THE CANCER LETTER

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FDA Staff Efforts To Issue Warning Letters On Procrit Ads Were Stopped By Counsel

By Paul Goldberg

Internal FDA documents show that the agency made a series of unsuccessful attempts to stop a direct-to-consumer advertising campaign that claimed that Johnson & Johnson's erythropoiesis-stimulating agent Proctit (epoetin alfa) improved "fatigue" associated with chemotherapy-induced anemia.

The advertising campaign, which is widely credited with making ESAs into the biggest-selling class of oncology drugs, was allowed to proceed with relatively minor changes after the FDA Office of Chief Counsel became involved in the controversy.

The details of the doomed effort by FDA staff to modify the Procrit

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Capitol Hill:

Report Calls For Reinvigorated Cancer Program With Increased Funding, Greater Collaboration

By Kirsten Boyd Goldberg

Cancer research in the U.S. needs to be "reinvigorated" and barriers to progress removed, according to a working group formed to advise Sen. Edward Kennedy (D-Mass.) and Sen. Kay Bailey Hutchison (R-Tex.).

"Sen. Hutchison and I will be introducing legislation in the coming days to make it clear that we must approach cancer comprehensively and not place emphasis on one type of cancer over another," said Kennedy, chairman of the Senate Health, Education, Labor, and Pension Committee, at the committee's May 8 hearing on cancer research and care. "This bill will renew our efforts to make progress in the battle against cancer, and to give patients and their families a renewed sense of hope."

Testifying at the hearing, Edward Benz, president of Dana-Farber Cancer Institute, presented the recommendations of the Research Working Group, a panel of physicians, scientists, advocates, and policy specialists.

Among the working group's recommendations:

—Form a special funding program in NCI for translational research.

—Provide additional Medicare payment for costs of participation in clinical trials.

—Increase support for biospecimen banking.

—Establish standards for biomarker development, testing, and validation.

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House Investigation Produces FDA Documents On Procrit

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campaign emerged in the nearly 80 pages of documents that were placed in the public record at the May 8 hearing of the Subcommittee on Oversight and Investigation of the House Committee on Energy and Commerce. The documents are posted at http://www.cancerletter.com/publications/special-reports.

The new information provides the factual backdrop to statements made by Richard Pazdur, director of the Office of Oncology Drug Products, at a meeting of the FDA Oncologic Drugs Advisory Committee nearly a year ago.

"Obviously, there is a great deal of concern that I have and that most of the clinical review staff have about these advertisements that were made," Pazdur said at the ODAC meeting May 11, 2007. "The FDA chief counsel's office, obviously, sets the tone for enforcement. We are looking into this whole issue of why these ads were allowed to go on, and I think that the FDA is responsible for giving the American public as well as the review staff that sits here the reasons why these ads were allowed to go on… FDA really does need to address this issue. Obviously, there is a fine line between the First Amendment free speech and the protection of the American population from false and misleading advertisement (The Cancer Letter, May 18, 2007)."

The agency hasn't announced the outcome of that internal inquiry.

Documents released by the committee indeed point to the role of FDA's Office of Chief Counsel. At the time the matter was resolved, the office was headed by Daniel Troy. Troy came to FDA in 2001, after representing pharmaceutical and tobacco clients, and stayed through 2004, to return to private practice, which recently apparently included a role as J&J's outside counsel on the Procrit matter, documents show.

Documents trace an effort by FDA staff to stop the Procrit advertising campaign, which ran for seven years between 1998 and 2005. Agency staff objected to many aspects of the ads, including the tagline "Strength for Living," which, according to an agency letter to J&J, was "misleading because it implies that Procrit improves strength and may improve survival when the outcomes have not been demonstrated by adequate and well-controlled clinical trials."

The agency turned down three applications for the quality of life indication for Procrit.

When FDA suggested that the models chosen for the ads looked healthier and more vigorous than a typical cancer patient, J&J responded with a question:

"Are the *very* physically active models in the current Celebrex broadcast advertisements or Dorothy Hamill in the Vioxx DTC print advertisement typical of the general population of osteoarthritis patients? Likewise, is Peggy Fleming typical of a patient with hyperlipidemia or Lance Armstrong typical of a testicular cancer patient?"

The two sides appeared to be were deadlocked.

However, OCC became involved in the matter, documents show. Handwritten notes from a May 29, 2002, teleconference titled "TC w/DDMAC re: Procrit" state: "Overall message fr. OCC—try to find middle ground. Fix in context rather than yanking material." DDMAC is FDA's Division of Drug Marketing, Advertising and Communications. The ad campaign ran through 2005.

On Feb. 27, 2007, when FDA was reviewing the ESA labels, Troy, by then an attorney with the firm of Sidley Austin, sent an email to his former colleagues in OCC.

"A woman named Leah Walker from Amgen has asked for a meeting with Tom Abrams, Lesley Frank and Mark Askine from DDMAC," Troy wrote. "It would be great if you could make sure that someone at OCC makes sure that people understand the limits of their authority. I will keep you posted about what I hear."

Troy's email was addressed to Jeffrey Senger, then the agency's deputy associate general counsel.

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A sequence of internal FDA emails released by the committee shows that Troy was inquiring about a call placed by Pazdur to Amgen and J&J. At the time, the agency was reviewing the ESA labels in light of toxicity and tumor promotion data that had just emerged from two Amgen studies. Apparently, Pazdur requested that the companies stop their direct-to-consumer advertising while the agency formulated the wording of the black box warning triggered by the new data.

Sources familiar with the situation said Troy represented J&J.

"Federal revolving door restrictions have many gaps, and often don't apply to government officials who make big-picture public policy decisions," said Scott Amey, general counsel for the Project on Government Oversight. "This issue, however, should be reviewed by FDA ethics officials to determine if a conflict of interest has occurred. At a minimum, the FDA should investigate whether any employee involved in formulating the advertising policy is now working for the other side."

Generally, former government employees are precluded from representing private clients in dealing with "particular matters" in which they participated "personally and substantially" while in government employ. In these situations, lawyers often face a life-long ban on representation.

During his stint at FDA, Troy had a clear agenda: to "pre-empt" product liability lawsuits from being filed in state courts. Also, he had the directive to become involved in issuance of warning letters.

Historically, the decisions to issue warning letters were made by FDA enforcement divisions. However, in November 2001, an HHS deputy secretary ordered that the Office of General Counsel sign off on all warning letters.

The preemption doctrine extends to regulation of advertising. For example, in September 2002, Troy was listed as "of counsel" in an amicus brief in the Paxil product liability case. FDA has the "comprehensive statutory and regulatory scheme governing prescription drug advertising" and "given the intent of Congress to centralize prescription drug advertisement regulation in the FDA, this court should defer to this agency's primary jurisdiction," the brief states.

Troy declined to discuss the matter.

After reviewing the documents, Howard Ozer, an expert in ESAs, said the documents point to political intervention. "I find this offensive," said Ozer, Eson professor and chief of hematology and oncology at the University of Oklahoma Cancer Center. "I think that J&J and FDA were doing what they should have been doing to represent their constituencies, namely that the pharma companies are pushing the envelope, and, thank God, the FDA is representing science and data. I think that what happened here is that one side had managed to get an FDA office supporting it, and that's wrong."

"Strength For Living"

At the hearing, Subcommittee Chairman Bart Stupak (D-Mich.) confronted Kim Taylor, president of Ortho Biotech, the J&J company that markets Procrit, with some of the memoranda.

"A year ago, at a public FDA advisory committee, Dr. Richard Pazdur, FDA's chief oncologist, remarked that the FDA and the Office of Chief Counsel owed the American people an explanation as to why Procrit TV ads were allowed to run for seven years," Stupak said. "Ms. Taylor, are you aware that the experts inside and outside the FDA consider the seven-year Procrit ad campaign to be false and misleading, because it constitutes off-label advertising for the treatment of fatigue, which it is not approved for by the FDA?"

TAYLOR: "No, sir. In fact, my understanding is that we had a reassurance that during the period concerned, the FDA was satisfied that we complied with regulations."

STUPAK: "You advertised for 'fatigue.' That's an off-label use of Procrit, isn't it."

TAYLOR: "No, our recommended use, approved use, for Procrit is for chemotherapy-induced anemia."

STUPAK: "Not for fatigue, right?"

TAYLOR: "And the symptoms of fatigue and weakness, which are cardinal symptoms which we used to describe for patient DTC."

STUPAK: "Isn't it true that Ortho Biotech and Johnson & Johnson were repeatedly cited by FDA for false and misleading advertising in connection with direct-to-consumer advertising of Procrit as a treatment for fatigue?"

Stupak cited three letters:

—One letter, dated Nov. 6, 1998, asks the company to modify an advertisement which read: "Are you a chemotherapy patient? Do you feel tired all the time? Please tell your doctor. There's a treatment for the tiredness."

In the letter, the agency states: "Procrit is intended, among other things, to treat anemia associated with certain chemotherapeutic regimens, not 'tiredness' in general. This information is considered to be both false and misleading under the [Food Drug and Cosmetics] Act."

—Another letter, dated June 30, 2000, objected

to the Procrit campaign, stating that "the claims made throughout the promotional materials are in violation of the Food Drug and Cosmetics Act and implementing regulations due to expanding the use of the product as a treatment for fatigue."

—On Dec. 21, 2001, the agency informed J&J about "false and misleading" advertising in television broadcasts titled "Anthem" and "Big Boy Bed."

Also, the letter states that "the tagline 'Strength for Living' is misleading because it implies that Procrit improves strength and may improve survival when these outcomes have not been demonstrated in adequate and well-controlled studies… The presentations imply that Procrit would improve fatigue and weakness in any chemotherapy patient when, in fact, Procrit only has been shown to increase red blood cells in chemotherapy patients with anemia. Chemotherapy patients may have fatigue and weakness due to factors other than anemia. Thus, increasing red blood cells with Procrit would not necessarily improve a patient's condition for weakness and fatigue."

Considering this language, how could the company claim that it kept within FDA guidelines, Stupak asked.

TAYLOR: "These were all part of a discussion, an ongoing discussion that went on with the FDA, and after each of these letters, there was further discussion and we complied or came to an agreement with the FDA."

STUPAK: "Why did the chief oncologist of the FDA then say we owe the American people an apology [sic.] for seven years of false and misleading advertising of Procrit?"

TAYLOR: "I am not sure. You would have to ask…"

STUPAK: "Let me ask you this one… If you are getting chemotherapy, you lose your hair, right?"

TAYLOR: "You can, yes."

STUPAK: "How come your ads don't have anyone in there who lost their hair from chemotherapy? That's a very simple thing you can do to have a fair ad… FDA said the models in your ads are not accurate, because you have people who still have hair, and we know in chemotherapy, you lose your hair… On Dec. 21, 2001, [FDA wrote]: 'The presentations are misleading, because the patient models depicted are not representative of the general population of chemotherapy patients, who would appear weaker and have hair loss, among other side effects.'

"Now, that doesn't sound like a discussion to me. I saw it as a directive on how you should be doing your ad. And you never presented a person without hair."

TAYLOR: "No, we didn't. I don't have the follow-up discussion, but I do believe that subsequent ads, which were agreed with FDA, and which did not have patients who had hair loss were accepted by FDA in the subsequent period."

STUPAK: "Anywhere in your advertising, did you say that use of Procrit for cancer patients who had tumors that Procrit would likely enlarge those tumors and endanger the lives of those patients?"

TAYLOR: "No, that was not a specific warning in the end."

STUPAK: "But the FDA told you about that, and you didn't put it in there. Don't you think people should know that before they take your drug, that, in fact, it could worsen their condition, not make it better, by making tumors swell more and shorten their lifespan?"

TAYLOR: "That is a theoretical concern that has been raised."

STUPAK: "It's been documented, right? That tumors would swell with your stuff, the greater the Procrit they got, the quicker the tumors swell."

TAYLOR: "I don't believe that that's accurate. What we did do with the ads is we included all of the side effects that were significantly different from placebo."

STUPAK: "That would be significantly different, wouldn't it, if you were a cancer patient and the tumors you have in your body swell when you took Procrit? Wouldn't that be significant, especially when it shortens your life?"

TAYLOR: "These are significant results as measured in clinical studies. So the side effects that were there, such as diarrhea and edema, were those that were significantly different from placebo."

STUPAK: "Can you submit to any of the documents you submitted—a couple thousand—anywhere where the FDA approved Procrit for off-label use for fatigue or weakness in patients? Can you point to any one document you submitted to our committee?"

TAYLOR: "Procrit has been approved for chemotherapy-induced anemia. Our advertisements were specifically looking at using language… that would be recognizable by a consumer."

STUPAK: "So I take it you answer is no… FDA wrote to you… telling you not to be using your ads for tiredness, for weakness. There isn't a letter from FDA that said you can advertise for that."

TAYLOR: "In fact, all the way through, there have been discussions with the FDA about…"

STUPAK: "I didn't ask about discussion. I asked about an approval letter for the way you marketed

Procrit for seven years or an off-label use that was not approved for Procrit. Do you have any document that can show me that?"

TAYLOR: "We have consistently throughout had reassurances that the way we were communicating the symptoms of anemia—such as fatigue and weakness—was appropriate to the patient group we were reaching with the DTC."

Symptom Improvement Claim Inserted In 2006

Taylor said the company discontinued the DTC ads because it had accomplished its goal of raising awareness of anemia.

"We discontinued our ads in 2005 [because] from our research we believed that there was a sufficient understanding of these symptoms and a recognition of them as being related to anemia," she said.

J&J's decision to stop the ads was made at the time when Procrit lost its dominant market share to the Amgen drug Aranesp (darbepoetin alfa). Marketing experts say that companies stop DTC ads when their products lose the dominant market share.

Amgen has never run DTC ads for Aranesp, but until recently, ran ads for the white blood cell growth factor Neulasta, which is administered earlier in the treatment cycle. Since Aranesp and Neulasta are sold in a bundling arrangement which allows doctors to earn rebates when they reach preset sales targets, doctors had the incentives to offer Aranesp as well.

The company said it recently stopped Neulasta DTC ads on television.

An analysis of the evolution of the Procrit label allows a careful reader to point to a place suggesting that the agent improves the symptoms of anemia.

On May 11, 2006, a year after Ortho stopped direct-to-consumer marketing, a symptom improvement claim mysteriously appeared in the patient version of the label. The label reads:

"Epogen is used to treat anemia (a lower than normal number of oxygen-carrying red blood cells). People with anemia may feel tired or may feel a lack of energy. They may also experience weakness, dizziness, difficulty with concentration, shortness of breath, chest pain, and feeling cold all the time. Your doctor has prescribed Epogen to treat your anemia. If your body responds to Epogen, your symptoms may improve…"

The language appeared during a reassessment of the label in the renal indication and was crossed out of the label less than a year later, during the March 9, 2007, revision.

Recently, David Steensma, associate professor of oncology at Mayo Clinic, pulled two Procrit ads from YouTube and showed them to hematology-oncology fellows last week during a teaching session on ESAs.

"Watching them made us all feel very uncomfortable," Steensma said in an email. "One of the fellows spoke out she felt slimy after seeing them and wanted to go take a shower. I had forgotten that the DTC ads talked about 'strength' (which physicians think of as ability to contract muscles) rather than fatigue or energy.

"There was also a statement in the ads we watched that only diarrhea and edema are more common than with placebo, which seems particularly naïve today—considering that these ads ran until 2005, and safety signals with ESAs in cancer patients were emerging in 2003-2004."

Capitol Hill:

Kennedy, Hutchison Plan Bill To Reinvigorate Research

(Continued from page 1)

—Enhance support for young investigators and oncology nursing.

—Expand the Bayh-Dole Act to permit academic, federal, and industry partnerships in cancer research.

—Increase federal appropriations to NCI and NIH.

"We've come a long way in fighting cancer since we passed the National Cancer Act 37 years ago," Kennedy said. "Since then, significant progress has been made. New methods to prevent and treat cancer have led to more beneficial and more humane ways of dealing with the illness. The expansion of basic research, the use of large scale clinical trials, the development of new drugs, and the enhanced focus on early detection have led to breakthroughs unimaginable only a generation ago. As a result, today cancer is no longer the automatic death sentence that it was a generation ago.

"But despite impressive achievements in fighting cancer, our society now faces a perfect storm of conditions have expanded the number of our citizens suffering from cancer—the aging of our population, new environmental issues, increased life expectancy and unhealthy behavior," Kennedy said. "As a result, today cancer is still the second highest cause of death in America.

"Clearly, we need a new way forward in battling this frightening disease," Kennedy said. "We must build on what the nation has already accomplished, and launch a new war on cancer for the 21st century."

Kennedy called for "new urgency to efforts to find cures for cancer," giving "equal priority" to cancer prevention and early diagnosis, and improved quality of care for all patients.

"We need to integrate our current fragmented and piecemeal system of addressing cancer," he said. "Front and center in our current system are the troubling divisions that separate research, prevention and treatment. Our current system treats these three aspects of cancer care as being inherently separate, rather than what they really are—different aspects in the continuum of comprehensive cancer care. The net effect of this fragmentation is the development of marked disparities in research progress, market innovation, access to care, and quality of care.

"We must move from a magic bullet approach to a mosaic of care in which advance becomes part of the larger picture of cancer care."

Kennedy's statement is available at http://kennedy.senate.gov/newsroom/press_releases.cfm. Hearing testimony is available at http://help.senate.gov/Hearings/2008_05_08/2008_05_08.html.

"Cancer Is Not A Priority"

Others testifying at the hearing supported increased federal funding for cancer research, improved access to care, and increased research collaboration between private and public sectors.

"I never saw the President at the President's Cancer Panel meetings," said Lance Armstrong, who recently completed his second term on the panel, established by the National Cancer Act to monitor the National Cancer Program.

"I think this issue has grown complacent," said Armstrong, founder of the Lance Armstrong Foundation. "We are conflicted in how we allocate money. [Cancer] is not a priority in our society to fight…. [NCI] has to be given proper priority and proper funding, and they don't have that. This is not a time when we should be decreasing our investment in research."

Armstrong also called for strategies that encourage collaborative team science, better coordination of research, and "a broad-based national cancer plan."

In his written testimony, Armstrong said a national cancer plan "should be a multi-disciplinary, cross agency approach that leverages the strengths of the various federal agencies and remains accountable for developing results in comprehensive cancer control and care."

Elizabeth Edwards, senior fellow at the Center for American Progress, and wife of former Sen. John Edwards, said Congress must solve the problem of lack of adequate health insurance in order to address disparities in cancer care and treatment outcomes.

Steve Case, chairman of Revolution Health and chairman of Accelerate Brain Cancer Cure, said funding should encourage greater collaboration between disease areas. "All too often, the battle for research money ends up pitting cancer groups against each other, in what they perceive to be a zero sum game," he said. "We are all in this together, and all of us will benefit from a more strategic, networked, technology-driven approach to cancer research.

"We need to come together as one community committed to tackling cancer and move away from the model that treats cancer based on where it appears in the body and toward a model where we focus on signaling pathways, new technologies, biomarkers and novel clinical trials," Case said. "As part of this strategic approach, we need to eliminate the restrictions that prevent NCI from pursing the most effective collaborative models. Policies now in place limit collaboration and slow innovation by making it difficult for the NCI to partner with for-profit companies."

The U.S. is facing a "cancer crisis," said Hala Moddelmog, president and CEO of Susan G. Komen for the Cure. "A crisis in our investment in prevention and early detection of cancers; a crisis in our dedication to innovative cancer research; and a crisis in patient access to the highest quality cancer care and treatment."

Gaps in research and care are due to "lack of investment in early detection of cancer, inadequate funding for cancer research and barriers that is difficult to translate basic research into patient treatments; and inconsistent access to high quality cancer care," Moddelmog said.

"Since 2003, the NIH has been consistently flat funded," she said. "When adjusted for inflation, flat funding translates to an actual decline in NIH purchasing power. According to the NCI, when funding is adjusted to reflect the Biomedical Research and Development Price Index, the NCI has experienced a significant loss in purchasing power each year since 2004, resulting in a 19 percent—or $1 billion—loss for FY 2008. We cannot engage in cutting edge science and maintain our status as the global leader in biomedical research without adequate NIH funding."

She also called for greater funding for young researchers and for translational research.

Greg Simon, president of FasterCures/The Center for Accelerating Medical Solutions, a center of the Milken Institute, said cancer research emphasizes studying biology rather than curing the disease.

"In funding deliberations at the NIH there is little emphasis on specific goals or milestones to cure disease or on achieving specific clinical results," Simon said in his testimony. "Researchers often insist that science cannot be managed, and that the role of the NIH is to provide ever-increasing funds and not to direct how those funds will be used. NIH program officers exercise little oversight over the use of NIH funds except to be sure that researchers are doing the work for which they were funded. As a result, the time from initial discovery to dissemination and commercialization is often measured in decades—an outcome simply unacceptable to the citizens who fund this research and expect to benefit from its fruits."

Peer review is too conservative and doesn't support high-risk proposals, Simon said. Nor does peer review effectively prioritize research projects, he said.

Replace Peer Review? With What?

Kennedy questioned Simon on his view of the NIH peer review system. "If peer-reviewed research is not working—that's the basic concept of our research. If that isn't working, I don't know what the substitute is," Kennedy said. "And I'm not getting a lot from you to tell me what it is."

NIH only can fund 19 to 20 percent of the grants and "we ought to do more," Kennedy said. "I'm sure there are a lot of things that can be improved upon, but if we are not for peer review, then I don't know what we ought to be for, particularly if we are starting out on a new course."

SIMON: "Peer review has two parts. Number one, 'Is this proposal scientifically rigorous?' The other part, which gets shortchanged all the time is, 'Is this meaningful? Does this help patients?' If something is scientifically rigorous, it often rises to the top even though there might be something else that is more meritorious. We have to be able to do both. We have to have strong science, but we have to be asking, 'Will this help people?'

"DARPA doesn't do it through peer review. They find a problem and ask people to fix it. They have a project manager for two years, and then they make a go/no-go decision at the end of two years. We don't do that in medicine."

KENNEDY: "That's entirely different from peer review. I'm familiar with DARPA, but that's an entirely different concept than peer-reviewed research. If you are talking about getting sound science, and grants that meet the best in terms of scientific capability and also have the best opportunity to help patients, I'm with you. I'm just concerned that we are getting into the questions about undermining peer review, we are talking about an entirely different approach. I don't know a lot of researchers who think we ought to throw peer review over the side."

SIMON: "I wouldn't propose that, Senator, not at all. We need to do more risky things than most peer review committees are willing to do, and we need the money to do those things."

BENZ: "I don't think the problem is with peer review. I think it would be very unfortunate if peer review as the mechanism for evaluating the quality of science were replaced by something else, because, like you, I can't imagine what would be better. Peer review, like all human systems, has its flaws. But having served on study sections and councils for several NIH institutes, what I can tell you is that peer reviewers do extremely well and sincerely with what they are charged with doing. The problem in the peer review system right now is what rules and what criteria are the peer reviewers asked to evaluate. If the primary mechanism for funding is the individual research grant in which individual productivity, individual accomplishment is a major parameter, we are going to fund things that favor individual accomplishment, probably at the expense of collaboration.

"A quick example from the Dana-Farber: in our strategic plan in 2003, we decided we needed to create these connections and overlaps between the clinic and basic research. We did that, but we funded it with philanthropy and institutional dollars, because there was no effective NIH mechanism at the time. So it's what we ask the peer reviewers to do that we should examine, not the process of peer review itself."

KENNEDY: "This is very interesting. We ought to try and sharpen that up. These are good suggestions."

Research Working Group Recommendations

Following are the recommendations of the Research Working Group:

I. Translational Research: The National Cancer Institute-supported effort to convert basic scientific findings into new and better therapies is not keeping pace with the advances in knowledge and technology over the past 40 years in cancer research. Among our recommendations to remedy this situation are: a special funding program to advance a select number of especially promising early research opportunities; joint NCI/industry funding of collaborative early translational research projects; and increased NCI interaction with foundations and advocacy groups to advance this type

of research.

II. Clinical Research: Clinical trials are becoming increasingly complex to conduct, and the NCI's per patient reimbursements are insufficient to cover the costs of such trials. Among our recommendations: additional Medicare payments to cover the additional time and resources involved in enrolling patients in trials; and group and individual health insurance mandates to cover the routine costs of participation in trials.

III. National Collection of Tissues/Biospecimens: Cutting-edge cancer research is impaired by the absence of either a centralized network of biospecimen and tissue collection banks, or consistent standards for retention and storage of such specimens. Among our recommendations: establishment of a National Cancer Biospecimen Network by linking existing public and private biospecimen and tissue collection banks; and guarantees of protections against genetic discrimination.

IV. Prevention and Early Detection Research: Despite the launching in 2000 of the Early Detection Research Network by the NCI, only a few biomarkers—substances in blood or other fluids that serve as telltale signs of cancer—are routinely used in oncology today. Discovery of new ones is hampered by the limitations of current technology. Among our recommendations: a standard process for developing, testing, and proving the value of biomarkers; support for high-quality biorepositories of samples of cancerous tissue across all stages of development and representative of all cancer sites; and federal and private health insurance coverage of new biomarker tests.

V. Young Investigator and Oncology Nurse Workforce: Teaching and mentoring the next generation of investigators is one of cancer scientists' most important jobs, but many of today's brightest young researchers are finding it increasingly difficult to establish independent careers in biomedical research and are leaving the field. Equally disturbing trends are threatening the vitality of the oncology nursing workforce, which is critical to quality care for patients. Among our recommendations: more stable funding streams to allow individuals and institutes to better plan projects and careers; more opportunities for non-U.S. citizens to emigrate and compete for training, postdoctoral and research awards; and fully funding for federal nurse loan repayment and scholarship programs.

VI. Collaboration: There is a lack of collaboration among NCI-funded cancer centers and programs, and a variety of barriers discourage partnerships between publicly and privately funded researchers. Pharmaceutical and biotechnology firms have little financial incentive to develop treatments for rare cancers. Among our recommendations: expansion of the Bayh-Dole Act to permit cancer-related partnerships between academia, nonprofit organizations, and private companies; and remove some restrictions on international sites that participate in NCI-funded trials.

VII. Federal Funding: Ten years ago, the nation made a bold, five-year investment in the National Institutes of Health and the National Cancer Institute, the primary federal vehicle for advancing cancer research. Between 1998 and 2003, NIH appropriations for cancer research essentially doubled, far outpacing the historic norm of 8.2% percent average annual increases. Since that period, however, the budget for such appropriations has been flat or declined. As the accompanying chart shows, had the five-year doubling never occurred and the 8.2% average been maintained each year since 1998, the appropriations budget would be significantly higher than it is today. Funding cuts for extramural research have been even more dramatic if one takes into account the allocations made for other NCI obligations. The result of this falloff is that many experienced researchers are struggling to obtain funding for more conservative, less-ambitious projects, while young investigators are increasingly abandoning the field. Without a renewed commitment to funding, the potential for new treatments, cures, and prevention strategies for cancer will continue to recede. Among our recommendations: consistent and sustained federal funding for research; support programs to improve the accuracy, completeness and accessibility of cancer data; and establish an office for rare cancers to ensure that research needs are met.

Conclusion: Decades of research have brought us to the point where some of the most dramatic advances in the history of the disease's treatment are coming into sight. The American public has made an investment in cancer research unequalled by that of any other nation, in the hope that such research will lead to better treatments and long-term cures. We have the opportunity, now, to honor that investment by ensuring a level of funding that will bring the promise of current cancer science to fruition. The Research Working Group encourages the members of the Senate Committee on Health, Education, Labor and Pensions to provide the financial, regulatory, and legislative tools to carry the War on Cancer to its decisive stage.

Funding Opportunities: PA-08-165: Stem Cells and Cancer. R21. Full text: http://www.grants.nih.gov/grants/guide/pa-files/PA-08-165.html. Inquiries: R. Allan Mufson, 301-496-7815; mufsonr@mail.nih.gov.

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