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NIH, FDA To Tighten Consulting Rules As Congressional Inquiry Continues

By Kirsten Boyd Goldberg

Responding to Congressional pressure, NIH Director Elias Zerhouni said he is ordering all employees to report the financial details of paid consulting agreements with pharmaceutical or biotechnology companies over the past five years.

About 500 NIH employees who have paid consulting agreements with pharmaceutical or biotech companies must comply with the new requirement, officials said. The details of the consulting agreements will be submitted to Congress.

In a related development, FDA Acting Commissioner Lester Crawford ordered a "comprehensive review" of all outside activity requests from agency employees in response to the revelation that an employee was consulting with a biotechnology firm that had the potential to be regulated by the agency.

At the May 18 hearing of the Subcommittee on Oversight and Investigations of the House Committee on Energy and Commerce, legislators

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Moonlighting By Scientists Liotta, Petricoin Conflicted With CRADA Work, Committee Says

By Kirsten Boyd Goldberg

A Congressional investigation of conflict of interest at NIH has spilled over to FDA, as lawmakers asked the HHS Inspector General to investigate FDA's approval in 2002 of microbiologist Emanuel Petricoin's consulting arrangement with Biospect Inc., a South San Francisco life sciences company.

"This review is needed to assure continued public confidence in the work of FDA," members of the Subcommittee on Oversight and Investigations of the House Committee on Energy and Commerce wrote in a May 17 letter to the IG.

The case "raises the ethical concern of whether the Biospect consulting agreement should have been approved in the first instance, since Biospect appears on its face to be a 'significantly regulated entity,' an organization for which FDA employees are generally prohibited from employment," the letter said.

In a hearing May 18, Subcommittee Chairman James Greenwood (R-Pa.) criticized "weaknesses" in the NIH and FDA ethics programs that allowed Petricoin and a collaborator, NCI scientist Lance Liotta, to work as paid consultants for Biospect while also working under a Cooperative

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Congress Places NIH Ethics Decisions Under Microscope

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grilled NCI and FDA officials and ethics officials in the Department of Health and Human Services and the Office of Government Ethics for five hours on decisions that allow employees to receive consulting payments from pharmaceutical and biotech companies.

The hearing was the second the subcommittee has held in its investigation of conflicts of interest at NIH, begun in response to a Los Angeles Times article published last December that found evidence of hundreds of consulting payments made to NIH officials by pharmaceutical and biotechnology companies.

Last week, legislators criticized as inadequate NIH's attempts to reform its policies through a review and recommendations by the NIH Blue Ribbon Committee on Conflict of Interest Policies (**The Cancer Letter**, May 14).

The May 18 hearing examined two specific instances that members of Congress called abuses of the public trust:

--A $40,000 prize presented by the University of Pittsburgh in 1997 to then-NCI Director Richard Klausner *(See story, page 6)*.

--Consulting payments made by Biospect Inc., a South San Francisco life sciences company, to NCI scientist Lance Liotta and FDA microbiologist Emanuel Petricoin, at the same time the two were working on a public-private partnership with a competitor, Correlogic Systems Inc., of Bethesda, Md. *(See story, page 1)*.

Klausner, who is also a co-founder of Biospect and a member of its board, was invited to the hearing, but didn't appear.

The two cases were presented as illustrations of lax oversight over ethics at NIH. The hearings are part of what appears to be a broad investigation of NIH, with a special focus on NCI activities over nearly a decade. The subcommittee continues its investigation of prizes Klausner received from NCI-funded institutions, his travel arrangements, his role in making controversial grants, and his business involvements after his departure from NCI.

The controversy is unfolding against the backdrop of Congressional discussion of recommendation by the Institute of Medicine that NCI should lose some of its special privileges.

The most recent hearing also touched on changes in the late 1990's that allowed NIH to hire scientists and administrators under a special program known as Title 42. The program was established by Congress to allow the government to hire "special experts" for short-term assignments at a higher pay scale than the civil service. Legislators said NIH has abused the program.

About 4,000 NIH employees currently have Title 42 status, according to Subcommittee Chairman James Greenwood (R-Pa.) *(See story, page 10)*. Altogether, NIH employs about 18,000 people and about 6,000 of them have M.D. and Ph.D. degrees.

"What happened to the public trust?" Greenwood said at the hearing.

"These decisions are the opposite of what people have the right to expect from their ethics officials," Rep. Henry Waxman (D-Calif.) said.

"This hearing shows that the committee is doing more than getting information," said Rep. Joe Barton (R-Tex.), chairman of the House Energy and Commerce Committee. "We are starting to achieve positive changes in NIH ethics policy for both consulting and awards."

As a result of the investigation, HHS ordered its agencies to collect information about the amounts of money paid to government scientists as part of the approval process for outside activities. The Office of Government Ethics is providing additional guidance to agencies regarding awards, Barton said. The committee also has prodded HHS to expand the number of NIH employees required to disclose financial Information.

"Much more needs to be done," Barton said.

Several subcommittee members said legislation may be needed to ban all paid consulting agreements

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between NIH employees and pharmaceutical and biotech companies.

"I have grave concerns about the Blue Ribbon Panel recommendations," said Rep. Diana DeGette (D-Colo.). "Unless there is a blanket restriction on outside compensation, serious conflicts of interest, and the appearance of conflicts of interest, will continue to exist."

At least one more hearing is expected to address broad ethical questions, with NIH Director Elias Zerhouni as a witness, in the near future, Capitol Hill sources said.

Consulting May Have Slowed Work On Ovarian Cancer Test

(Continued from page 1)

Research and Development Agreement with that company's competitor, Correlogic Systems Inc., of Bethesda, Md.

The consulting arrangement may have slowed down NCI's work with Correlogic, lawmakers said.

Because of the scientists' financial arrangement with Biospect, "progress appears to have slowed on a public-private partnership that could have led to prompt commercialization of life-saving ovarian cancer diagnostic tests," said Rep. Joe Barton (R-Tex.), chairman of the House Committee on Energy and Commerce. "Public trust has been damaged."

In April 2002, Correlogic and NCI entered into a CRADA for research on a blood test for early-stage ovarian cancer. For the past two years, the company and NCI have been negotiating over a second CRADA to pursue clinical trials.

NCI decided to unilaterally sponsor clinical trials on the ovarian cancer test, instead of conducting the trials under a CRADA with Correlogic, Greenwood said.

"The NIH and the FDA allowed government scientists, who are co-inventors and CRADA partners with Correlogic, to secretly provide consulting services, without the knowledge or consent of Correlogic, to Correlogic's competitor," Greenwood said. "What happened to the public trust?

"The way things were handled in the Correlogic case, a private company entering into a CRADA with NIH cannot protect itself," Greenwood said. "It risks its government partners taking the insight, knowledge, and prestige gained from the CRADA to consult with the competition—and all under the cover of an ethics approval.

"What company will want to enter a CRADA with NIH if this is the way conflict of interest issues are managed? This is an outrage."

NIH Director Elias Zerhouni has said he disapproves of Liotta's consulting arrangement, the Los Angeles Times reported May 18. Biospect changed its name on May 17 to Predicant Biosciences.

Petricoin, a senior investigator in the Office of Cell Tissue and Gene Therapies at FDA's Center for Biologics Evaluation and Research, testified that he "immediately and without hesitation" ended his consulting for Biospect on May 7, after FDA officials informed him that a review--done as a result of the Congressional investigation--determined that the company was considered a "significantly regulated entity."

"I believe that my outside activities, all of which were submitted, reviewed and approved according to the procedures in place, were performed to the highest ethical standards," Petricoin said at the hearing. "I believe I followed, to the best of my ability, not only the instructions, but also the intent of the ethics guidelines."

Liotta, chief of the NCI Laboratory of Pathology, said he, too, "immediately withdrew" from the consulting arrangement last week, after learning that Biospect had at one point requested publicly available data from the NCI-FDA Clinical Proteomics Program that he and Petricoin head.

Liotta said the NCI Technology Transfer Branch, in preparation for the hearing, had found a document that indicated a request from Biospect for the data.

As a result, Liotta said, "I could not be completely, absolutely sure that they weren't going to be studying something that might overlap with my government work."

Liotta and Petricoin formed the proteomics program in 1998 to develop applications for laser capture microdissection in cancer diagnostics. They applied mass spectrometry for fingerprinting analysis to microdissected tissue and analyzed the mass spectral data using visual graphing and pattern recognition software that was commercially available.

Petricoin has said, and it has been reported in the press, that he mentioned the work to Peter Levine, an acquaintance and an attorney who was interested in biotechnology. As a result, Levine formed Correlogic Systems to develop pattern recognition software to analyze mass spectral data.

In February 2002, the scientists and the company reported in a paper published in the Lancet that the

method they developed to use mass spectral fingerprints in serum had correctly identified ovarian cancer in a study of 116 women. Liotta and Petricoin have published six papers with Correlogic Systems. Another paper is scheduled for publication next month.

Correlogic and the government signed a CRADA in April 2002 for "joint research in the identification of patterns of protein expression that detect diseases such as cancer," according to a press release issued by the company. The company also said it has a licensing arrangement with NCI for "the shared invention of using patterns of protein expression to detect disease."

Liotta characterized the work differently. "The CRADA was aimed at evaluating the use of Correlogic's software for additional research topics," Liotta testified. "At that time, Correlogic was a software company with an established proprietary pattern recognition software using a genetic algorithm with a lead cluster analysis."

That CRADA expired last month, a spokesman for Correlogic Systems said.

In late 2002, Liotta and Petricoin were approached by Biospect, which had been formed earlier that year.

Biospect described itself in a 2003 press release as "an emerging life sciences company developing systems for detecting biomarker patterns."

The company has attracted three former NCI officials. Richard Klausner, the former NCI director, serves on the company's board of directors. Carol Dahl, formerly director of the NCI Office of Technology and Industrial Relations, is vice president of strategic partnerships. Svetlana Shtrom, an NCI technology transfer specialist who worked on the Correlogic-NCI CRADA, also is an executive at the firm.

"My understanding was that Correlogic was a software company, in contrast with Biospect, that I understood to be a scientific instrument company," Liotta testified. "When I began consulting with Biospect, I understood Biospect was in the early stages of developing a new instrument and scientific technology which employed its proprietary chemistry to separate and identify molecules. I understood Biospect desired to explore the use of blood and body fluids from animal and human sources with the goal of discovering molecules for biological and medical applications."

This explanation is "an attempt to split hairs," an industry scientist who is not involved with either company said to **The Cancer Letter**.

"Both companies have the same aim—to identify putative biomarkers through the analysis of differential protein expression," the scientist said, speaking on condition that his name not be used. "One is providing a portion of the answer with software, while the other is trying to provide the whole answer with a more comprehensive approach involving instrumentation. If you want to split hairs, you could say Correlogic is a software company, and Biospect is a service company. But the ultimate aim of both groups is to find candidate diagnostic markers, or biomarkers."

On its Web site, Biospect says it plans to develop "an integrated system incorporating proprietary separation, detection, and informatics technologies to provide reliable, reproducible and sensitive measurements for protein pattern discovery and clinical assay."

According to the hearing testimony, Biospect retained Liotta and Petricoin to work two days a month for $5,000 a month, initially. Later, the work dropped to one day a month for $3,250 a month.

Petricoin said his role as a consultant was "to survey the public domain for applications of their technology, including selling the machine itself, all the way to environmental monitoring, to discovering new molecules associated with disease."

Liotta and Petricoin said they did this work sitting at their computers at home, filing occasional reports to the company.

Under questioning, Petricoin testified that he did not know Biospect was working on "pattern analysis" until his superior, CBER Director Jesse Goodman, told him last week.

GREENWOOD: "Was it not abundantly clear that this company was interested in getting FDA approval for its equipment?"

PETRICOIN: "It was not abundantly clear to me. My understanding was they were looking at every aspect of science and technology—science and technology being such a huge field."

GREENWOOD: "Isn't the wonderful promise of this technique that it is going to be able to allow for us to have very advanced diagnosis of potential cancer victims?"

PETRICOIN: "Not to my understanding. They had really no specific application. They had developed a technology, a platform, and they were looking at avenues to use it. That's what my consultation was, to look at the public domain, where any application where technology such as this could possibly be used."

GREENWOOD: "Why do you think they wanted you?"

PETRICOIN: "I assume because of my expertise, my reputation. At no time did I give advice on FDA."

FDA ethics officials also approved Petricoin's

request to accept an honorarium to speak at a conference organized by ImClone Systems and Bristol-Myers Squibb Co. last February. Petricoin said he was unaware that it was an industry-sponsored event, even though the companies were listed on an agenda that was attached to his activity request. When he learned the companies sponsored the event, he withdrew his request, he said.

Shared Secretarial Services

Petricoin said Correlogic president and CEO Levine learned that Liotta and Petricoin were consulting with Biospect when the two scientists went to an office on Democracy Boulevard in Bethesda that provided secretarial services that, ironically, were shared by both companies.

PETRICOIN: "Mr. Levine saw us and asked what we were doing there—we weren't having a CRADA meeting."

GREENWOOD: "Why wouldn't you have volunteered that information to him?"

PETRICOIN: "I didn't see any need to. There was no overlap in my mind. Correlogic, in my mind, sir, was a software company that was using algorithms to look for hidden patterns in mass spec data, and those would be fingerprints that could be used for diagnosis. Biospect, my understanding was, was an instrument company, building a platform for protein separation. It was entirely different, and thus, in my mind, there was really no reason to talk to Mr. Levine."

GREENWOOD: "When you were first made aware of the concerns Mr. Levine had, did you consider terminating your consulting agreement with Biospect?"

PETRICOIN: "No, because I thought those concerns really related to the number of former NCI employees [involved in Biospect]…

"I think he was unhappy that Dr. Liotta and I had an outside activity that perhaps was taking away our time. My recollection of the conversation was that he expressed some question about why there were so many former NCI employees in the company."

GREENWOOD: "Why do you think he had that concern?"

PETRICOIN: "I guess he felt this was nepotism going on here. I don't know. He just said that it didn't smell right to him. I said I didn't know that that was illegal."

NCI Re-Review, Re-Approval

Anna Barker, NCI deputy director for advanced technologies and strategic partnerships, said NCI Director Andrew von Eschenbach told her in July 2003 that a consultant for Correlogic Systems was concerned about Liotta's work for Biospect, a potential competitor.

Barker asked Carl Barrett, director of the NCI Center for Cancer Research, to re-review the consulting arrangement. "At that time, the question on the table was whether there was any conflict between the outside activity and the ongoing CRADA we had with Correlogic," Barrett said.

Barrett and Maureen Wilson, the NCI ethics officer, re-approved the consulting arrangement.

Liotta's consulting agreement with Biospect states that, "Services will exclude protein microarrays, tissue microdissection, and serum proteomic pattern analysis using genetic algorithms and self-organizing maps."

Barker and Barrett testified that it appeared that Biospect's mission changed over time. "The Biospect scope is certainly expanded relative to what Dr. Liotta was led to believe the scope of that company was," Barker said. "The issue of pattern recognition was never actually a part of what Dr. Barrett actually reviewed when he re-approved this."

"At the time of the original approval and the time of re-review, there were basically three areas that I was focusing on. One was whether or not there was overlap with the official duties of Dr. Liotta—there were not," Barrett said. "In fact, the consulting agreement had very specific exclusionary language to assure that to be the case. When that was approved, that was added to the language to assure that. When I re-met with Dr. Liotta, he reaffirmed that that was true.

"The second issue was whether there was any non-public information that was being revealed, and there was not," Barrett said.

"The third issue was whether or not this influenced his performance or official duties, and in particular, this related to the CRADA. It was my discussion with Dr. Petricoin and Dr. Liotta, that, in fact, we were doing everything we possibly could to facilitate the development of the clinical trials to confirm and extend the original findings.

"The issue of direct competition between the two companies was one that was less clear in the past than it is currently," Barrett said. "So, it is really that appearance of potential conflict based on that information that has led us to be more cautionary."

Barrett said NIH officials need more clear definitions of conflict of interest. "It is very difficult in these relationships to understand how two entities might be competitors or not," he said. "We tried to do

due diligence in these circumstances and tried to define very clearly the scope of the consulting activities, yet we seem to have this appearance of conflict."

Liotta maintained that it's not clear to him whether the companies are competitors. "Even today, I have no information that that directly shows that Biospect is working in the same area that is covered by the scope of the Correlogic CRADA," he said. "In my mind, Correlogic and Biospect were completely different companies with completely different missions. It didn't seem like it would even be relative."

Liotta said he thought the situation "shows that the way the ethics system works, it produces very good results."

Barker said she was surprised at the amount of review that was done for Liotta's outside activity request. "I think there is no fault here relative to our intent to look at this carefully," she said. "I think that review worked pretty well.

"Having been in the biotechnology industry at some phase in my life, you never quite know where a company might go from where they start," Barker said.

She suggested that NIH consider a policy to have investigators "reveal who they are working for, who they might be consulting with, or what relationships they might have, and let the companies make their decisions on that basis.

"There is no downside to sharing information if in fact we can actually continue the same success rate with our CRADAs.," Barker said. "The thing we want to be careful of is that we don't make it more bureaucratic or more difficult to do a CRADA."

IG Review Of BSC Conflicts

Last year, NIH and NCI officials received a report by the HHS Inspector General on a conflict of interest allegation concerning a Board of Scientific Counselors ad hoc reviewer, according to Rep. Cliff Stearns (R-Fla.)

The report recommended that NCI "modify its process for selecting ad hoc reviewers to allow a principal investigator to object in writing to the BSC if he or she believes the selected BSC ad hoc reviewer has a conflict of interest," Stearns said.

His questions led to this exchange with NIH Deputy Director Raynard Kington:

STEARNS: "NIH intramural researchers know in advance who is on the list of ad hoc reviewers and can object if they think a reviewer has a conflict of interest. Given that intramural researchers have this right, shouldn't a private partner negotiating a CRADA with intramural researchers know if those researchers are consulting for the competition? Shouldn't the private partner have the right to know that and have the right to object to a perceived conflict of interest?"

KINGTON: "Clearly, anytime there's a situation in which the government has entered into an agreement with a private company, we have decided that's the best way to achieve a scientific goal. We should be very concerned if there is an appearance of conflict with an employee who might be involved with the competitor. So, yes, it should be something that's of concern."

STEARNS: "The intramural researcher knows this information, whereas the private partner does not. We are saying that shouldn't this private partner have this right, too, so we have transparency here. Does that make sense?"

KINGTON: "On the face of it, yes. We absolutely want our partners to have faith that we are reasonable partners, that we are actually committed to working with them. So, yes, we should be concerned about appearance of conflict of interest."

STEARNS: "So this private partner should be told, should have the right to know, and the opportunity to object to this perceived conflict of interest?"

KINGTON: "There's no question that we could do whatever's necessary to remove the possibility of a serious conflict or appearance of conflict of interest. We are committed to that."

HHS Lawyer Tells Of Pressure To Allow Award To Klausner

By Paul Goldberg

The recommendation of the NCI ethics officer was disregarded and HHS ethics attorneys were pressured to allow former NCI Director Richard Klausner to accept a prestigious prize and a check for $40,000 from the University of Pittsburgh, a Congressional panel was told earlier this week.

The extraordinary effort to clear the way for Klausner to receive the 1997 Dickson Prize in Medicine was described in testimony at the May 18 hearing of the Oversight and Investigations Subcommittee of the House Committee on Energy and Commerce.

Klausner's acceptance of that prize remains controversial not only because Pitt receives NCI funding, but also because the institution and the government were named as defendants in a law suit stemming from the firing of breast cancer researcher Bernard Fisher.

Klausner, who became the NCI director in 1995, was first selected to receive the Dickson Prize in 1996,

documents show. However, the plan for his acceptance was abandoned, since government ethics officials were concerned about conflicts stemming from the Fisher litigation.

The Fisher suit was settled in August 1997, with NCI contributing $300,000 toward its resolution, and weeks later, the Dickson award was once again offered to Klausner. This time, the NCI director was allowed to accept.

Lawmakers raised questions about Klausner's eligibility to receive the award in the first place. According to Pitt documents, the prize is given to medical professionals who had "made the most progress in the United States for the year in question."

"Although the rules for the prize state that the award should be given to the individual who made the most progress in medicine for the year in question, Dr. Klausner was honored for achievements that occurred prior to becoming director in 1995," said Rep. James Greenwood (R-Pa.), chairman of the subcommittee. "Giving the prize to Dr. Klausner in 1997 was like giving the Academy Award to a well-liked actor who didn't make any movies that year."

A spokesman for Pitt said the award to Klausner was made by an independent committee, and was proper.

"The University of Pittsburgh awarded the 1997-1998 Dickson Prize to eminent scientist Dr. Richard Klausner, a member of the National Academy of Sciences, for his contributions to furthering human health," Robert Hill, vice chancellor for public affairs, said in a statement. "Dr. Klausner was recommended for the prize--as is the case for all recipients--by a committee of medical school faculty, which reviewed his superb record of achievement in cell and molecular biology.

"The University of Pittsburgh has cooperated with the requests of the House Energy and Commerce Oversight and Investigations Subcommittee concerning NIH ethics concern," the statement said. "The evidence solicited by the subcommittee counsel and produced by the University of Pittsburgh shows clearly that there was no connection between the legal settlement with Dr. Fisher and the Dickson Prize in Medicine awarded to Dr. Klausner.

"The Dickson Prize, awarded by the University of Pittsburgh since 1970, is widely recognized for honoring the nation's outstanding leaders in science and medicine, several of whom have later won the Nobel Prize."

A Maureen Wilson Memo

Documents show that throughout the Dickson Prize controversy NCI Deputy Ethics Counselor Maureen Wilson recommended that Klausner decline the award.

In a memorandum dated Oct. 1, 1996, and addressed to Klausner, Wilson wrote:

"It is my recommendation that you decline acceptance of the award… The University of Pittsburgh is a grantee, contractor and cooperative group trial participant funded by NCI. Under these circumstances, the university is clearly a prohibited source, as defined by the Office of Government Ethics Standards of Conduct at 5 CFR 2635.203 (d).

"This is reaffirmed in the Supplemental Standards of Conduct for Employees of [HHS] issued July 30, 1996 at 5 CFR 5501.102… The NIH Manual 2300-735-4 on 'Outside Work, Financial Interests and Related Activities,' also clearly states that it is NIH policy not to accept awards from organizations, the interests of which may be affected by the performance or non-performance of the employee's official duties.

"Although you as Director, NCI, do not actually sign either grants or contracts, you are the ultimate responsible party for all of the Institute activities, unless you have disqualified yourself from matters involving a specific party. Because the Institute is currently a co-defendant with the University in a suit by Dr. Bernard Fisher, it would be inappropriate for you to be disqualified from dealing with the University of Pittsburgh.

"Therefore, it is difficult for you to accept the award in your official capacity, and it is clearly inappropriate for you to accept the award as an outside or personal activity, as the University clearly both does business with us and is seeking action from the Institute and thus, from you as its director."

The Office of Government Ethics concurred with Wilson's interpretation. "Given the current litigation involving NCI, the University and Dr. Fisher, the recent audit by NCI regarding costs charged to contracts by the University of Pittsburgh, and the fact that the University is a grantee, OGE felt that all of these were more than sufficient to indicate that the University has interests that could be affected by the performance or non-performance of duties by the Director of NCI," HHS attorney Michele Russell-Einhorn wrote in an Oct. 7, 1996, email to Wilson.

The Fisher suit was settled on Aug. 27, 1997, with a $2.7 million payment from Pitt and other entities to Fisher (**The Cancer Letter**, Sept. 5, 1997). Though Klausner was apparently involved in the settlement, his role is documented only in hand-written notes taken by

a staff member.

"Available evidence indicates that Klausner orally approved a $300,000 payment from the government as a contribution to the settlement," Greenwood said at the hearing.

After the suit was settled, the Dickson Prize Committee, which is made up of Pitt faculty members, once again recommended Klausner to receive the award. In letter dated Sept. 18, 1997, Michael Lotze, chief of surgical oncology at Pitt, wrote that "a majority of the committee were in favor of Richard Klausner, a prominent physician and scientist involved in the study of protein packaging and transport, the T-Cell receptor chains, and suppress ocomogene [sic]."

In the letter, addressed to a dean, Lotze wrote that Klausner was chosen as a result of three separate meetings in late spring and summer of 1997. Scientists that the committee rejected included Gunter Blobel, who went on to win the 1999 Nobel Prize in Physiology or Medicine. Other runners-up were: "James Allison, Floyd Bloom, James Darnell, Stephen Elledge, David Ho, Richard Horwitz, James Ihle, Mario Capecchi, Richard Kolodner, James Rothman, Erkki Ruoslahti, Robert Tjian, and Don Wiley."

"Richard Horwitz" may be a misidentification of H. Robert Horvitz, a 2002 Nobel laureate.

"I have inquired at the NCI, and it is clear that [Klausner] is capable of receiving this award," Lotze wrote.

Lotze was invited to the hearing, but was unable to appear, Greenwood said.

Another Wilson Memo

Asked to take another look at the prize, NCI Deputy Ethics Counselor Wilson once again recommended that Klausner decline.

In a memo dated Oct. 1, 1997, and addressed to Klausner, Wilson wrote that the Dickson award is paid out of interest accrued on a bequest made to Pitt, rather than by a foundation separate from the university.

"As there is no foundation, but simply a bank account, we cannot formally separate the business structure of the Dickson Foundation from the University of Pittsburgh and must look at the selection process and its level of independence from the University," she wrote. "Clearly, because the selection committee appears to be drawn from Pittsburgh staff, we cannot distinguish between the University and the Foundation."

Wilson wrote that, with approval from HHS Secretary, it would be possible to obtain a waiver that would state that Klausner's scientific work was separate from his duties as NCI director. The waiver would recognize that the award is based "on your scientific achievements and not your association with NCI," Wilson wrote.

However, the appearances of Klausner accepting the prize so soon after settlement of the Fisher suit was a concern, she wrote. "The issues created by the recent litigation are more nebulous, because they involve obligations incurred by NCI to permit Dr. Fisher's continued access to data and ability to participate in the grant/contract application/award process which, of necessity, involve the University of Pittsburgh and other grantees/contractors… Given that the litigation was only recently settled, the major issue to be overcome is the appearance that the NCI agreed to cooperate with Pittsburgh to settle the litigation, including the monetary payments as well as other tangibles and intangibles, and that this award is being made as a result of that agreement.

"It is the prerogative of the Department to authorize acceptance of the award despite this appearance…

"Realizing that we are exploring your ability to accept an award not yet made, had this question occurred at least 12 months post-settlement, a generally acceptable cooling off period, the implication that the decision to award derived from NCI's cooperation in the litigation would be of less concern," Wilson wrote.

Directive to Disregard Appearances

The hearing produced a step-by-step account of the decision by HHS officials to disregard Wilson's concerns.

"I was the one who signed that approval, and it's not a decision that I look back on with fondness and pride," said Edgar Swindell, associate general counsel for ethics at the HHS Office of the General Counsel. "I think the situation was one where I relied too uncritically on the direction and information provided to me by [HHS] General Counsel [Harriet] Rabb."

Swindell said several attorneys at HHS were assigned to evaluate Klausner's request to accept the award. Many of these attorneys voiced misgivings about the request, but ultimately, Rabb personally pressed for approval, Swindell said.

At the time, ethics lawyers at HHS were instructed to analyze such requests strictly from the legal perspective, refraining from considering appearances of impropriety.

"We and other attorneys in the Office of General Counsel at that time had been specifically instructed to provide advice and evaluate issues based upon whether

any reasonable argument could be made as to particular course of action was leally supported," Swindell said. "The view was that the decision-makers, the political appointees and other senior officials, were to be responsible and accountable themselves for the choices they made. To say 'No' to anything, the lawyers would have to demonstrate that that was the only possible answer."

In 1994, three years before Klausner award, Swindell wrote a memo to the file, which he read at the hearing:

"My supervisor indicated to me that the General Counsel instructed him to confine ethics advice to purely legal answers. We are no longer to provide observations about the wisdom of a particular actions or policies, for how things may appear on the front page of The Washington Post, for possible political ramifications. These matters are for policymakers... My supervisor, in turn, instructed me to carry out the General Counsel's wishes. He said that he had written a not to the file to document that instruction, and advised me to do the same."

"I've got the gist of it," interrupted Rep. Joe Barton (R-Tex.), chairman of the Committee on Energy and Commerce. "Basically, you are saying is that as long as at some point in the past you've written a note to the file to cover your bottom, it's okay. Whatever the guys on top tell you to do, you are going to find a way to do… As I understand that note, the direction is that even though you are the ethics division, you are not supposed to use any ethics… Is it ever ethical to just resign, or say 'I can't do that?'"

SWINDELL: "The bar rules require lawyers to provide counsel on ethics, political, social, and so forth. But they also say the client can waive those."

"Technically, the Emperor Has Clothes On…"

Swindell said the Klausner request to accept the Dickson prize caused concern among HHS lawyers.

"Do you agree with the NCI ethics advisor that there is an appearance issue to be overcome?" Greenwood asked Swindell. "And you knew that there was an appearance issue."

SWINDELL: "A number of us were concerned about the looks of that. Sure."

GREENWOOD: "As the designated ethics official for HHS, did you advise Dr. Klausner about the appearance of undue influence or conflict of interest in his accepting a $40,000 cash gift from a grantee institution involved in a lawsuit with NCI which had recently been settled?"

SWINDELL: "I didn't personally give him the advice, other than what was in the opinion."

GREENWOOD: "Did you know whether anyone said to him, 'This looks like hell'?"

SWINDELL: "The communications with Klausner were from the General Counsel..."

GREENWOOD: "In your memo to Klausner, did you address the appearance issue, or did you just address the strictly legalistic response, pursuant to what you had been instructed to do by your superiors?"

SWINDELL: "You are correct. It doesn't look like I stressed that issue with him."

GREENWOOD: "You weren't supposed to, right? Basically, you said that, technically, the emperor has clothes on, but the fact that it appeared to everybody else that he had no clothes on, you didn't bother to incorporate that in your memo."

SWINDELL: "I was in a difficult situation back then. I was new. I was an acting person…"

GREENWOOD: "Was there a reason to believe that if you didn't follow the instruction to ignore appearance issues, that that might affect you getting a permanent appointment?"

SWINDELL: "At the time, there was actual concern that the whole ethics division would be dissolved and merged into what was called the business and administrative law division."

Swindell said he was puzzled by Rabb's interest in the Klausner request.

"I do not know why this was so special," he said. "Because she wanted an answer. She was somewhat inscrutable, because she also seemed to understand that this was unseemly. But nonetheless… I don't know what her directions were."

Rep. Greg WALDEN (R-Ore.): "What makes you say that she seemed to understand that it was unseemly?"

SWINDELL: "That she would frown about the fact that he is trying to make a big deal about getting some money."

WALDEN: "Do you recall Harriett Rabb contacting you on behalf of any other official for this kind of reward? Was this just a very unique situation?"

SWINDELL: "I thought it was very unique. Yes."

Rabb could not be reached for comment.

In previous correspondence, the subcommittee raised questions about Klausner's acceptance of a $3,000 Donald Ware Waddell Award from the Arizona Cancer Center, a $4,000 lecture award from Van Andel Research Institute, and a $15,000 Block Lectureship

Award from Ohio State University (**The Cancer Letter**, July 4, 2003).

The subcommittee is also investigating Klausner's role in awarding a $40 million contract to Harvard at a time when he sought to become president of that institution (**The Cancer Letter**, Nov. 14, 2003).

Klausner, too, could not be reached for comment.

Obvious Appearance Problems

The HHS approval of the award was inappropriate, said Jack Maskell, a legislative attorney with the American Law Division of the Congressional Research Service.

"An agency of the federal government makes grants for research or clinical studies to a private laboratory or a clinic in the sum of tens of millions of dollars a year," Maskell said in his testimony. "That private laboratory or clinic then gives a cash 'award' or 'prize' of several thousand dollars to the director of the very federal agency making those grants.

"One doesn't need to have an intricately detailed knowledge of federal law and regulations on ethics to see the obvious 'appearance' problems and potentials for more serious consequences in that scenario," Maskell said. "In fact, preventing appearances of impropriety and increasing confidence in the public's perception of the fairness of the administration of federal programs is one of the principal purposes behind federal ethics regulations and laws."

The problem with this scenario reaches beyond appearances, Maskell said.

"Simply put, it appears that an agency head, with administrative and operational authority over all aspects of that agency's functions and programs, should not under federal law and regulation be accepting cash gifts, 'awards' or 'prizes' from a private grantee of his own agency, that is, a private source that is dependant upon and so interested in the official duties, responsibilities and powers of that administrator," he said. "This is particularly the case with certain private clinics and laboratories which have a continuing 'certification,' as well as a substantial and continuing grant, relationship with the agency.

"It would strain credibility to argue that a grantee regularly receiving millions of dollars in grants from a federal agency is 'detached from' or 'disinterested in' or 'independent of' the duties, powers, and responsibilities of the Director of that agency," Maskell said.

"Even when the agency head or other supervisory personnel are not directly participating in the award of a grant, or actually participating in certifying the private entity as a 'comprehensive' treatment facility, the actual authority over those subordinate employees making the decisions, the inherent influence of supervisors and agency heads over such subordinate employees, and the natural inclination of employees to want to please their superiors, all counsel against such agency heads and management personnel receiving cash awards from these private grantees under the regulation," he said.

The text of Maskell's testimony, along with other testimony submitted for the hearing is posted at http://energycommerce.house.gov/108/Hearings/05182004hearing1275/hearing.htm

Varmus Calls For Enhanced Review Of Conflicts At NIH

By Paul Goldberg

Former NIH Director Harold Varmus said that when he relaxed restrictions on outside activities by intramural researchers, he envisioned a system that would review such activities, detecting conflicts of interest.

"I lifted the restrictions as another step towards making the NIH intramural program more welcoming to outstanding scientists, with the explicit understanding that all outside activities would be carefully reviewed by ethics officers to insure that they did not interfere with the conduct of official duties," Varmus said at the May 18 hearing of the Oversight and Investigations Subcommittee of the House Committee on Energy and Commerce. "

Varmus, head of the Memorial Sloan-Kettering Cancer Center, said he agrees with most of the recommendations of a panel of experts appointed by Elias Zerhouni, his successor at NIH, appointed to study conflicts of interest.

"I believe that exclusion of senior Institute and Center personnel from consulting for industry or academia should be based on function (namely, formulation or funding of extramural programs as opposed to direction of intramural research), rather than seniority or title," Varmus said. "I also believe that exemptions should be permitted from the ban on reimbursement with equities if reviewed favorably by the trans-NIH conflict of interest committee."

Varmus said his approach to conflicts of interest has evolved over the years, and the policies he would develop today would differ from those he enacted at NIH between 1993 and 1999.

"We've heard a lot about the problems of managing this kind of outside activities, and the difficulties of appearance of conflicts," Varmus said. "I would do it somewhat differently."

The problem of conflicts and appearances of conflicts at NIH is spilling over into academia, Varmus said.

"Even those of us outside of government, in the academic sector, feel this very acutely," he said. "We've all been revising our rules, changing the ways in which we monitor our investigators, to avoid the same kind of conflicts you are worried about, because, indeed, many of our people are supported with public money received from NIH, and many of them at public institutions like state universities have other kinds of public money. So, these are major concerns."

Growth of Title 42 Program

At the hearing, Varmus acknowledged his surprise at the growth of the Title 42 program at NIH and the practice by the Institutes to bring in nearly all their new scientists and other experts under the program.

"Wasn't its origin the notion that sometimes you need to bring in specialists, for a limited period of time, to consult?" subcommittee chairman James Greenwood (R-Penn.) asked Varmus. "That's why Congress created that opportunity. It was never Congress's intent to say, all the new guys come in under Title 42."

VARMUS: "It wasn't my idea that it would be all the new guys, either. We were bringing in people to do high-level positions, who would not be tenured. They would come in for a few years, serve as experts."

GREENWOOD: "Do you have any idea how many people at NIH are under Title 42 now?"

VARMUS: "I am told it's a lot… Probably in the range of several hundred or a thousand?"

GREENWOOD: "Would you be surprised if I told you it was more like 4,000?"

VARMUS: "I am somewhat surprised, but under the circumstances, I wouldn't react to it."

GREENWOOD: "You wouldn't be shocked to know that the policy you enacted on your way out has enabled 4,000 people…

VARMIS: "I didn't enact the policy. I asked for permission to enlarge… I didn't know a lot about Title 42 to begin with, but I began to learn about it, and it looked like a reasonable mechanism for us to use in these circumstances to recruit people who were being paid very high salaries in academia."

GREENWOOD: "But the text of the law says 'special circumstances.' And when I tell you that there are 4,000 people at NIH who are now paid as 'special consultants,' does that not strike you as something run amok?"

VARMUS: "I would say the number surprises me. I wouldn't have thought it was that large."

Rep. Diana DeGette (D-Colo.) said scientists may be willing to accept lower pay and limitations on outside activities in exchange for the prestige of working for NIH.

"Dr. Varmus, when you assumed the directorship of the NIH, did you find that the Institute was populated with second-rate scientists?" DeGette asked.

VARMUS: "Yes. There were many reasons to believe that the review processes had not been stringent enough, that NIH had not been able to recruit the best people to come into these positions, and there was much reason to believe that the NIH intramural program was not held in the esteem in which in was held 10 to 20 years earlier."

DEGETTE: "Did you think that was mainly or solely because of the issue of outside compensation?"

VARMUS: "Only partly. There were many other reasons having to do with management and review processes. It's a complex situation, and we tried to deal with matters across the board… Not all the outside activities are concerned with industrial relations. In many cases this is just a matter of honoraria for talks and special publications. When I came to NIH, the whole program was under the honorarium ban. Writings, special kinds of review articles, giving lectures couldn't be compensated as they were for people on the outside."

DEGETTE: "This happens to members of Congress all the time. I get invited to speak to groups, and they might invite someone from private industry to speak, and give them a cash award. And when I go, I get a really nice plaque. We all have rooms full of them. But for me, it's the honor of going and speaking to the group. It's about the prestige of the event."

VARMUS: "As a former Presidential appointee, I feel your pain."

DEGETTE: "It's actually not painful."

VARMUS: "You have to recognize that an intramural scientist is very different from a legislator. It creates an atmosphere when people are making choices of jobs, and they can go to a place where the world seems open to them, and where very similar work is being done, at a university laboratory, for example."

Varmus's testimony is posted at http://energycommerce.house.gov/108/Hearings/05182004hearing1275/Varmus2007.htm

In Brief:

ASCO To Award $4.4 Million For Career Development

AMERICAN SOCIETY of Clinical Oncology Foundation will award more than $4.4 million to recipients of its 2004 first Advanced Clinical Research Award, Career Development Awards, and Young Investigator Awards. **Vered Stearns**, Johns Hopkins University, is the winner of the ACRA Award. Stearns will receive $450,000 paid in three annual increments of $150,000 on July 1. The winners of the CDA awards are: **Sylvia Adams**, New York University School of Medicine; **Shabbir Alibhai**, University of Toronto; **Nancy Baxter**, University of Minnesota; **Jacqueline Casillas**, University of California, Los Angeles; **Sophie Dessureault**, H. Lee Moffitt Cancer Center; **Kavita Dhodapkar**, Rockefeller University; **John Heymach**, Dana-Farber Cancer Institute; **Jennifer Ligibel**, Dana-Farber Cancer Institute; **William Matsui**, Johns Hopkins University; **Yael Mosse**, Children's Hospital of Philadelphia; **John Pagel**, Fred Hutchinson Cancer Research Center; **Michael Sawyer**, Cross Cancer Institute; **Melanie Thomas**, M.D. Anderson Cancer Center; **Martin Weiser**, Sloan-Kettering Cancer Center; **Margaret Yu**, University of Utah; CDA awardees will receive a three-year grant totaling $170,100 to test a hypothesis or accomplish intended research. The awards will be presented at the ASCO 40th Annual Meeting in New Orleans, June 5-8**.**

Funding Opportunities:

RFA Available

RFA-CA-05-018: Cancer Intervention and Surveillance Modeling Network (CISNET)

Letter of Intent Receipt Date: Sept. 14, 2004

Application Receipt Date: Oct. 14, 2004

NCI Division of Cancer Control and Population Sciences invites applications from domestic and foreign applicants for collaborative research using simulation and other modeling techniques to describe the impact of interventions (i.e., primary prevention, screening, and treatment) in population-based settings in the United States or in non-U.S. settings that will shed light on U.S. population-based trends. The primary goals of this research are: 1) to determine the impact of cancer control interventions on observed trends in incidence and/or mortality; and 2) to determine if recommended interventions are having their expected population impact by examining discrepancies between controlled cancer intervention study results and the population experience. The RFA will use the NIH U01 is a cooperative agreement award mechanism. The RFA is available at http://grants.nih.gov/grants/guide/rfa-files/RFA-CA-05-018.html.

Inquiries: Eric Feuer, Division of Cancer Control and Population Sciences, NCI, phone 301-496-5029; fax 301-480-2046; e-mail rf41u@nih.gov.

Addendum: Community Networks To Reduce Cancer Health Disparities

This is to inform applicants of the following change in RFA CA-05-012, "Community Networks to Reduce Cancer Health Disparities." The RFA states that within the phase I goals, applicants are required to "form at least four collaborations with other NCI programs (i.e., NCI Centers/Divisions/Offices other than the NCI CRCHD) to reduce cancer health disparities with other than NCI CRCHD programs. In this section, "other NCI programs" should be interpreted, in the case of NCI extramural Centers/Divisions/Offices, to mean programs (e.g., research projects, program projects, centers, networks and consortia) funded by the NCI through those Centers/Divisions/Offices.

There will be a pre-application conference on May 26, from 3-5 p.m. at Bldg.10; Lipsett Auditorium; 9000 Rockville Pike; Bethesda, MD 20892. For reservations, contact Tara Scibelli, phone 301-529-0799 or e-mail tscibelli@novaresearch.com. See the Community Networks Program Web site at http://crchd.nci.nih.gov/RFA/index.htm for updates and additional information.

Inquiries: Kenneth Chu, Center to Reduce Cancer Health Disparities, phone 301-496-8589; fax 301-435-9225; e-mail kc10d@nih.gov.

Mesothelioma Research Grants

Application deadline: Aug. 15, 2004

Mesothelioma Applied Research Foundation is accepting applications for developmental projects advancing pleural or peritoneal mesothelioma treatment. Projects may relate to benchwork or clinical research, must not be presently funded or pending review, and may be conducted through any not-for-profit academic, medical or research institution, in the U.S. or abroad. Grant amounts: $100,000 over two years.

Inquiries: Full details, review criteria and application form are posted at: www.marf.org.

Call For Nominations

AACR-Cancer Research and Prevention Foundation Award for Excellence in Cancer Prevention Research

Online nomination deadline: July 1, 2004.

AACR is accepting nominations for the award given to a scientist for seminal contributions in basic, translational, clinical, epidemiological, or behavioral science investigations in cancer prevention research. The winner will present an Award lecture at the Frontiers in Cancer Prevention Research Conference. Inquiries: For information or instructions on submitting a nomination, visit the Web site at www.aacr.org/1620.asp.

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