and chemical countermeasures, and up to $10 million for the Director's discretionary fund.

The Common Fund is supported as a set-aside within the Office of the Director at the statutory minimum of $495 million, rather than through an assessment of institute and center budgets. The bill also provides $40 million for NIH buildings and facilities.

The bill includes language requested by the administration permitting NIH institutes and centers to use their appropriation for renovation and improvement of facilities, up to $2.5 million per project and up to a total of $35 million across NIH.

Support for SPOREs, Minority Cancer Center

In the report, the House committee encouraged NCI to emphasize research in a variety of cancers. Of note, the report:

—urged NCI to "consider using separate pay lines for each cancer" within the Specialized Programs of Research Excellence grants.

—encouraged NCI to conduct randomized trials to validate biomarkers for the early detection of ovarian cancer.

—suggested that NCI support the establishment of a comprehensive cancer center at a "minority institution focused on research, treatment, and prevention of cancer in African American and other minority communities."

The full text of the NCI section of the House report follows:

Mission—NCI conducts and supports basic and applied cancer research in early detection, diagnosis, prevention, treatment, and rehabilitation. NCI provides training support for research scientists, clinicians and educators, and maintains a national network of cancer centers, clinical cooperative groups, and community clinical oncology programs, along with cancer prevention and control initiatives and outreach programs to rapidly translate basic research findings into clinical practice.

Unprecedented gains—The committee is pleased to note the important gains returned by the nation's investment in cancer research. These investments are proving to be important steps toward advances in diagnosis, treatment and prevention for many cancers. For example, the Cancer Biomedical Informatics Grid will allow investigators to manage and share clinical data in real time in a move toward "digital biology." The Cancer Genetic Markers of Susceptibility initiative will scan the entire human genome and identify genetic changes associated with either increased or decreased risk for breast and prostate cancer. The Cancer Genome Atlas, done in conjunction with NHGRI, will test the complex science and technology framework needed to systematically identify and characterize genomic changes associated with cancer. The repository named REMBRANDT developed by NCI and NINDS is a publicly available bioinformatics knowledge base of primary brain tumor data. The new Clinical Proteomics Program is developing the standards needed to characterize patterns of protein markers in human serum for very early detection of cancer. The Nanotechnology Alliance for Cancer began harnessing nanotechnologies for cancer diagnostics, targeted imaging, and drug delivery.

Cancer metastasis to bone—A frequent complication of cancer is its spread to bone (bone metastasis) that occurs in up to 80 percent of patients with myeloma and 70 percent of patients with either breast or prostate cancer--causing severe bone pain and pathologic fractures. Only 20 percent of breast cancer

patients and five percent of lung cancer patients survive more than five years after discovery of bone metastasis. The committee understands that immune response plays a role in cancer metastasis and encourages NCI to focus research in the emerging area of osteoimmunology. The committee encourages NCI, as well as NIAMS, NIA, and NIDDK, to support research to determine mechanisms to identify, block and treat cancer metastasis to bone. Furthermore, the committee encourages NCI to expand research on osteosarcoma to improve survival and quality of life and to prevent metastatic osteosarcoma in children and teenagers who develop this cancer. In addition, NCI is encouraged to strengthen research on tumor dormancy as it relates to bone metastasis.

Gynecologic cancers—Today, in the United States, one woman will be diagnosed with a gynecologic cancer every seven minutes. That is almost 200 per day and 80,000 in a given year. Furthermore, almost 30,000 women die from a gynecologic cancer each year. Existing NCI funding for specialized programs of research excellence (SPOREs), program projects, the early detection network, and investigator initiated grants has accelerated basic, molecular-based research discoveries for gynecologic cancers. The committee encourages NCI to give priority to gynecologic cancers under its nanotechnology plan, its oncology biomarker qualifications initiative, and its cancer genomics atlas project, jointly conducted with NHGRI. This will allow laboratory discoveries to be translated into clinical applications at the bedside causing a decrease in the mortality rates for women with gynecologic cancer.

Gynecologic oncology clinical trials—The committee recognizes NCI's longstanding commitment to improving the health of women through gynecologic oncology clinical trials. These trials have led to the identification of new therapeutic agents and techniques for treating gynecologic cancers. This effort has directly produced improved outcomes for ovarian cancer patients as a result of changes in the way ovarian cancer is treated and the development of a vaccine for preventing the virus that causes cervical cancer. The committee encourages NCI to continue its support of gynecologic oncology clinical trials through public-private partnerships with the pharmaceutical and biotechnology industries and the NCI-sponsored cancer centers and cooperative groups.

HPV Vaccine and cervical cancer—The committee encourages NCI to study if there are clinical and cost benefits of prospectively tracking pap test results and outcomes in women who have been vaccinated for human papillomavirus. The committee encourages NCI to support research that will identify the most cost-effective management strategy for cervical cancer screening in the era of HPV vaccines and to identify the circumstances where pap test/HPV screening fails in vaccinated women.

Liver cancer—The committee notes that the incidence of primary liver cancer continues to increase. Liver cancer is one of the few cancers experiencing continuing increases in mortality, and treatment options remain very limited. The committee encourages NCI to work closely with NIDDK to develop a basic, clinical and translational research program designed to reverse these trends and enhance survivability.

Pancreatic cancer—The committee recognizes that pancreatic cancer is the country's fourth leading cause of cancer death among men and women. While NCI support for pancreatic cancer research has increased during the past several years, unfunded opportunities remain. The committee strongly encourages the Institute to continue to support the existing pancreatic cancer SPORES and to consider using separate pay lines for each cancer within the SPORE program.

Lymphoma—The incidence rates for non-Hodgkin lymphoma in the general population have doubled since the 1970s. The reasons for its increased incidence are not clear. The committee recommends an enhanced commitment to research focusing on the possible environmental links to lymphoma. The committee suggests that NCI direct funds to: (1) studies on the identification of environmental-genetic interactions which may influence the development of lymphoma; (2) studies of adequate scope to assure the identification of environmental risk factors for specific subtypes of lymphoma; (3) small studies designed to improve detection and quantification of historically difficult-to-measure environmental factors; (4) studies that are directed toward enhancing the understanding of the role of the immune system in the initiation and progression of lymphoma; and, (5) studies that examine the simultaneous presence of a wide profile of infectious agents among individuals with lymphoma. Lymphoma is often diagnosed in young adulthood and middle age, and survivors may experience immediate, but also late and long-term effects of the disease and treatment. Although there are effective treatments for Hodgkin lymphoma, survivors of this form of lymphoma may have a wide range of side effects from the disease and will require long-term monitoring and follow-up care to address the long-term effects. The committee encourages NCI to dedicate some of its survivorship research to problems confronted by lymphoma survivors.

Lymphatic research and lymphatic diseases—The committee recommends that NCI support research on lymphedema, a chronic, progressive and historically neglected complication that must be endured by many cancer survivors. The committee also encourages the Institute to support the study of lymphangiogenesis and lymphatic imaging, which are critical to a greater understanding of cancer metastasis and lymphedema.

Ovarian cancer—Today, in the United States, there is no widely available screening test for ovarian cancer. More than 22,000 women will be diagnosed with ovarian cancer this year and 16,000 women are expected to die from it. Ovarian cancer has a high mortality rate, 55 percent over five years, mainly because there is no proven effective method for early detection. Research is being conducted on glycomic profiling which may identify unique patterns of glycosylation that may be more sensitive and specific than CA-125, an existing blood marker, in identification of early stage ovarian cancer. Circulating plasma proteins, another blood marker, could also possibly serve as biomarkers to differentiate women with ovarian cancer from healthy women. The committee encourages NCI to make randomized, prospective studies that would lead to the validation and acceptance of these and other biomarkers for the early detection of ovarian cancer a priority.

Clinical trial participation—Despite efforts to improve participation in cancer clinical trials, only three percent of adult cancer patients participate in trials, and the participation by senior citizens is even more limited. The committee strongly encourages NCI to support research to investigate decision-making by patients, particularly with respect to barriers to, and decisions on, participation in clinical trials. This research effort should be undertaken to inform strategies to enhance accrual in cancer clinical trials. Current low levels of accrual are often rate-limiting in the development of novel treatment approaches, and solving this problem would ultimately improve outcomes for cancer patients.

Cancer centers—The committee commends NCI on the success of its cancer centers program. Given that minority populations suffer disproportionately from virtually every form of cancer, the committee encourages NCI to consider supporting the establishment of a comprehensive center at a minority institution focused on research, treatment, and prevention of cancer in African American and other minority communities. The committee is pleased with NCI's attention to this important matter.

Tissue repositories—Cancer biorepositories, because they centralize and standardize molecular annotation of tissues, have the potential to accelerate the understanding of cancer and the discovery and development of new biomarkers, new diagnostics and new therapeutic approaches. The committee encourages NCI to continue to support efforts to centralize the collection and distribution of tissue and pursue programs to make them available to researchers.

Neuroblastoma—The committee notes with concern the incidence of neuroblastoma, an aggressive pediatric cancer with poor survival rates among Stage III and Stage IV patients. The committee encourages NCI to accelerate support for neuroblastoma research with a focus on clinical trials for high-risk patients. The committee requests a comprehensive report on NCI's research in this area, including planned clinical and translational research initiatives, as part of NCI's fiscal year 2009 budget justification.

Radioisotope research—The committee encourages NCI to continue and enhance its support for radioisotope-targeted therapy and research. This research ultimately benefits cancer patients worldwide by developing new, productive avenues for the use of nuclear stockpile materials previously earmarked for weapons development.

NCI Programs:

Advisors Approve Plans To Renew 8 Grant Programs

By Kirsten Boyd Goldberg

NCI advisors approved eight concepts for grant programs that will fund $213.25 million worth of research over the next five years.

The NCI Board of Scientific Advisors voted June 28 to approved the institute's plans for reissuing Requests for Applications for the eight existing grant programs. At the same meeting, the board approved NCI's plans for a new biospecimen research program (The Cancer Letter, July 6).

Excerpts from the concept statements for the eight existing programs follow:

AIDS Cancer Specimen Resource. Concept for a RFA reissue, cooperative agreement, estimated total cost $18 million over five years, for four awards. Division of Cancer Treatment and Diagnosis, program director: Rebecca Liddell Huppi.

The primary purpose in renewing the AIDS Cancer Specimen Resource RFA is to continue to provide investigators access to high quality, HN-associated, human tumor tissue with associated histopathologic and demographic data. It is hoped that the availability of such specimens will enable investigators to identify therapeutic targets and gain further

insight into the pathogenesis and treatment of cancer in the HN-infected population. The purpose for the year extension and the Biospecimen Research Evaluation Tool (BRET) was to inform program staff and the Executive Committee of resource strengths and weaknesses. The AIDS Malignancy Program's primary goal, if granted the reissuance, would be to re-write the RFA to incorporate suggested improvements for the resource. ACSR principal investigators would then be expected to address these changes in their proposals, and if funded, carry out these improvements. The AMP expects the ACSR investigators to continue to collect, process and handle specimens in a way that assures that the specimens are of the highest quality and suitable for a wide variety of studies and technologies. In order to ensure the availability of suitable specimens for patient diagnosis and quality control of research specimens, the ACSR Steering Committee includes an experienced surgical or anatomical pathologist, actively involved in the operation of a pathology laboratory with demonstrated access to human cancer tissues. Although separate awards will be made to individual institutions, awardees will be required to work collaboratively.

General operating policies are established by the Steering Committee (consisting of the principal investigators plus one additional representative from each participating institution and a representative from the NCI), which oversees standards for quality control, equitable policies for distributing specimens, processing and biohazard procedures and policies for addressing the legal, ethical, and human subjects issues related to the use of human specimens for research.

Cooperative Human Tissue Network. Concept for an RFA reissue, estimated cost $29 million over five years, for six awards. Division of Cancer Treatment and Diagnosis, program director: Yaffa Rubinstein.

This initiative is to provide funding to continue the Cooperative Human Tissue Network for an additional five years. The CHTN was established in 1987 to collect and distribute high quality human tissue specimens to facilitate basic and developmental cancer research. The CHTN is primarily a prospective tissue procurement service, in which custom procurement and processing are performed for specific investigator-initiated protocols. The CHTN pioneered the procurement and distribution model and has distributed tens of thousands of high quality specimens to the scientific community. Continuation of the CHTN is critical, not only to provide specimens for a wide variety of basic and developmental studies in cancer research, but also to catalyze the evolution of high quality practices for the collection, storage and use of human specimens for the translation of basic research findings into clinical practice.

The initial RFA in 1986 invited applications from institutions willing to provide access to high quality human tissues for cancer research to help meet the needs of scientists applying emerging molecular approaches to cancer biology and diagnosis. Three organizations were funded by the NCI. Those were University of Alabama at Birmingham, National Disease Research Interchange in conjunction with the hospital of the University of Pennsylvania, Ohio State University, with a subcontract to Children's Hospital in Columbus, Ohio (representing the Children's Cancer Group). During the second funding period, 1991-1995, Case Western Reserve University joined the CHTN and Children's Hospital in Columbus, Ohio, became an independent group. During the third funding period, 1996-2001, the award to NDRI was transferred to the University of Pennsylvania. The fourth funding period, 2001-2006, saw the addition of University of Virginia, and Vanderbilt University replaced Case Western Reserve University. When the concept to reissue the RF A for the CHTN was brought to the Executive Committee in 2004, a decision was made to provide two years of supplement funding, through March 31, 2008, while the NCI reviewed the institute's specimen resource infrastructure.

The intent of this RFA is to request applications for cooperative agreements from current CHTN participating organizations. The CHTN network will continue to provide access to high quality human tumor tissue with associated histopathologic and demographic data to investigators throughout North America and other countries. The network provides large numbers of tumor specimens from a wide variety of cancers and access to specimens from rare tumor types when possible. Normal, malignant and benign human tissue will continue to be collected based on requests and prepared to meet specific researcher requirements. Specimens will be obtained from excess materials collected during the course of routine medical care or at autopsy. While the network is not a tumor bank, it will store specimens pending completion of shipments and bank rare tumors that would not otherwise be available. Premalignant lesions, when available, could also be stored for future distribution to facilitate early detection research. Data routinely provided continue to be limited to histopathological and demographic information such as diagnosis, sex, age and race. Other clinical data may be provided if requested at the time of the initial application. Members of the network will be expected to follow, implement and when necessary uniformly improve upon the procedures established by the CHTN to collect, process and handle specimens to assure that they are of the highest quality and suitable for a wide variety of studies and technologies. In order to ensure the availability of suitable specimens for patient diagnosis and quality control of research specimens, the principal investigator of each participating group must be an experienced surgical or anatomic pathologist, actively involved in the operation of a pathology laboratory with demonstrated access to human cancer tissues. Although separate awards will be made to individual institutions, awardees will be required to work collaboratively with the other network members.

General operating policies are established by the Coordinating Committee (consisting of the principal investigators plus one additional representative from each participating institution and a representative from the NCI), which oversees standards for quality control, equitable

policies for distributing specimens, processing and handling processing fees, biohazard procedures and policies for addressing the legal, ethical, and human subjects issues related to the use of human specimens for research.

The estimated average cost of each of the six divisions is $966,667 per year for a total of $5.8 million per year for five years. Total direct cost over five years: $29 million. This represents an 8 percent increase over current funding since the groups have not had any increase over the last two years. The NCI Best Practices will require some upgrading of the informatics and increased frequency of molecular characterization.

Cooperative Family Registry for Epidemiologic Studies in Colon Cancer. Concept for an RFA reissue, cooperative agreement, estimated total $32 million over four years for six awards. Division of Cancer Control and Population Sciences, program director: Daniela Seminara.

The purpose of this concept is to request approval for continued support (four years) for the Colon Cancer Family Registry (C-CFR), a hypothesis-driven research infrastructure. This request has two parts.

—Re-issuance of the RFA that supports the core activities of the C-CFR. This RFA will target the core activities necessary for the maintenance of the infrastructure to respond to the cutting edge scientific questions in colon cancer research.

—RFP solicitation for a contract to support a centralized biospecimen repository which will provide high-quality biospecimen management and distribution to all projects relying on the CFR's inftastructure. This Centralized Biorepository will house aliquots of all C-CFR biospecimens, with the exception of tissues. The C-CFR participating sites will retain back-up aliquots of blood-derived biospecimens. A Virtual Tissue Repository is being developed for studies requiring tissue specimen and is not part of this request. The CRB is deemed essential to the optimal use of this outstanding research resource. The feasibility to establish the CRB at the NCI Frederick biorepository facilities is being explored.

An additional component to the plans for C-CFR is the issuance of a Program Announcement with special review to solicit R01s for projects proposing to use the CFR resource.

The C-CFR is an international consortium of six registries and an Informatics Support Center. The participating centers are the University of Hawaii, Honolulu; Fred Hutchinson Cancer Research Center; Mayo Clinic, Rochester; University of Southern California; University of Melbourne; and Cancer Care Ontario. The ISC is run from the Research Triangle Institute.

Recruitment will be guided by two areas of high research priority that build on the unique strengths of the C-CFR: Identification of more MMR mutation carriers and identification of more "Type X" families. Population-based recruitment will no longer be necessary and will be discontinued. Targeted minority recruitment will be deleted and supported through grants.

Comprehensive Minority Institution Cancer Center Partnership (U54). Concept for an RFA resissue, estimated cost $37.5 million over five years for three awards. Office of the Director, program director: Peter Ogunbiyi.

The purpose of the U54 MI/CCP is to foster and support intensive collaborations among Minority-Serving Institutions and the cancer centers in order to develop stronger national cancer programs aimed at understanding the reasons behind the significant cancer disparities and related impacts on racial and ethnic minority and socio-economically disadvantaged populations. The MI/CCP U54 grant targets four areas: cancer research, cancer training, cancer outreach, and cancer education. The U54 grant must address the first three target areas, cancer education is optional.

While MI/CCP grants are expected to give projects/programs every chance to succeed, they are not entitlement programs. Every pilot and full project/program funded should meet the highest standard of scientific merit and relevance to the program. All of these activities are intended to generate competitively funded peer reviewed support.

The U54 provides support for administrative costs, planning and evaluation, developmental core funds, pilot cancer research projects or pilot cancer training and career development, up to three full projects/programs per year, interim support, resources and infrastructure, and start-up packages for new investigators.

Innovative Molecular Analysis Technologies Program. Concept for an RFA reissue, estimated cost $52.5 million over five years, about 50 awards per year. Office of Technology and Industrial Relations, program directors: Carolyn Compton and Mahin Khatami.

The IMAT program has encompassed three thematic areas with separate RFAs. These include innovative technologies for the molecular analysis of cancer, applications of emerging technologies for cancer research, and innovations in cancer sample preparation. The RFAs were developed as trans-NCI initiatives specifically to support technology development and early phase applications of technologies to cancer research. These RFAs piloted the use of the R21/33 Phased Innovation mechanism that allows for a feasibility or proof-of-principle phase followed by a developmental phase. The RFAs have supported a wide range of innovative molecular. analysis technology development projects spanning a variety of disciplines. Building on the success of some of the originally funded IMAT technologies, some investigators have begun to apply their technologies to clinically relevant issues in projects that are supported by other NCI and NIH program announcements. Other investigators have gone on to develop and expand businesses based on their technologies and yet many others have formed strategic collaborations to continue to develop cancer their technologies in cancer-relevant areas.

Programmatic reorganization is being proposed that will integrate the program with other NCI programs to increase synergy and return on investment. Restructuring will also take

advantage of the new NCI/NIH focus on and consolidation of small business developmental support through the new NCI SBIR Development Center.

The proposed program renewal would continue to use the R21 and R33 funding mechanisms and will permanently eliminate the phased innovation (R21/33) awards that were temporarily suspended in FY07. This will be done to minimize the impact of long-term commitments for R33 transitions and assure that R33-supported development occurs only for the most meritorious technologies with the highest commercialization potential as judged by independent expert peer review.

The program would be renewed under the following structure:

1. Innovative Technologies for the Molecular Analysis of Cancer. Feasibility and early development of highly innovative technologies with high-risk/high-payoff potential. Key areas described but open to any cancer-relevant technology that is novel or highly innovative, particularly within the fields of nanotechnology, proteomics, genomics, and epigenomics. R21 and R33 projects, and SBIR/STTR projects.

2. Application of Emerging Technologies for Cancer Research. Extended development and quality assessment for high-need/high-impact technologies. Emphasis on potential of technology to impact biological and clinical questions. R21 and R33 projects (eliminating phase innovation R21/33 awards. SBIR/STTR projects.

3. Innovations in Cancer Sample Preparation (Re-assigned to OBBR's Biospecimen Research Network Program). Development of high-need/high-impact technologies for improving efficiency and quality of biologic sample retrieval, storage, and/or use. Emphasis on high-quality sample isolation, storage, processing, and/or quality assessment, especially for analysis platforms used in the fields of nanotechnology, proteomics, genomics, and epigenomics. R21 and R33 projects (eliminating phase innovation R21/33 awards). SBIR/STTR awards.

Multidisciplinary Career Development Award: Fellowships in Cancer Nanotechnology Research. Concept for an RFA reissue, estimated total $2.25 million over three years for 11 awards.

This reissuance aims to continue supporting the career development of investigators for multi-disciplinary nano-oncology research and provide career development initiatives to accelerate the translation of nanotechnology platforms in clinical research. The goal is to support the entry of qualified scientists over the next three to five years with formal training in the application of nanotechnology to cancer biology who can lead new programs in technology development through the cancer research enterprise towards clinical applications.

NCI will support career development for individual researchers through F33 Ntional Research Service Awards for Senior Fellows and F32 Ruth L. Kirschstein National Research Service Awards for postdoctoral training in biomedical, behavioral, or clinical research that serves health-related sciences.

Network for Translation Research in Optical Imaging. Concept for an RFA reissue, estimated total $24 million over five years for four awards. DCTD program director: Houston Baker.

The Cancer Imaging Program proposes to reissue the RFA for the NTROI with expanded goals and updated strategies to incorporate a broader set of emerging imaging platforms that includes multi-modality molecular imaging systems, with more emphasis on consensus validation as opposed to their development. The goal of the open competition will be to accelerate productivity by networking research teams to validate and translate multi-modality platforms (combined imaging systems) that must include optical imaging/spectroscopy with other imaging systems. There will be a strong emphasis on validation for specific pre-clinical or clinical cancer investigations focused on a specific organ, cancer, or area of oncology. The proposed continuation will increase focus on translation of more advanced multi-modal platforms, increase emphasis to create and share access to resources for validation of platforms developed and implemented by the different teams, increase focus and support for inter-team working groups, SPORE and other center collaborations, and for broader support of working group activities. The scope of a new application may include early cancer detection, diagnosis, imaging guided drug delivery, and drug response evaluation as the validation methods may be similar.

Adult Brain Tumor Consortium. Concept for an RFA reissue, estimated total $18.07 million over five years for one award. DCTD program director: Jeffrey Abrams.

The NCI-sponsored adult brain tumor consortia, NABTT (New Approaches to Primary Brain Tumors) and NABTC (North American Brain Tumor Consortium) have played a key role in demonstrating that studies of new agents can be safely and effectively carried out in patients with brain tumors. The successful completion of multiple clinical trials by the consortia has clearly increased the willingness of biotechnology and pharmaceutical firms to pursue clinical development of their new agents in brain tumors.

Over the last two grant cycles (nearly 10 years), NABTC and NABTT combined have enrolled over 2,000 patients on nearly 50 phase I/II trials.

To increase the success rate of drug discovery, the next generation of consortia studies will require an increased emphasis on PK-PD relationships, and other mechanistic endpoints based on tissue, imaging, and biomarkers. In view of this more resource-intensive approach required by the science, NCI has elected to limit the recompetition of this RFA to a single, consolidated consortium for which only the leadership of the two existing consortiums, NABTT and NABTC, can apply. By consolidating the two separate consortia into a single entity, NCI can streamline the organizational infrastructure.

This should allow the consortium, with NCI assistance, to more easily prioritize new agents for study, and to focus more intensively the required resources (tissue acquisition, PK/PD, and imaging) on the selected trials. This approach leverages the past decade of NCI support for these two consortia by maintaining the intellectual capital of both in the new single entity. The proven ability of the consortia to conduct multi-site phase I and II trials should permit a smooth transition to a consolidated entity without significant down-time, which would not be the case if totally new entities were allowed to compete. This approach is also preferable to a competition between the two consortia as both groups have made important contributions, provided excellent leadership, and contain highly experienced member sites. However, to ensure that the consortium is dynamic and that its institutions are among the most capable in North America for conducting early phase clinical trials in brain tumors, the consortium will be required to compete the membership of those institutions in the lower tertile of performance (by year 2 of the new award). This will allow capable institutions that are not currently members of the consortium to contend for one of the approximately 15 membership slots.

In the Cancer Centers:

City Of Hope Names Mortimer To Direct Phase I Programs

(Continued from page 1)

for Cancer Control, a community-based participatory research network that brings cancer education, prevention, and screening activities to the community level in rural areas of Alabama and neighboring states.

He is also principal investigator for the Morehouse School of Medicine/Tuskegee University/UAB Comprehensive Cancer Center Partnership, a grant that links UAB investigators with those at the historically black universities to enhance cancer health disparity research.

Partridge is chairman of the board of the Mid South Division of the American Cancer Society and serves on the ACS National Board of Directors.

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JOANNE MORTIMER was named administrative director of phase I programs, associate director for affiliate programs and professor, Division of Medical Oncology and Experimental Therapeutics at City of Hope Comprehensive Cancer Center. She will head her own breast cancer research and will oversee existing collaborations with off-site affiliated programs that enroll patients in clinical trials at City of Hope. She was deputy director for clinical oncology at the Moores Cancer Center at the University of California, San Diego. Her research includes using functional imaging techniques to determine response to breast cancer therapies, investigating agents for advanced breast cancer treatment, finding effective management for cancer pain and increasing participation in clinical trials. She is a member of the FDA Oncologic Drugs Advisory Committee. . . . **MATTHEW LOSCALZO** was named administrative director of the Sheri and Les Biller Patient and Family Resource Center at City of Hope. The center offers a comprehensive range of supportive care and education services. He was professor of medicine in hematology-oncology and co-director of the palliative care program at Moores Cancer Center at University of California, San Diego. . . . **MEMORIAL SLOAN-KETTERING** Cancer Center announced appointments and awards. **Ephraim Casper** was named head of the newly formed Division of Network Medicine Services, Department of Medicine and will oversee medical services at the MSKCC Regional Care Network sites. His responsibilities include oversight of clinical trials at the regional locations. **Jimmie Holland**, attending psychiatrist, received the Association of Professional Chaplains Distinguished Service Award. She was recognized as a "dedicated advocate for pastoral care." **Hedvig Hricak**, chairman of the Department of Radiology, was honored by the Association of University Radiologists for service and dedication to academic radiology. **Paul Marks**, president emeritus, was elected to the American Philosophical Society. Also, M.D. Anderson Cancer Center honored two MSKCC researchers. **Malcolm Moore**, of the cell biology program, received the Jeffrey A. Gottlieb Memorial Award for cancer therapeutic research; and **Charles Sawyers**, chairman of the human oncology and pathogenesis program, received the Emil J. Freireich Award for clinical cancer therapeutics. . . . **ARIZONA CANCER CENTER** established the Skin Cancer Institute with a mission to prevent and cure skin cancer in the state of Arizona. The goals include bringing together laboratory researchers, clinicians, and health educators into one multidisciplinary, collaborative group, said **Robin Harris**, associate professor of public health and deputy director of the institute. To address early detection and treatment, the institute also has opened the Pigmented Lesion Clinic. The clinic provides comprehensive evaluations and tracks changes in skin lesions using total body digital photography. Funding comes from the Bert W. Martin Foundation, which donated $400,000 in 2005 and recently made a second donation of $290,000 to provide partial funding of institute activities.

NCCN National Comprehensive Cancer Network®

NCCN EMPLOYMENT OPPORTUNITIES

The National Comprehensive Cancer Network (NCCN), a not-for-profit alliance of 21 of the world's leading cancer centers, is dedicated to improving the quality and effectiveness of care provided to patients with cancer. The NCCN is currently offering several exciting and challenging opportunities in our suburban Philadelphia office for individuals seeking to impact the practice of oncology.

Medical Director, Information and Informatics

For a medical oncologist seeking to impact oncology nationally and internationally, this position provides clinical guidance and informatics expertise to NCCN information programs, including NCCN Clinical Practice Guidelines in Oncology™ and CE programs. This staff physician works collaboratively with NCCN physicians and non-physician staff to ensure production of accurate, clinically relevant, and multi-functional information products. Opportunity also exists to work on the Oncology Outcomes Database Project and Oncology Research Program.

Requirements:

- An MD or DO with recent clinical experience and board certification or eligibility in medical oncology, hematology, or other oncology-related specialty
- A current and broad understanding of the issues and literature in managing cancer patients
- Expertise in medical informatics, including EMR and clinical decision-assist systems
- Excellent writing skills, strong interpersonal skills, the ability to interact effectively with personnel at various levels, and the organizational proficiency to manage multiple projects and meet deadlines
- Experience in outcomes research and/or health services research a plus.

Oncology Scientist – Compendium

This position develops and maintains the NCCN Drugs and Biologics Compendium™ and the NCCN Standard Chemotherapy Order Templates, working collaboratively with physician and non-physician staff to ensure prompt and accurate incorporation of new drug indications into the Compendium. This individual will work with NCCN clinical pharmacist representatives and others to develop and maintain the Order Templates, develop and maintain a Not-Indicated List for each disease site, and review FDA indications to update Compendium to reflect changes.

Requirements:

- A PhD in pharmacology or PharmD with ability to evaluate clinical research
- Extensive expertise in and experience with cancer treatment modalities
- Ability to evaluate medical and drug use recommendations and translate them into different formats
- Proficiency in MS Office products
- Strong interpersonal communication skills and the ability to interact effectively with internal and external personnel at various levels
- Excellent writing skills and the ability to formulate medical information in a clear and concise manner
- Experience in scientific/medical writing preferred, and understanding of implications of compendium and order set products for utilization and coverage policy is a plus.

Oncology Scientist/Medical Writer

This position will work with NCCN expert panels to develop content for the NCCN Clinical Practice Guidelines in Oncology™, NCCN Drugs and Biologics Compendium™, and other projects as required.

Requirements:

- An MD, PhD, or PharmD and experience in oncology
- Excellent writing skills and the ability to formulate medical information in a clear and concise manner
- Ability to understand and evaluate medical literature, to abstract information concisely, and to work to deadlines
- Proficiency in MS Office products
- Strong interpersonal communication skills and the ability to interact effectively with internal and external personnel at various levels

Policy Fellow

The NCCN Policy Fellowship offers the opportunity for a clinical professional or individual with related training to gain understanding of the coverage and reimbursement policies that influence access to and availability of diagnostics and therapeutics in cancer care. The fellow will learn directly about policy development and also research, evaluate, and track coverage policies of public and private payors. The fellow will compare coverage policies to the NCCN Clinical Practice Guidelines in Oncology™, the NCCN Drugs and Biologics Compendium™ and other clinically relevant recommendations and follow-up with payors to attempt to reconcile differences. This position is funded for a 1-year term, but additional funding may extend its duration.

Requirements:

- An MD, Pharmacist, Nurse Practitioner, or PhD in health policy, public health or related discipline
- Understanding of clinical aspects in oncology
- Ability to self start, strong critical appraisal and analytic skills
- Strong interpersonal communication skills, the ability to work effectively in teams and independently, and the ability to interact effectively with internal and external staff at various levels
- Proven organizational skills and absolute attention to detail
- Proficiency in MS Office products

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