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Rep. Bliley Challenges FDA On Failure To Approve Oral Colon Cancer Drug UFT

Claiming that FDA's handling of the drug UFT places the agency outside the mainstream of clinical oncology, the chairman of the House Commerce Committee directed the agency to state its reasons for not approving the oral treatment for advanced colorectal cancer.

The letter from Rep. Tom Bliley (R-VA) to FDA Commissioner Jane Henney asks the agency to explain why UFT was not approved, notwithstanding a unanimous recommendation from the FDA Oncologic

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In Brief:

Five Advocates Named To SWOG Committees; NCI, NASA Sign Nanotechnology Agreement

SOUTHWEST ONCOLOGY GROUP appointed five lay advocates to its committee on Women and Special Populations and to the Disease and Disciplines Committee, after a national search. Appointed to five-year terms are: **Dale Eastman**, founder and president of the Alamo Breast Cancer Foundation and state coordinator for the Texas National Breast Cancer Coalition; **Helen Friend**, Grant/Riverside Regional Cancer Institute volunteer and former advocate on the U.S. Army Medical Research and Materiel Command 1997 Breast Cancer Research Program; **Anna Gottlieb**, Gilda's Club Seattle executive director and research project coordinator for the Women's Health Initiative at the Fred Hutchinson Research Cancer Center; **Henry Porterfield**, former chairman of the United Fund and chairman of US TOO Partners group and US TOO Initiative for Underserved and Minorities—support and education programs he initiated for prostate cancer patients and their partners; **Susan Stewart**, Blood and Bone Marrow newsletter editor and member of the NCI Director's Consumer Liaison Group. . . . **NASA AND NCI** signed a Memorandum of Understanding last week to develop new biomedical technologies that can detect, diagnose and treat disease. NASA Administrator **Daniel Goldin** and NCI Director **Richard Klausner** signed the agreement April 13 in a ceremony on Capitol Hill. The collaboration comes as NASA and NCI move forward with initiatives requiring major advances in technology. NCI is attempting to define cancer for the first time based on the unique molecular characteristics of tumors. NASA is seeking to develop a new form of patient care—"microscopic explorers"—that would travel through the human body looking for disease. This technology will allow NASA to monitor astronaut health and treat

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FDA "Outside The Mainstream" Of Oncology, Bliley Writes

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Drugs Advisory Committee.

"This pointless exercise in regulation for its own sake puts the agency outside the mainstream of clinical research and lowers its stature in the field it attempts to regulate," Bliley wrote in the letter dated April 17.

Capitol Hill sources said Bliley's challenge is unusual because Congress tends to defer to FDA on issues of science. In this letter, science emerges as the focus of the inquiry. [The text of the letter appears on page ZX.]

An investigation by **The Cancer Letter** suggests that in this controversy, FDA would be unlikely to receive much support from mainstream oncologists, including members of the agency's Oncologic Drugs Advisory Committee. Further, if the matter comes to Congressional hearings, Henney, an oncologist, may have difficulty defending the statements and actions of her subordinates.

Based on public record, UFT was not approved for two reasons. First, the agency was not convinced that the drug was truly equivalent to the Mayo Clinic Regimen of 5-FU/LV, and launched an internal effort to formulate methodology for assessing clinical trials that seek to prove equivalence. Second, the agency invoked an obscure regulation to demand that UFT sponsor Bristol-Myers Squibb demonstrate the contribution of the agent uracil to the "fixed combination" of uracil and tegafur that make up UFT.

Oncologists, including ODAC Chairman Richard Schilsky, say neither issue is relevant in the clinic:

—Equivalence standards, no matter how meticulously characterized by statisticians and drug regulators, can never provide a substitute for clinical judgment, Schilsky said to **The Cancer Letter**. "I don't think that you can have generic equivalence standards," Schilsky said. "Equivalence standards need to be individualized, based upon what the treatment is, what the disease is, and what the goals of treatment are."

—The contribution of uracil, a naturally occurring, non-toxic substance used to prolong the breakdown of 5-FU generated from tegafur, is well described in the medical literature and does not merit clinical trials, Schilsky and other clinicians said. "We know from studies of other drugs that even if you induce extremely high levels of uracil in the plasma, it has no toxic effects on patients," said Schilsky, professor and associate dean, clinical research, at the University of Chicago and chairman of Cancer and Leukemia Group B. "The amount of uracil in UFT is not even likely to influence the plasma uracil levels. So it's a non-issue."

ODAC was unanimous in its recommendation that UFT was a useful treatment for advanced colorectal cancer, and that a combination of UFT/LV was an acceptable alternative to the Mayo Clinic Regimen of 5-FU/LV, which at the time represented the standard of care in colorectal cancer.

Since that time, the recommended standard of care has changed to a combination of 5-FU/LV and CPT-11, which demonstrates a survival advantage over the Mayo Clinic Regimen (**The Cancer Letter**, March 24). However, that regimen is more toxic, which points to UFT/LV as an appropriate treatment for patients opting for a less less-toxic, more convenient treatment, colon cancer experts say.

"There are lots of understandable reasons why oncologists would use 5-FU/LV, and in those situations, if one wishes to use an oral regimen, that choice should be available," said Norman Wolmark, chairman of the National Surgical Adjuvant Breast & Bowel Project. NSABP is conducting a trial of UFT/LV for adjuvant treatment of colorectal cancer.

Richard Goldberg, chairman of the gastrointestinal oncology program at Mayo Clinic, said

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the UFT situation reminds him of The Trial, Franz Kafka's novel about the triumph of procedure over facts.

"Presumably, BMS met with FDA to determine what clinical trials needed to be done," Goldberg said to **The Cancer Letter**. "Then they successfully completed the trials, presumably met the requirements, only to be told by FDA that, in retrospect, the agency decided that the comparator arm is no longer a reasonable comparator arm. This sort of apparently capricious government policy seems Kafkaesque." Goldberg, who is also chairman of the gastrointestinal program at the North Central Cancer Treatment Group, is not involved in the development of the drug.

BMS withdrew its application for UFT on March 17, the day before the agency was obligated to issue a "not approvable" letter for the therapy. "The company elected to withdraw and resubmit these applications to afford the FDA additional time to review new analyses of existing data provided by BMS during the review process," the company said in a press release at the time.

The company resubmitted the application on April 20. Since the drug's first go-around at FDA raised profound questions about the agency's approval standards, the pharmaceutical companies are paying close attention to the outcome of Bristol's second try.

The outcome would be of immediate significance to two companies, Hoffmann-LaRoche and GlaxoWellcome, sponsors of oral equivalents of 5-FU. Both companies are comparing their drugs with the Mayo Clinic Regimen. Congress is watching, too. "FDA's hard-line regulatory position may have implications beyond this therapy," Bliley wrote in his letter to Henney. "Indeed, an argument can be made that equivalence and fixed combination standards could have relevance beyond cancer."

The agency's position on UFT is unlikely to get support from patient advocacy groups.

"Patients need treatment options, and if UFT provides viable options for some patients, we urge all involved to resolve this issue swiftly, with the needs of the patients at the forefront," said Kevin Lewis, chairman of the Colon Cancer Alliance.

Ellen Stovall, executive director of the National Coalition for Cancer Survivorship, said the controversy around UFT merits an investigation.

"Those of us advocating for expedient review and approval of safe and effective cancer therapies rely on the credibility and intellectual integrity of the scientific review processes at FDA," Stovall said to **The Cancer Letter**. "When it appears as though there has been a breach in these processes that allows the agency to thoughtlessly apply rules that may work in some contexts, but are not appropriate for the approval of oncology products, we want that investigated."

FDA officials declined to comment on the Bliley letter, citing agency policy not to discuss letters from members of Congress until those letters are answered. Richard Pazdur, director of the Division of Oncology Drug Products, declined a request for an interview. According to a spokesman, Pazdur, who conducted the pivotal trial of UFT before coming to the agency, was recused from reviewing the BMS application for the drug.

A Toxic Placebo?

At the ODAC meeting last September, the agency argued that the Mayo Clinic Regimen could be a "placebo" incapable of extending survival in advanced colorectal cancer (**The Cancer Letter**, Sept. 24, 1999).

The company's pivotal trial, which enrolled 816 patients, was designed to demonstrate statistical equivalence in survival between UFT/LV and the Mayo Clinic Regimen of 5-FU/LV.

The median survival in the Mayo Clinic regimen arm was 13.4 months, and on the UFT/LV arm survival was 12.4 months. The result favored the Mayo Clinic Regimen arm, but did not reach statistical significance. The p value was 0.391.

The hazard ratio was 0.933, with a lower bound of the 95 percent confidence interval of the hazard ratio of 0.794, which meant that in the worst-case scenario UFT/LV could be about 20 percent less efficacious than the Mayo Clinic Regimen.

However, if the Mayo Clinic Regimen has no impact on survival, then UFT could be less efficacious than a placebo. This could make UFT a "toxic placebo," the FDA medical reviewer said to ODAC.

"This goes back to the basic efficacy of 5-FU/LV in this disease, and it is felt to have no impact on survival," FDA medical officer Robert White said, answering a question from a committee member.

"If the true effect of the 5-FU/LV regimen is less than 2.68 months, then the UFT regimen may be a placebo or worse than a placebo in its effect on median survival time," White said, describing one scenario.

Though the impact of 5-FU/LV on survival in

advanced colorectal cancer cannot be shown unequivocally, "placebo" may be a poor choice of words to describe it. At least three randomized trials show a moderate survival advantage of up to six months, experts say.

"I am unimpressed with the comparison that we have just heard that UFT is a placebo or worse than a placebo," ODAC member David Kelsen, chief of the Gastrointestinal Oncology Service at Memorial Sloan-Kettering Cancer Center, said at the committee meeting. "Placebo-controlled trials regularly give a very brief median survival of about five or six months. 5-FU/LV has modest activity, and this drug has modest activity."

Richard Kaplan, the NCI Cancer Therapy Evaluation Program coordinator of colon cancer trials, agrees that it would be inappropriate to describe the Mayo Clinic Regimen as ineffective.

"The Mayo Clinic Regimen works in a minority of patients, but for that minority, it is often associated with very meaningful benefits," Kaplan said to **The Cancer Letter**. "We are talking about objective responses that have always been observed in a small proportion of patients. If 5-FU/LV is ineffective, then why did its application in an earlier setting, as an adjuvant, actually lead to an improved rate of long-term disease control? That's not a placebo effect."

NSABP Chairman Wolmark said little can be gained by questioning the efficacy of the Mayo Clinic Regimen. "It's an approved regimen," Wolmark said to **The Cancer Letter**. "If you want to go back and reassess efficacy of every regimen that's been approved, you are going to spend all your time reviewing old regimens."

From Toxic Placebo To Evaluation Criteria

The issue of activity of control is anything but moot to Robert Temple, director of the FDA Office of Drug Evaluation I, who is spearheading the internal FDA efforts to develop standards on equivalence trials.

For nearly two decades, Temple has been publishing papers on the flaws inherent in such trials. In December, at an ODAC meeting that observers immediately recognized to be about UFT, Temple addressed the issues in general:

"When you do an equivalence or a non-inferiority trial, there is always the question, did the active control drug have an effect?" Temple asked. "If it didn't, then equivalence is completely meaningless, because the equivalent, or non-inferior, drug could have no effect at all."

After a discussion of what can go wrong in equivalence trials, Temple said: "When you see a difference between treatments, and you really have very little assurance of what the active control did in this particular study… you are up a creek."

Was UFT up a creek?

"We recently reviewed flouorouracil results, and the improved survival varies from half a month to three to four months," Temple continued. "What does that mean in any given trial? Was this one where the effect was half a month, in which case the equivalence was uninformative, or was it three to four months, where the equivalence trial might be informative?

"And there isn't any way to know."

FDA recently formed an internal working group to develop the criteria for assessment of equivalence trials, a process that could involve a fundamental re-examination of approval criteria (**The Cancer Letter**, Dec. 17, 1999). Though a biostatistician's dream, the process is unlikely to satisfy clinicians.

The issue of equivalence boils down to a level of tolerance of the possibility that a new therapy could be inferior, ODAC Chairman Schilsky said to **The Cancer Letter**.

"Unless you have an enormous clinical trial, it becomes a question of how much inferiority are you willing to tolerate, and that level of tolerance is going to vary, depending on the toxicity profile of the agent and the patient population in which it would be studied.

"It's a clinical judgment," Schilsky said.

Will Patients Take Oral Drugs?

Temple's uncertainty about UFT is based partly on doubts that patients would comply with oral regimens, thereby eroding the quality of care they receive.

Thus, clicking on the final slide in his review of UFT, FDA medical reviewer White announced: "And finally, we have one last slide that is added at the request of Dr. Temple."

The slide read: "It is not clear to the FDA that an oral formulation of a cytotoxic anticancer drug is an advantage over a parenteral formulation because of the uncertainty of the amount actually taken by the patient and the narrow safety margin. This uncertainty is less important with drugs for other conditions, where the safety margin is much greater."

This argument may be a tad far-fetched, clinicians say. "This business about uncertainty

regarding the amount of drug actually taken by the patient when oral agents are used is quite curious," Goldberg said to **The Cancer Letter**. "Does that mean that we should withdraw approval for tamoxifen? My patients want a response to treatment even more than I want a response for them. Perhaps in Dr. Temple's experience in his oncology practice, he has patients with different priorities."

Temple is board-certified in internal medicine and clinical pharmacology.

"While patient compliance is an important issue, cancer patients are often active participants in their treatment decisions and are capable of complying with an oral chemo regimen," said Colon Cancer Alliance Chairman Lewis. "Decisions such as this are best left to the patient and the clinician."

The issue that finally sank UFT—the exact contribution made by uracil to the "fixed combination" capsule—was so clinically irrelevant that ODAC Chairman Schilsky apparently didn't immediately appreciate its importance.

The committee voted 12-0 in favor of approval, "if the FDA concludes the contribution of uracil to the UFT capsule to be adequately shown."

In the next question to the committee, FDA said it could consider waiving the obscure requirement if the committee decided that that UFT/LV constituted "an important therapeutic advance."

Does UFT constitute such an advance? Of course not, the committee said, voting 8-0 with four abstentions. The vote was a knee-jerk reaction on the part of the committee that repeatedly upholds survival advantage as the gold standard in colorectal cancer.

"The wording of the question was ambiguous in terms of the kind of response that it might have generated," Schilsky said. "The committee took the question at face value with respect to does this represent a therapeutic advance, meaning, does it clearly show improved efficacy? Had the question been asked in a different way, or had the committee considered the issue of therapeutic index, as opposed to just outright improvement in efficacy, the question might have been answered differently.

"I personally would have voted in favor of the question of it being a therapeutic advance," Schilsky said. "That would have been consistent with the committee's view that UFT should be approved."

FT vs. UFT; Kafka's Trial?

Since no one can recall FDA invoking the "fixed combinations" requirement in oncology, the committee could not have fully appreciated the significance of its vote.

The requirement dates back to 1975, when the agency was trying to figure out how to dispense with combinations of drugs that hit the market before Congress passed a law that required that drugs should be efficacious.

Occasionally over the years, the regulation has been applied to diuretics, analgesics, and antibiotics.

Since BMS officials declined to discuss UFT with **The Cancer Letter**, it is unclear how much data on the contribution of uracil FDA requested and how much data the company was able to provide.

In the late 1970s, when parenteral tegafur was used in the U.S., the drug was found to be excessively toxic and inferior to 5-FU. Ultimately, the drug was abandoned by Mead Johnson, a subsidiary of Bristol-Myers.

In 1983, an oral combination of tegafur and uracil was approved in Japan, where it is used widely and for many indications, BMS officials said in their presentation to ODAC.

However, it appears that randomized clinical trials, the ultimate method for assessment of the contribution of uracil to UFT, may not be an option for the company. The hypothesis for such trials would be guaranteed to underwhelm: FT would be expected to produce greater toxicity and less efficacy than UFT.

"It would be unethical, with the information that's available on tegafur and uracil, to do a clinical trial," said Robert Comis, chairman of Eastern Cooperative Oncology Group. "It's been shown that tegafur by itself is not as active as 5-FU; uracil is not active, but together there is a pharmacologic interaction which clearly shows activity.

"I don't think there is a clinical trials-oriented person in the US who would consider designing and executing a study like that."

Bliley's Letter

The excerpted text of Bliley's letter to FDA Commissioner Henney follows:

I am writing you to bring to your attention an unusual matter that appears to reflect regulatory overreach and unfairness in the drug approval process that could set a terrible precedent for drug development in the United States, and has implications for the ability of seriously ill Americans to get access to the newest therapies.

The matter concerns the FDA's regulatory position on UFT, an oral therapy for advanced colorectal cancer. On September 16-17, 1999, the FDA's Oncologic Drugs Advisory Committee recommended approval for UFT capsules in combination with leucovorin calcium tablets for the first-line treatment of metastatic colorectal cancer. The data that supported this recommendation reportedly showed acceptable therapeutic equivalence between UFT (the oral drug) with the standard of care, 5-FU/LV, an injectable drug. At an ODAC meeting last December, Robert Temple, Director of the FDA Office of Drug Evaluation I, said the FDA needed to develop standards for evaluation of such claims since approvals based on equivalence can erode standards of care. According to the March 24, 2000 Cancer Letter, "though no specific examples were mentioned at that session of ODAC, industry observers recognized veiled references to the Mayo Clinic Regimen of 5-FU/LV to which [UFT] was being compared." In two separate votes on March 16, 2000, the ODAC changed the standard of care for colorectal cancer, thus dropping the use of 5-FU/LV as a standard first-line comparator. The change in the standard of care immediately raised questions about the approval standards for UFT and the entire class of oral equivalents of 5-FU/LV. On March 17, 2000, the day the FDA was obliged to issue an "approvable" or "not approvable" letter for UFT, the company withdrew its application.

My understanding from Committee staff is as follows: The withdrawal of the application for UFT, an oral therapy for advanced colorectal cancer, was prompted by the FDA for two reasons. First, the agency was doubtful about the benefit of the Mayo Clinic Regimen to which the drug was being compared. Second, the agency was not satisfied with the quality of data on the contribution made by uracil, a naturally-occurring substance that is a component of UFT.

UFT is a drug that was eagerly expected by patients and physicians across the U.S. Though not a breakthrough therapy capable of extending survival among metastatic colon cancer patients, UFT is gentler than the proposed new standard of care, 5-FU/LV in combination with CPT-11, which was approved at the March 16 meeting of the FDA Oncologic Drugs Advisory Committee. It is also comparable in efficacy and has a more favorable safety profile than the previous standard of care, the FDA-approved Mayo Clinic Regimen of 5-FU/LV. This regimen was the accepted control when ODAC made its approvability recommendation.

UFT's main advantage is convenience. Though the therapy is likely surpassed by 5-FU/LV and CPT-11 in terms of survival, physicians and patients believe that UFT should be available to patents who are unable or unwilling to take a more toxic intravenous therapy. These patients are paying the price for the agency's actions that led the sponsor, Bristol-Myers Squibb Co., to withdraw its application for approval of the therapy. The company withdrew that application when it became clear that the FDA was about to issue a letter stating that the UFT application was "not approvable."

Based on information presented at ODAC, UFT has been tested against the Mayo Clinic Regimen in a pivotal trial involving over 800 patients, reportedly the largest registration trial ever performed in advanced colorectal cancer. The drug was found by the committee to have a favorable safety and efficacy profile. Further, UFT has been available in Japan for over two decades, a clinical experience that has generated vast safety data.

Even before the recommended standards of care for colon cancer changed from 5-FU/LV to a combination of 5-FU/LV and CPT-11, a conclusive comparison of FT and UFT would not have been feasible. Physicians would not have been sufficiently interested in the contribution on uracil to UFT to put patients on phase III clinical trials comparing FT to UFT. Besides, FT and UFT have been tested in phase II trials, and the data suggests that UFT is as active as and less toxic that FT.

Uracil plays a protective role in this therapy, and has no anticancer activity of its own. Although it would have been ideal to have unequivocal data on uracil's contribution to UFT, the question has no clinical relevance. This regulatory stance looks less like an effort to benefit colon cancer patients and more like an unthinking, insensitive demand for clinically irrelevant information. This pointless exercise in regulation for its own sake puts the agency outside the mainstream of clinical cancer research and lowers its stature in the field it attempts to regulate. No one is protected by this, and many patients—and FDA—are harmed.

Moreover, FDA's hard-line regulatory position may have implications beyond this therapy. Two other oral therapies are being developed by other sponsors for this disease. Those drugs, too, are being compared

to the Mayo Clinic Regimen. Indeed, an argument can be made that equivalence and fixed combination standards could have relevance beyond cancer.

To assist this inquiry, please provide written responses to the following questions by May 1, 2000. In addressing the following questions, please be advised that the agency's answers may be subjected to review by a panel of prominent oncologists, biostatisticians, and patient advocates.

1. Please explain why UFT was not approved, despite the unanimous vote by ODAC in favor of approval. Why was the company given a 90-day extension to provide additional data? Why was the company data provided following the ODAC vote insufficient to support approval?

2. Is it the FDA position that the Mayo Clinic Regimen, which was approved by the agency, is not effective in colon cancer?

3. What is the status of the Agency's efforts to develop equivalence standards? When will these standards by completed? Will they be made public? Will they be reviewed by physicians and biostatisticians who are external to FDA and the ODAC prior to being enforced?

4. Was the sponsor informed that company-sponsored trials of UFT would be inadequate before launching an expensive clinical development program? Please supply all records relating to minutes of meetings with the sponsor.

5. When was the last time the "fixed combination" regulations were applied to oncology? What is the history and rationale of these regulations? How much data would be required from a sponsor to demonstrate each agent's contribution to a multi-component therapy under the "fixed combination" regulations? What would be required: Pre-clinical data? Pharmacokinetics? Phase I data? Phase II data? Side-by-side trials? Please supply answers that would address these questions in general terms and specifically for UFT. Why wasn't ODAC asked about the standards for demonstrating the contribution of uracil under the "fixed combination" regulations?

6. Would efforts to define the contribution of uracil to UFT have any clinical value?

7. What is the nature of Robert Temple's expertise on oncology? How many oncology patients has he treated and how recently?

8. All records relating to communications to and from Robert Temple relating to the development of standards for evaluation for claims based on equivalence since January 1, 1999.

Funding Opportunities:

IRB Protocol Approval Not Required Prior To NIH Review

NIH has revised its policy for IRB review of human subjects protocols in grant applications by no longer requiring prior IRB approval preceding NIH peer review.

The revised policy will begin with applications submitted for the January 2001 council funding round—applications submitted for the June/July 2000 receipt dates.

The change in NIH policy, provided only to IRBs at this time, is intended to give institutions the flexibility to reduce the workload burdens that many IRBs are currently facing. However, the institution may still determine that certain lines of research or mechanisms of research should receive IRB review prior to submission of the application.

Due to PHS policy language, applications including research with animals will continue to require review by the Institutional Animal Care and Use Committee at the time of submission or within 60 days thereafter.

NCI Program Announcement

PA: Geographic-based Research in Cancer Control and Epidemiology

The goal of the program announcement is to promote epidemiologic research to pursue questions that emerge from the recently-released Atlas of Cancer Mortality in the United States, 1950-94, located at the following website address: http://www.nci.nih.gov/atlas. Applicants also are encouraged to use Geographic Information Systems for epidemiologic behavioral research, cancer surveillance and cancer control surveillance research, to facilitate the integration of appropriate types and levels of data in program planning, implementation and evaluation, and to develop GIS methodology in support of these applications.

Inquiries:Burdette Erickson, program director, Biometry/SBIR/STTR, DCCPS, NCI, NIH, phone 301-435-4913; e-mail: be13u@nih.gov

In Brief:

ASA Honors Bernard Fisher With Surgeons' Highest Award

(Continued from page 1)

conditions in space. . . . **BERNARD FISHER**, University of Pittsburgh Distinguished Service Professor, scientific director of the National Surgical Adjuvant Breast and Bowel Project and its former chairman and a founding member, was awarded the American Surgical Association Medallion for Scientific Achievement. Fisher, whose pioneering breast cancer studies changed the way in which breast cancer is managed, becomes one of only 14 individuals to receive the highest honor bestowed by the ASA in 120 years. . . **RAYMOND DUBOIS**, Mina Cobb Wallace Professor of Gastroenterology and Cancer Prevention, director of gastroenterology and associate director for cancer prevention in the Vanderbilt-Ingram Cancer Center, received the Outstanding Investigator Award in clinical science from the American Federation for Medical Research. The award recognizes his work on the enzyme cyclooxygenase-2 in colon cancer, which paved the way for the testing of new drugs that selectively target COX-2 for chemoprevention in humans. DuBois is a national co-investigator of a trial to test one of the new selective COX-2 inhibitors, celecoxib. . . . **NIH OFFICE** of Research on Minority Health launched a new web site to offer the public and scientific community information about ITS Minority Health Initiative. The MHI multi-year program supports biomedical and behavioral research into health improvement for minorities and for research training programs aimed at increasing minority representation in biomedical and behavioral research. For access to the ORMH web site: http://www1.od.nih.gov/ormh. . . . **DAVID BEACH** and **CHARLES SHERR** shared the Bristol Myers-Squibb Award for Distinguished Achievement in Cancer Research and its $50,000 prize. Beach, founder and director of Mitoxis Inc., founder and president of Genetica Inc. and Wolfson Chair at the Hugh and Catherine Stevenson Institute in London, is best known for his discovery of the regulatory role of cyclins in the cell division cycle. Sherr, chairman of the department of tumor cell biology at St. Jude's Children's Research Hospital and a Howard Hughes Medical Institute Investigator, is recognized for his contributions to the mechanisms of cell growth control and neoplastic transformation, particularly as they pertain to the mammalian cell division cycle. . . . **NATIONAL SCIENCE** and Technology Council released a report, "Ensuring a Strong U.S. Scientific, Technical, and Engineering Workforce in the 21st Century." Although the U.S. has enjoyed a leadership position due to its ability to attract foreign nationals to its high-tech workforce, the growing economic role of science, technology, and engineering has increased the need for workers from within the U.S., the report said. "If current trends persist, our nation may begin to fall far short of the talent needed to spur the innovation process that has given America such a strong economy and high quality of life," the report said. To draw all population groups into the high-tech workforce, human resource policies must "ensure that our scientific and technical workplace reflects the face of America," the report said. The report is available at http://www.whitehouse.gov/WH/EOP/OSTP/html/workforcerpt.html. . . . **NATIONAL COMPREHENSIVE** Cancer Network and American Cancer Society have issued "Colon and Rectal Cancer Treatment Guidelines for Patients." For a copy phone 800-ACS-2345 or 888-909-NCCN; or visit web sites http://www.cancer.org and http://www.nccn.org . . . . **MOLECULAR TARGET LABORATORY** pre-solicitation conference at the Doubletree Hotel in Rockville, MD, has been rescheduled to May 18, from 1-5 pm. For a draft solicitation contact Heather Wells phone 301-846-1520; fax: 301-846-5414. . . . **HHS SECRETARY DONNA SHALALA** made the following statement earlier this week regarding R.J. Reynolds' new product, Eclipse: "We have significant concerns about the marketing plans R.J. Reynolds is announcing for its new product, Eclipse. It is not at all clear that a sufficient science base exists to support a bold claim that this tobacco product may reduce the risk of cancer. Nor is it clear what advice doctors should give their smoking patients who wonder if they should switch to a product like Eclipse. What we do know is that cigarettes and other tobacco products in any form are unsafe, dangerous, and cause great pain, suffering and death. We know that Congress has it within its power to pass legislation to give FDA clear jurisdiction over tobacco products. But we need to know much more about the extent of any reduction in exposure to toxins, and whether this actually reduces the overall risk of smoking in a meaningful way. Until then, smokers should be very careful about assuming that products like Eclipse are in any way safer than cigarettes."

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