THE CANCER LETTER

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*News Analysis:*

## NCI's Use Of Dialogue For NBN Blueprint Raises Legal, Procedural Questions

In a column published recently on the NCI Web site, Institute Director Andrew von Eschenbach announced that a plan for a national tissue bank had been posted for "public comment."

"The NBN Blueprint, developed through the National Dialogue on Cancer's Cancer Research Team in collaboration with NCI, is currently available for public comment on the National Dialogue on Cancer Web site," von Eschenbach wrote in his "Director's Update" Nov. 18.

Under ordinary circumstances, it is laudable for federal agencies to

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*In Brief:*

## Stillman Named President, Cold Spring Harbor, Watson Is Chancellor; Pollin Prize Honors Four

**BRUCE STILLMAN**, director of Cold Spring Harbor Laboratory since 1994, was named president and CEO, replacing **James Watson**. Watson was named chancellor of CSHL. Stillman has been director of the cancer center at CSHL since 1992, a position he still holds. In 1994, Stillman succeeded Watson as director. . . . **POLLIN PRIZE** in Pediatric Research will be presented to four senior investigators for lifetime achievement in pediatric biomedical research on Dec. 19, in New York. The winners are **Emil Frei,** physician-in-chief emeritus, Dana-Farber Cancer Institute; **Emil Freireich,** director, Adult Leukemia Research Program, M.D. Anderson Cancer Center; **Donald Pinkel,** professor of pediatrics, University of Southern California; and **James Holland**, Distinguished Professor of Neoplastic Diseases, Mount Sinai School of Medicine. The award, given by Irene and Abe Pollin, of Chevy Chase, Md., and administered by the New York-Presbyterian Hospital, consists of a $100,000 award to the recipients and a $100,000 fellowship stipend to be assigned by the recipients to a young investigator at one of their institutions. . . . **CHRISTOPHER WILLETT** was named chairman of the Department of Radiation Oncology at Duke University Medical Center, effective March 1. Willett is clinical director of radiation oncology at Massachusetts General Hospital and professor of radiation oncology at Harvard Medical School. He succeeds **Edward Halperin**, who was named vice dean at Duke University School of Medicine and associate vice chancellor for academic affairs, Duke University Medical Center. **Leonard Prosnitz**, has been interim acting chairman. . . . **LARRY**

(Continued to page 8)



### The Cancer Letter Takes Winter Break

This issue of **The Cancer Letter** is the final publication for the year. The next issue, Vol. 30 No. 1, is scheduled for publication on Jan. 2, 2004.

**The Cancer Letter** is published 46 times a year, with publication breaks in August and December.

## NBN Proposal Shows Dialogue Functions As Advisory Group

(Continued from page 1)

seek public comment. Yet, in this case, von Eschenbach's discussion of the controversial, multi-million-dollar National Biospecimen Network warrants a close reading.

Why was a proposal that was largely funded by the Institute and that involves commitment of millions of taxpayers' dollars be posted on the site of the Dialogue, a non-profit group?

It would be difficult to argue that the Dialogue is an impartial third party. Heavily funded by pharmaceutical companies, the group is vying to operate the proposed public-private project. Von Eschenbach is an interested party, too. In addition to running the Institute, he serves as vice chairman of the Dialogue's board of directors.

More than money is at stake in discussion of the proposed NBN. Skeptics say the development of the network could harm existing tissue banks just as genomic techniques are making it possible to analyze the specimens collected over three decades.

As the Dialogue fields comments on the NBN proposal, NCI appears to be putting it into action. Last month, the Institute proposed changing the method of funding the groups' tissue banks from grants to contracts. Institute officials describe this as an effort to give more money to the cash-starved groups, but insiders see this offer as a Trojan horse, a plan to use the leverage of government contracts to assert control over tissue resources and the intellectual property of the groups. This would be consistent with recommendations in the NBN blueprint.

"I don't have a view about the basic issue—whether or not it's better to have the national tissue bank or tissue banks operated by cooperative groups—but I think that such an important issue with respect to spending federal funds would be of interest to Congress," said Jeffrey Lubbers, professor of administrative law at American University's Washington College of Law.

Lubbers said the Dialogue seems to be functioning as an advisory committee to NCI, and, therefore, its work should be subject to open meetings requirements.

"It appears that there is a very close relationship between the National Dialogue on Cancer and NCI," Lubbers said to **The Cancer Letter**. "It appears that NCI is looking for recommendations from the Dialogue on issues related to tissue banking. The fact that the head of NCI is the vice chairman of the board of the Dialogue seems to be an indication that NCI is likely to rely on the recommendations of the group.

"Therefore, it appears that the Dialogue fits within the definition of an advisory committee under the Federal Advisory Committee Act, because it is a group with outside members that is being relied upon to render specific advice and recommendations to a federal agency. If that's the case, then its operations have to be open, and the documents it uses to make the recommendations have to be made available to the public."

### More Than a Simple Collaboration

The NBN blueprint wasn't the only document posted for "public comment" by the Dialogue. The organization also published the results of an NCI-funded study that serves as the foundation of the proposal.

"The Blueprint development process was informed by a second report, 'Case Studies of Existing Human Tissue Repositories: Best Practices for a Biospecimen Resource for the Genomic and Proteomic Era,' prepared by the RAND Corp.," von Eschenbach wrote. "A pre-publication version of this second report is also available from the NDC Web site."

The NCI director didn't mention that the Institute

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**Editor & Publisher:** Kirsten Boyd Goldberg
**Editor:** Paul Goldberg
**Editorial Assistant:** Shelley Whitmore Wolfe

**Editorial: 202-362-1809 Fax: 202-318-4030**
**PO Box 9905, Washington DC 20016**
E-mail: news@cancerletter.com

**Customer Service: 800-513-7042**
**PO Box 40724, Nashville TN 37204-0724**
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funded the RAND study through a sole-source contract, a rare practice at NIH (**The Cancer Letter**, Aug. 8).

Publishing a study on the Web site of a non-profit group where the director of the funding institution happens to serve as an officer is not a common practice in the government.

"Ordinarily, one would expect to see, at a minimum, some disclaimer that addresses this possible appearance of a conflict to mitigate the chance that a member of the public could get the otherwise apparently reasonable impression that there is a government approval or government sponsorship involved," said Michael Clark, an attorney with the Houston law firm of Hamel Bowers & Clark. "One would expect to have members of a federal government agency affirmatively disclosing any financial or otherwise potentially important interests that they may have with an entity, to avoid, at a minimum, the appearance of impropriety."

John Engel, an attorney with the Washington firm of Engel and Novitt, said the partnership between NCI and the Dialogue appears to be more than an ordinary collaboration.

"NCI appears to have played a pivotal role in developing the blueprint," Engel said. "The apparent depth of NCI support for the blueprint and the dynamic nature of the Institute's involvement in its development suggest that the blueprint represents as much in the way of NCI recommendations as it does proposals of the NDC. "

The RAND study and the NBN blueprint would be open for "public comment" for about six weeks, von Eschenbach wrote. "The public comment period for both reports will last until Dec. 31, 2003, and a summary of comments received will be posted on the NDC Web site," he wrote.

Von Eschenbach's use of the words "public comment" to describe the posting may raise some eyebrows.

In the federal government, "public comment" signifies publication of materials in the Federal Register or in the NIH Guide to create administrative record that accompanies rulemaking or to ensure compliance with the open meetings requirements. A non-profit organization like the Dialogue is free to present its documents for "comment" from the public, but referring to this as "public comment" may create an appearance of openness for a closed process.

Von Eschenbach's decision to provide a link from his column to the Dialogue Web site was unusual, too. Though this violates no law, federal agencies rarely link to sites outside the government, mostly out concern about creating an appearance of favoring some organizations over others.

**Loose Use of Language?**

Lubbers said NCI should not rely on the Dialogue to respond to comment.

"I am all in favor of public comment, but I would hope that NCI would react and respond to the public comment itself," he said.

Von Eschenbach's reference to "public comment" is puzzling, lawyers say.

"The concept of the Administrative Procedure Act and its core notice-and-comment requirements was to provide a meaningful proxy for entities in the executive branch of government to use, so that members of the regulated community that will be required to adhere to the rulemaking will have a chance to voice their concerns and to suggest necessary changes that should be made," said Clark, a former federal prosecutor.

"Only after this is done can any rulemaking be said to have provided basic protections of fairness and openness in government," Clark said.

It is unclear why anyone, least of all a public official, would misuse these words, Engel said.

"Under these circumstances, it is unclear what the purpose is of noting the availability of the blueprint from the NDC for 'public comment,' and of linking to the NDC website from the NCI Web site," Engel said. "Is it intended to somehow suggest that the traditional avenues for public notice and opportunity for comment are being followed? Certainly, neither NCI nor its attorneys would suggest that it comports with the notice-and-comment standards governing agency actions under the APA."

This is not the first time the Dialogue borrowed the language of the federal government to describe its procedures. In 1999, the organization spun off the National Cancer Legislation Advisory Committee, which was unlike any other advisory committee in the federal government.

The committee had no charter, was funded by ACS, met behind closed doors, and was advisory to Sen. Dianne Feinstein (D-Calif.), who is also the vice chairman of the Dialogue (**The Cancer Letter**, Jan. 21, 2000). After that committee concluded its work, the resulting "white paper" was posted for what was described as "public comment" on a privately-owned cancer information Web site.

**Dialogue Vies For NBN**

A member of the public who chooses to comment on the NBN blueprint would do well to start reading on page 88, where the report suggests the Dialogue as a candidate for running the mega-project. The same suggestion appears on page 97.

Begun by the American Cancer Society in an apparent bid to place itself in a leading role in cancer politics, the Dialogue is funded primarily by the Atlanta-based society and by the pharmaceutical industry. According to internal documents, ACS committed $5 million to the organization. AstraZeneca, Aventis Oncology, Bristol-Myers Squibb, GlaxoSmithKline and Pharmacia contributed $1.5 million each, and Novartis pledged $1 million. The American Legacy Foundation, an anti-tobacco group funded through tobacco industry's settlements with state attorneys general, contributed $3 million, primarily in order to stoke the Dialogue's interest in tobacco control, foundation officials said.

Proponents of NBN argue that a new, uniform system of tumor collection is needed to give scientists relatively easy access to tissues in order to analyze tumors on the molecular level. NBN is controversial in part because it is being proposed less than a year after NCI refused to provide additional grant funding to the cooperative group tissue banks, and one month after the Institute proposed that tissue bank funding be changed to contracts.

The groups started collecting tissue in the 1970s. Since samples are collected as part of clinical trials, it is possible to correlate tissues with outcomes observed in prospectively designed experiments.

Unlike the groups, NBN seeks to collect tissue outside clinical trials and follow the donors, possibly for the rest of their lives. While tissue preservation techniques in this system would likely be consistent with today's standards, the rigor of monitoring treatments and measurement of outcomes would not match that of samples collected by the groups.

"Statistical significance is not our goal," Paula Kim, co-chairman of the NBN development committee explained in an interview earlier this year. "What we are talking about here in the NBN is developing a resource [for] the researchers, so they could do their research, a resource that will have tissue, and ultimately, it will be a resource that will have tissue and data (**The Cancer Letter,** Aug. 8)

Kim, who is also head of the Pancreatic Cancer Action Network, a non-profit group, and secretary of the board of the Dialogue, co-chaired the NBN committee with Jeffrey Trent, president and scientific director of the Translational Genomics Research Institute in Phoenix, Arizona.

Tissues collected over the years by the cooperative groups are becoming extraordinarily valuable as genomic analysis is making it possible to reanalyze them on the molecular level. For example, in a study reported last week, Genomic Health, a biotechnology firm, and the National Surgical Adjuvant Breast & Bowel Project, a cooperative group, used pathology samples collected between 1982 and 1988 in the NSABP B-14 clinical trial to develop a prognostic index for breast cancer.

NSABP and Genomic Health designed a blinded, prospective validation using surgical tissue samples from 668 patients, who were node-negative, estrogen receptor positive, and treated with tamoxifen.

Using RNA analysis, the study evaluated Genomic Health's breast cancer assay to determine the likelihood of breast cancer recurrence as defined by a recurrence score. The recurrence score was able to accurately assign patients into high and low risk groups.

"This trial represents a practical advance in breast cancer diagnosis because the assay uses tumor tissue that is routinely obtained and stored for every patient," NSABP chairman Norman Wolmark said in a statement. "Based on our studies, the recurrence score becomes as important a prognostic measure for this group of node-negative patients as nodal status is for all patients."

These results were presented at the San Antonio Breast Cancer Symposium Dec. 4.

**"Legacy Systems" To "Existing Resources"**

The published version of the NBN blueprint differs significantly from a confidential final draft obtained by **The Cancer Letter** last summer.

In the earlier version, the report referred to existing tissue banks as "legacy systems." This has been changed to less pejorative "existing resources." The cost estimate for operating the proposed system has been reduced by the factor of about 25. Also, the published version of the plan includes a provision for a three-year pilot project.

The choice of words "legacy systems" could not have been an accidental slip. This term appeared 29 times in the draft report. Also, Anna Barker, NCI Deputy Director for Strategic Scientific Initiatives, used this phrase in a presentation to the NCI Board of Scientific Advisors earlier this year (**The Cancer**

**Letter**, July 11). Barker is also a Dialogue board member and the point person for both organizations in development of NBN.

In the environment of von Eschenbach's NCI, insiders interpreted this choice of words as an expression of the Institute director's low opinion of the cooperative groups. Von Eschenbach's funding priorities and statements give credence to this interpretation.

The Institute leadership withheld a scheduled 3 percent funding increase to the groups last fiscal year, and plans to begin a top-to-bottom study of the clinical trials system, even though a study completed in 1997 recommended increasing funding for the groups.

Insiders say that in discussions, von Eschenbach has been known to accuse the groups of conducting clinical trials of trivial significance, referring to such experiments as "Coke vs. Pepsi" (**The Cancer Letter**, June 27.)

In his stump speech, the director describes his strategy for battling cancer as "ready, fire, steer," which he distinguishes from "ready, aim, fire," a strategy that he says is "unfortunately, too often, 'ready, aim, aim, aim, and then fire.'" (**The Cancer Letter**, Oct. 31).

Since von Eschenbach is a man in a hurry—he has taken a vow to end "suffering and death from cancer" by the year 2015, alas, without presenting a detailed plan for reaching this goal—at least on the rhetorical level he does not seem to approve of aiming.

**Cost Deflation: $1.25 Billion To $50 Million**

The writers of the draft version of the blueprint appeared to take pride in describing the project's gigantic scale and enormous cost.

"It is more like the space station or a particle accelerator than a traditional medical science initiative," the report stated in its draft version. At that time, operating costs—excluding initial investment and the cost of analysis of biospecimens—could reach $1.25 billion a year, the draft report estimated. This was simple arithmetic: it costs $2,000 to $5,000 to track a specimen.

"Even using the low estimate, tracking 250,000 samples is expected to cost $0.5 billion per year." According to the draft, NIH spent about $53 million on tissue banks today.

Compare this jarring estimate—an equivalent of about a quarter of the NCI budget—with the relatively tame numbers that appear in the published version of the report:

"Determining the precise cost per specimen is difficult since there are many complexities. Providing 250,000 samples at $200 each would have an annual cost of $50 million (exclusive of start-up costs). The cost would, of course, scale if the marginal cost of specimens were greater than $200. By comparison, approximately $40 million is allocated currently by the NIH to extramural programs for `tissue banks.'"

The report section describing participation of for-profit companies was extensively revised. The draft contained this description of commercial opportunities:

"The inclusion of for-profit partners in the collaborative model has been seen in the past as a challenge. The prevailing thought is that patients only want their samples to be used as a public service, as opposed to generating profit. However, studies have shown that patients are happy to donate their tissues for research in general, even if it is to a for-profit company. If new drugs are to be developed, commercial entities (pharmaceutical and biotech companies) must be allowed to make a profit from their investments."

This language didn't survive the final cut, but the opportunities for collaboration for companies are noted in the new draft:

"As the NBN provides pre-competitive access to specimens and data and takes no intellectual property position relative to findings from research using the specimens, users' ability to retain intellectual property rights should enhance participation," the published version of the report states. "It is probably unrealistic to expect the NBN to be self-sustaining for several years, if at all. Institutions and individuals that benefit from this system would be expected to help support it financially, either directly or in-kind."

Under the existing system, the groups retain intellectual property rights to their data.

**The Question of Authorship**

The published version of the blueprint doesn't reflect the authorship as clearly as the draft.

Instead of listing all the individuals involved in preparing the NBN blueprint, the report offers extensive acknowledgments and lists the participants of a design team meeting held last July.

The draft report was more informative. It contained an appendix that listed the names of "ad hoc" advisors who worked in groups that designed specific sections of the blueprint.

The crucial "business plan and operations" group included three participants and two staff members

of Constella Health Sciences, a company that put together the proposal under a contract with NCI and the Dialogue.

The three ad hoc advisors include two NCI staff members: Roger Aamodt, chief of resources development branch at the Cancer Diagnosis Program, and Peter Covitz, director of core infrastructure at the Center for Bioinformatics.

The third person on the three-member team was Anthony Dennis, president of Omeris Inc., a Columbus, Ohio, based technology transfer organization funded partly by the state. Dennis is married to the NCI and Dialogue official Barker.

In December 2002, months before the draft report of the NBN was completed, Dennis filed a letter of intent to seek $8 million in Ohio state funds for creation of a "National Oncology Tissue Repository and Genetic/Proteomic Database."

Listing himself as the principal investigator of the project, Dennis described a venture that would include NCI, the Dialogue, and the International Genomics Consortium, an Arizona-based entity founded by Trent, co-chairman of the Dialogue working group that designed NBN. Other participants were to include Ohio State University, Proctor & Gamble Pharmaceuticals, Roche and Eli Lilly.

Last August, in a written response to questions from **The Cancer Letter**, Dennis confirmed that he took part in designing NBN. He said the letter of intent was submitted as a "placeholder," and no final application was filed.

"We elected not to follow up on this letter of intent with a formal proposal, as our existing and long-standing tissue resources and clinical centers were sufficiently advanced that we felt that the desired outcomes would emerge without further organization," Dennis said at the time (**The Cancer Letter**, Aug. 8).

The published version of the NBN Blueprint doesn't acknowledge Dennis's contribution, and his name doesn't figure in the report.

**Pilot Project Proposes Contract Funding**

The NBN Blueprint recommends a three-year demonstration project that, according to the document, would cost between $15 million and $20 million.

"The demonstration project should be able to perform the basic functions of the NBN, address specific challenges discussed in this Blueprint report, and meet performance characteristics to evaluate success," the document states. "In addition, the demonstration project should be capable of quickly expanding to operate on a national scale."

Attorney Engel said it would be shortsighted for NCI to attempt to implement the NBN plan.

"If the NDC blueprint were somehow to be transmogrified into a formal NCI policy and effectively presented as a *fait accompli*—a result that some might perceive as having been presaged by the Institute's integral role in its development—the NCI and NIH attorneys undoubtedly would want to take all necessary steps to provide all parties affected by any such 'adoption' of the blueprint with a meaningful opportunity to participate in that NCI policymaking process," Engel said.

"Particularly in light of the potential impact of such action on existing repositories like the cooperative group tissue banks, it would seem that the government's attorneys would want to be particularly vigilant to these fundamental procedural requirements to ensure that any such action by NCI could withstand legal scrutiny based upon reasoned consideration of an administrative record compiled by the Institute," he said.

Nonetheless, implementation of the plan has begun.

Last month, the Institute proposed switching the cooperative group tissue banks to the contract mechanism, a change consistent with the NBN recommendation for starting a pilot project for the network.

"As a starting point, the NBN Design Team considered strengths in existing NCI resources in tissue collection and bioinformatics, and expertise in patient privacy issues," the NBN report states. "In addition, the expertise of private sector entities in establishing business operations and systems to collect, process, and distribute biospecimens to the research community is also valued. The Design Team considered and recommended a business model for the demonstration project that included the use of contracting mechanisms to build on these existing resources."

The NCI proposal to the Board of Scientific Advisors mentioned the NBN blueprint. BSA members came to the defense of the groups, chastising Institute officials for failure to discuss the plan with group chairmen before presenting it to BSA (**The Cancer Letter**, Nov. 21).

"You need input from the people who are currently doing the work," BSA member Thomas Curran said at the meeting. "Maybe we can learn

from their wisdom, and maybe export some of the ideas they have developed."

The board sent the proposal back to the NCI Executive Committee to reconsider the funding mechanism. NCI will discuss the plan with the chairmen of the cooperative groups on Dec. 12.

**New Name For Dialogue?**

The National Dialogue on Cancer was designed by Shandwick International, a public relations firm which has since merged into Weber Shandwick Worldwide.

Working for the American Cancer Society, Shandwick put together a plan for development of an overarching cancer agenda.

The Dialogue is a dream project for a PR firm, an opportunity to tap into a pack of multi-billion-dollar industries, including health care, pharmaceuticals and food. Unfortunately, the PR firms involved have been unable to steer away from another multi-billion-dollar industry: tobacco.

Initially, Shandwick and ACS recruited former President George Bush and Feinstein to lead this effort. Yet, soon after the Dialogue began its work, **The Cancer Letter** reported that Shandwick also represented R.J. Reynolds Tobacco Holdings Inc. As a result of that disclosure in January 2000, the society fired Shandwick.

Tobacco industry documents released earlier this year show that at the time Shandwick was designing the Dialogue for ACS, it was also helping British American Tobacco in its effort to thwart the World Health Organization's Framework Convention on Tobacco Control. This was accomplished through the "social reporting process," which bears striking resemblance to the Dialogue (**The Cancer Letter**, July 25).

Setbacks notwithstanding, the Dialogue continued, holding meetings behind closed doors at Washington hotels, at the George Bush Presidential Library and Museum, and at the Bush family compound in Kennebunkport. After George W. Bush became President, he appointed von Eschenbach, a urologist at M.D. Anderson Cancer Center and one of the Dialogue founders, to lead NCI.

Now, the Dialogue's public relations are handled by Edelman, a firm that also represents food companies, and through international affiliates, tobacco companies. Last summer, **The Cancer Letter** reported that Edelman also represented BAT Malaysia, where it promoted social reporting, the process designed by Shandwick. Responding to the news report, the company dropped that client.

Edelman has been involved in the NBN proposal, too. The names of the firm's employees appeared alongside the names of NCI employees on press releases announcing the tissue banking initiative (**The Cancer Letter**, July 25).

Recently, internal Dialogue communications indicated that the organization is considering changing its name. Documents filed with the U.S. Patent and Trademark Office show that the Dialogue has filed an application to trademark C-CHANGE.

C-CHANGE would provide "association services, namely promoting the public interest and awareness in cancer research, prevention, detection and clinical trials, access to quality cancer care and state cancer plans," the Dialogue' application states.

The history of the Dialogue and its connection to von Eschenbach's 2015 goal are traced in two special reports available at www.cancerletter.com.

Von Eschenbach's "Director's Update" is available at www.cancer.gov/directorscorner/directorsupdate-11-18-2003. The NBN blueprint is available at www.ndoc.org.

*Obituary:*

## Joyce LeMaistre, 71, Wife Of Former M.D. Anderson Head

Joyce LeMaistre, the wife of retired M.D. Anderson Cancer Center president Charles A. "Mickey" LeMaistre, died Dec. 5 in San Antonio from complications caused by cancer. She was 71.

LeMaistre was well-known in Houston during her husband's 18-year tenure as M.D. Anderson president from 1978 to 1996. On his retirement, the University of Texas System Board of Regents issued a resolution of appreciation to her.

She is survived by her husband of 51 years, sons Charles F. "Fred" LeMaistre, of San Antonio, and William LeMaistre, of Fort Worth; daughters Joyce Anne LeMaistre and Helen Meyer, of San Antonio; and brother, Dewey Trapp, of Aliceville, Ala.

## NCI Contract Awards

Title: NCI SEER Program. Contractors: $21,268,854 Connecticut; $16,222,050 Emory; $32,519,107 Northern California Cancer Center; $13,624,072 Univ. of Hawaii; $18,217,304 Univ. of New Mexico; $40,535,164 Univ. of Southern California; $10,833,704 Univ. of Utah; $23,564,038 Fred Hutchinson Cancer Research Center; $39,915,140 Iowa; $37,883,095 Wayne State Univ.

*In Brief:*

## ASTRO Opens DC Office; UCLA, Drew Win NCI Grant

(Continued from page 1)

**SCHAAF** was named director of the Clinical Treatment Unit at Arthur G. James Cancer Hospital and Richard J. Solove Research Institute. He was director of oncology, clinical pharmacology, for Pharmacia Corp. and held the same title at Pfizer Corp. before joining Ohio State Univ. . . . **AMERICAN SOCIETY** of Therapeutic Radiology and Oncology has opened a satellite office at 1101 Pennsylvania Avenue NW, in Washington, D.C. . . . **UCLA JONSSON CANCER CENTER** and **Charles R. Drew University of Medicine and Science** formed a partnership to study the burden of cancer on the working poor and minority communities of South Central Los Angeles, funded in part by a two-year, $500,000 grant from NCI, said Jonsson Director **Judith Gasson**. . . . **LEUKEMIA & LYMPHOMA Society** presented the Stohlman Scholar Award for blood cancer research to: **Alan Friedman**, associate professor, Johns Hopkins Univ.; **Warren Pear**, associate professor of pathology and laboratory medicine, Univ. of Pennsylvania; **Edward Scott**, director, Stem Cell Biology and Regenerative Medicine Program, Florida Shands Cancer Center; **Richard Van Etten**, professor of medicine and director of hematologic malignancies, Molecular Oncology Research Institute, Tufts-New England Medical Center; **Dong-Er Zhang**, associate professor, Scripps Research Institute. . . . **GERALD KEUSCH**, director, Fogarty International Center and NIH associate director for international research, accepted the positions of assistant provost for global health at Boston Univ. Medical Campus and associate dean for global health at Boston Univ. School of Public Health. **Sharon Hrynkow**, deputy director of FIC since 2000, will serve as acting director. . . . **TUSKEGEE UNIV.** was awarded a $14 million NIH grant for its National Center for Bioethics in Research and Health Care. The grant will provide research and teaching facilities. . . **SCP COMMUNICATIONS INC.** sold its publishing subsidiaries Cliggott Publishing and The Oncology Group to United Business Media. The Oncology Group, formerly PRR, publishes ONCOLOGY and Oncology News International. UBM paid $37.5 million in cash. The sale was handled by Berkery, Noyes & Co. LLC.

THE CANCER LETTER

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# Business & Regulatory Report

*Clinical Trials:*

## FDA Lifts Clinical Hold On Phase III Trials Of Oncophage Vaccine By Antigenics

**Antigenics Inc.** (NASDAQ:AGEN) of New York said FDA has lifted the partial clinical hold on its two phase III trials of the cancer vaccine Oncophage (HSPPC-96).

The decision to lift the hold comes 13 weeks after a request for product characterization information in September 2003, the company said.

Antigenics will resume patient enrollment in the trial, the company said.

FDA had placed two Antigenics studies on partial clinical hold to

(Continued to page 2)

*Product Approvals & Applications:*

## NCI, FDA Say They Are Collaborating On Electronic IND Submission, Training

**NCI** and **FDA** said they are collaborating on two initiatives for the development of cancer treatments.

The initiatives result from ongoing work from the interagency oncology task force, established in May 2003 to improve the efficiency cancer drug development and regulatory review.

The initiatives include a system for submitting investigational new drug applications electronically under the Cancer Biomedical Informatics Grid project.

FDA has agreed to work with NCI to develop clinical trial management software for cancer research groups and FDA, and to build tools for electronic interaction, focusing in particular on IND applications.

The initiatives would link cancer researchers electronically to FDA, reducing the time it takes for clinical trial drug testing, the institutes said. Now, FDA reviews IND applications in 30 days or less.

The collaboration would also initiate the cancer fellowship training programs that would allow fellows to work in clinical oncology programs at NCI and in the technical and regulatory review programs at FDA.

* * *

**Tufts Center for the Study of Drug Development** in Boston said the FDA Fast-Track program cut drug development by three years

The study found clinical development time for Fast-Track drugs approved between 1998 and 2003 was, on average, 2 to 2.5 years shorter than for non-Fast Track drugs.

"The fast track program has clearly made a difference," said

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PO Box 9905
Washington DC 20016
Telephone 202-362-1809

## FDA Lifts Hold On Antigenics' Trials Of Oncophage Vaccine

(Continued from page 1)

review product characterization data, the company said. All other Oncophage trials, including phase I and II studies, were unaffected by the hold.

* * *

**Light Sciences Corp.** of Seattle said it has begun a new trial site in the phase II study of Light Infusion Technology for liver metastases from colorectal cancer.

The added trial will be at University of Pennsylvania in Philadelphia. Other sites include: Allegheny General Hospital, Pittsburgh; Presbyterian/ St. Luke's Medical Center, Denver; and Johann Wolfgang Goethe-University Hospital, Frankfurt.

The trial will enroll up to 25 patients with inoperable chemotherapy-resistant liver metastases that develop from primary colorectal cancer.

Litx is a photodynamic therapy platform in which the drug, LS11 (talaporfin sodium) is activated by light from the light-emitting diode-based light infusion device.

* * *

**National Surgical Adjuvant Breast and Bowel Project** of San Antonio and **Genomic Health Inc.** said their prospective trial met its defined endpoints and validated the Genomic Health breast cancer assay from fixed paraffin-embedded tissue.

The assay can quantify breast cancer recurrence for newly diagnosed breast cancer. The study also showed that the recurrence score determined by the assay provides a level of correlation to breast cancer recurrence and performance that exceeds standard measures, such as patient age, tumor size and tumor grade, the groups said.

The results are the first large-scale, multi-center validation of a multi-gene assay. It is also the first time that such a study has been conducted using thin sections from standard diagnostic pathology specimens (fixed paraffin-embedded tissue) that are routinely available.

"We are excited about the results of this trial, which represent a practical advance in breast cancer diagnosis because the assay uses tumor tissue that is routinely obtained and stored for every patient," said Norman Wolmark, chairman of the NSABP, and the Department of Human Oncology at Allegheny General Hospital in Pittsburgh. "Based on our studies, the recurrence score becomes as important a prognostic measure for this group of node-negative patients as nodal status is for all patients."

Using the NSABP patient database, NSABP and Genomic Health designed a blinded, prospective validation using surgical tissue samples from 668 patients, who were node-negative, ER-positive and tamoxifen-treated.

The tissue samples were from patients who enrolled in the NSABP B-14 clinical trial from 1982-1988 and whose outcomes have been tracked over time by NSABP sites. Using RNA analysis of tumor tissues, the study evaluated the Genomic breast cancer assay to determine the likelihood of breast cancer recurrence as defined by a recurrence score from 0-100.

The recurrence score was able to accurately assign patients into high and low risk groups ($p<0.00001$), and when the recurrence score was examined together with age and tumor size in a multivariate analysis only recurrence score remained a significant predictor of patient outcome ($p<0.00001$).

"The results of this trial demonstrate a major advance in molecular pathology by showing that the performance of this genomic assay exceeds the standard measures of patient age, tumor size and tumor grade, characteristics that clinicians have used to predict prognosis for the better part of a century," said Soonmyung Paik, director, Division of Pathology, NSABP. "Even more important is the fact that we can perform this assay in a reproducible and accurate

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manner using routinely available diagnostic biopsy tissue, unlike other genome based assays which require special handling, such as snap freezing in liquid nitrogen. We believe our findings will provide critical information for this substantial group of patients."

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**Therion Biologics Corp**. of Cambridge, Mass., said it began a multi-center randomized, double-blind phase II trial to test the safety and efficacy of Prostvac-VF for prostate cancer.

Prostvac-VF targets prostate specific antigen and is designed to stimulate and sustain an immune response against prostate cancer tumor cells.

The study builds on the clinical data of a phase II trial which demonstrated that therapy with a PSA-based vaccine stabilized PSA levels in 52 percent of early metastatic prostate cancer patients, with no significant adverse events attributed to the study vaccine reported.

The new phase II study would enroll 120 patients with metastatic prostate cancer at 40 treatment centers in the U. S., the company said.

Participants will be randomized to receive either Prostvac-VF or placebo. The treatment group will receive a priming dose of Prostvac-VF in combination with GM-CSF, followed by six monthly booster vaccinations. The control arm will receive inactive vaccine. The primary endpoint of the study is progression-free survival.

The study will be led by Philip Kantoff, director of the Lank Center for Genitourinary Oncology and chief, Division of Solid Tumor Oncology at the Dana-Farber Cancer Institute.

* * *

**ViaCell Inc**. of Boston said it would begin enrollment in a phase I/II trial of CB001, a highly purified population of stem cells isolated from umbilical cord blood and multiplied using the ViaCell patented Selective Amplification technology.

The trial would assess the safety of CB001 and the rate and durability of blood and immune system reconstitution using CB001 for advanced stages of hematologic cancers where high dose chemotherapy and radiation treatment has occurred.

"While cord blood stem cell transplants are routinely and successfully used in the treatment of hematologic disease in children, they are not typically used in adults because of the limited number of stem cells available in cord blood," said Mary Laughlin, director of the Allogeneic Transplant Program, University Hospitals of Cleveland, and associate professor of medicine and pathology, Department of Medicine, Division of Hematology/Oncology, Case Western Reserve University.

"This study is exciting because the ViaCell technology has demonstrated the ability to expand a highly purified population of stem cells and will potentially allow many more patients to be treated with cord blood," she said.

The technology yields an increased number of defined, pharmaceutical grade stem cells capable of enhancing engraftment success, the company said.

"The potential of this cell expansion platform may well extend to both hematologic and non-hematologic therapy applications," said John Wagner, professor of pediatrics and scientific director of clinical research of the Blood and Marrow Transplantation Program and Stem Cell Institute.

The trial will be conducted at sites in the U.S., including University Hospitals of Cleveland, Cleveland; and University of Minnesota, Minneapolis. Mary Laughlin, and John Wagner will serve as investigators.

Adults with advanced stages of leukemia and myelodysplastic syndrome who are in need of a hematopoietic stem cell transplant and are unable to find a suitable donor will be eligible to participate, the company said.

*Deals & Collaborations:*

## Applied Molecular Evolution To Merge With Eli Lilly

**Eli Lilly and Co**. (NYSE: LLY) of Indianapolis and **Applied Molecular Evolution Inc.** (Nasdaq: AMEV) of San Diego said they have mutually agreed to the AME merger into Lilly.

The boards of directors of Lilly and AME have given their approval to the transaction, which is subject to approval of AME shareholders, the companies said.

"We are confident that the synergies this merger creates will accelerate our ability to discover and optimize biotherapeutic drugs for cancer, inflammatory diseases, and critical care, as well as diabetes and obesity—areas where proteins, such as monoclonal antibodies, are of great therapeutic benefit," said Steven Paul, executive vice president, science and technology for Lilly

AME will retain its name but become a wholly-owned subsidiary of Lilly and integrate with the Lilly research organization, the companies said.

Under the terms of the agreement, AME shareholders will receive $18 for each outstanding AME share at closing, the companies said. AME shareholders may elect to receive the $18 in cash or shares of Lilly common stock based on the closing price of Lilly stock on the closing date, subject to proration such that the total purchase price paid by Lilly is 80 percent stock and 20 percent cash. The value of the transaction is expected to be $400 million, net of cash.

The transaction is expected to close in the first quarter of 2004, the companies said.

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**GE Medical Systems**, a unit of General Electric Co. (NYSE:GE) Waukesha, Wis., said it has signed a clinical trial agreement with the **NCI Cancer Imaging Program** for multi-site trials of 18F-Fluorothymidine as an agent for positron emission tomography , for cancer management.

FLT is a PET radiopharmaceutical used to image DNA synthesis, showing contrast in the presence of cellular proliferation in tumors and other proliferating tissues, the company said.

NCI will sponsor clinical trials at Johns Hopkins, Virginia Commonwealth University Medical Center, Massachusetts General Hospital, the University of Washington, and the NIH Clinical Center, the company said. GE Medical will provide TRACERlab FX synthesis systems to produce FLT for the clinical work done at the sites.

FLT will be one of the first PET agents for which there will be an FDA investigational new drug proceeding for the NCI-sponsored multi-site trials, the company said.

"By using agents like FLT that can specifically image proliferation and other aspects of tumor biology, we can look at tumors before and soon after treatment to determine reliably whether a given therapy will be effective or not," said James Thrall, chief of radiology, Massachusetts General Hospital. "The idea is to personalize therapy by using PET imaging of the cancer to choose the right treatment and enable the patient to avoid inappropriate therapy."

Besides the TRACERlab FXN synthesis equipment, four out of five of the clinical sites will use GE Medical PET/CT or PET systems, the company said.

Under the terms of the agreement with NCI, GE Medical Systems also will be responsible for developing the standard FLT synthesis software and procedures, the company said.

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**Hologic Inc.** (Nasdaq:HOLX) of Bedford, Mass., and **Confirma Inc.** of Kirkland, Wash., said they have formed an agreement to distribute the Confirma CADstream MRI CAD system.

The agreement gives Hologic non-exclusive distribution rights for CADstream, a computer-aided-detection system which automates the processing of data-intensive breast magnetic resonance imaging studies and assists with study interpretation.

Confirma said it is also integrating its CADstream-processed breast MRI studies and system to function with the Hologic full-field digital Lorad Selenia system, to provide simultaneous mammography and breast MRI study viewing capability.

The CADstream determines the extent of breast disease, evaluates surgical margins, and monitors response to treatment.

The Lorad Selenia is an FDA-approved full field digital mammography system using direct capture technology and the M-IV and Affinity Series of screen-film mammography systems.

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**Ingenuity Systems** of Mountain View, Calif., said the **Genomics Institute of the Novartis Research Foundation** has licensed its Ingenuity Pathways Analysis application for their research programs.

The technology is a Web-delivered application that enables biologists to discover, visualize, and explore therapeutically relevant networks significant to their experimental results, the company said.

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**Odyssey Thera Inc.** of San Ramon, Calif., said it has entered into an agreement with **Pfizer Inc.** to profile compounds across the Odyssey Thera panel of cell-based assays to characterize mechanism of action and pathway activity.

The Protein-fragment Complementation Assay technology measures pathway activity within living cells and is applied across signaling pathways relevant to drug discovery in therapeutic areas, the company said. The project with Pfizer will focus on compounds in one therapeutic area.

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**Prolexys Pharmaceuticals Inc.** of Salt Lake City said it has formed a chemiproteomics research collaboration agreement with **Whitehead Institute for Biomedical Research** of Cambridge, Mass.

The research is based on the investigation of



interactions between small molecule drug candidates and proteins in oncology, the company said. The Prolexys mass spectrometry proteomics technology platform, HySpec, will identify proteins that bind to pharmacologically active compounds. The information will be used to identify therapeutically active compounds that have the desired anti-cancer activity without significant toxicity and side effect liability.

The two-year agreement calls for sharing of compounds from the laboratory of Brent Stockwell for chemiproteomic analysis at Prolexys, the company said. The Stockwell library of compounds is a source of starting compounds; the lab also has expertise in medicinal chemistry allowing for the modification of original compounds based on the results of the proteomic studies.

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**Southern Research Institute** and **Genome Explorations Inc**. of Birmingham, Ala., entered into a collaborative agreement for joint development programs in pharmaceutical target identification using gene expression profiling, and to co-market individual and combined services.

Gene expression profiling uses collections of thousands of human genes arranged on gene chips known as DNA microarrays, the company said. Researchers distinguish between cancers based on the presence or absence of proteins that are expressed within cancer cells. Recent studies have examined the expression of genes in leukemias, lymphomas, and melanomas, as well as colorectal, pancreatic, ovarian, prostate and breast cancers.

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**SRI International** of Menlo Park, Calif., an independent research and development organization, said it has received a three-year, $1.52 million contract from NCI to synthesize chemical carcinogens, derivatives of polynuclear aromatic hydrocarbons and chemopreventive agents.

The compounds will be offered to researchers through the NCI Chemical Carcinogen Reference Standard Repository, the company said.

Under the contract, SRI will synthesize, isolate, purify, and characterize compounds as authentic standards and substrates pathways of carcinogen metabolic activation and molecular mechanisms of action, the company said.

* * *

**Tularik Inc.** (Nasdaq: TLRK) of South San Francisco said it has achieved the first milestones under its collaboration agreement with **Amgen Inc**. (Nasdaq: AMGN) to discover, develop and commercialize therapeutics for oncology targets.

Amgen has two compounds identified by Tularik for optimization, each directed against a different target, resulting in the payment of two milestones, the company said.

In May, Tularik and Amgen entered into a five-year collaboration that included multiple drug discovery and development programs. In addition to committed funding of $125 million, Tularik will receive royalty payments and escalating milestone payments as compounds are selected and progress to market approval, the company said. Aggregate milestone payments for compounds active against each oncology target could reach $21 million.

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**Ventana Medical Systems Inc.** (Nasdaq:VMSI) of Tucson, Ariz., said it has entered into a long-term antibody development agreement with **Epitomics Inc**. Burlingame, Calif., under which Epitomics will create rabbit monoclonal antibodies for Ventana.

Rabbit monoclonal antibodies are reagents for diagnostic applications in anatomical and clinical pathology and proteomics, the company said. The collaboration combines the Ventana edge slide staining technologies with next generation antibody chemistry.

*Oncology Management:*

## CMS Says Oncura Cryotherapy To Be Reimbursed In 2004

**Center for Medicare and Medicaid Services** of Philadelphia said the **Oncura** cryotherapy for minimally invasive prostate cancer would be accessible to Medicare beneficiaries based on updated Medicare outpatient hospital reimbursement for 2004.

The ultra thin cryotherapy needle technology does not require a major surgical procedure thereby avoiding the increased risk of incontinence associated with surgery, the center said.

The cryroablation needles are reimbursed separately on a pass through payment basis, which will expire at the end of the year, the center said. The pass through payment and procedural payment will be replaced by a cryotherapy procedure a national average payment of $6,545.86.

"CMS's decision to reimburse each prostate cryotherapy procedure at over $6,500 is clearly the result of an extensive review of the data supporting

this option," said Jim Matons, vice president and general manager of the Americas at Oncura.

Oncura, an Amersham business, was created through the merger of the Amersham (LSE, NYSE, OSE: AHM) brachytherapy business with the Galil Medical Ltd urology business.

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**American Society for Gastrointestinal Endoscopy Technology Assessment Committee** of Oak Brook, Ill., said it has recommended standard colonoscopy rather than virtual colonoscopy.

The term virtual colonoscopy refers to the use of radiological techniques, including computed tomography and magnetic resonance scanning, with computers to produce pictures or images of the colon, the committee said. Supporters of virtual colonoscopy recommend the test as an alternative to standard colonoscopy performed with an endoscope.

Like standard colonoscopy, virtual colonoscopy requires a bowel preparation to cleanse the colon and the insertion of a device into the rectum, the committee said. While sedation is used to reduce or eliminate discomfort associated with standard colonoscopy, sedation is not necessary for virtual colonoscopy. Unlike standard colonoscopy, virtual colonoscopy only provides images of the colon and does not allow for biopsy or polyp removal at the time of the exam. Some abnormalities detected during virtual colonoscopy will require standard colonoscopy for confirmation and management, the committee said.

Virtual colonoscopy may be indicated for obstructing colon cancer and for incomplete colonoscopy, the committee said. However, there is insufficient evidence to support the use of virtual colonoscopy for symptoms related to the lower digestive tract or for routine colon cancer screening.

Standard colonoscopy has been proven effective for detection of colon cancer and pre-cancerous polyps, the committee said. Moreover, in the National Polyp Study, periodic colonoscopy with removal of polyps was demonstrated to prevent death due to colorectal cancer. This benefit has not been demonstrated for virtual colonoscopy. Therefore, the American Cancer Society, the U.S. Multi-Society Task Force on Colorectal Cancer, and the U.S. Preventive Services Task Force have not recommended virtual colonoscopy for colorectal cancer screening or surveillance.

"Advertisements for total body scanning and virtual colonoscopy may promote potential benefits that have not been documented by clinical studies," said Gregory Ginsberg, University of PA Hospitals and chairman of the ASGE Technology Committee. "Patients who undergo virtual colonoscopy may expose themselves to false-negative and false-positive results leading to additional testing, and to unnecessary expense and radiation exposure."

*Product Approvals & Applications:*

## Fast-Track Process Effective, In Speeding Approvals

(Continued from page 1)

Christopher-Paul Milne, associate director at the Tufts Center. "By 1997, the FDA's five-year-old accelerated approval regulations had resulted in about 20 approvals; within its first five years the fast track program led to 200 fast track product development designations and another two dozen approvals."

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**FDA** said it has approved the new drug application to market Plenaxis (abarelix) for advanced prostate cancer where no alternative therapy exists.

The drug will be marketed under a voluntary risk management program agreed to and administered by the sponsor because of an increased risk of serious, and life-threatening allergic reactions, FDA said.

Plenaxis is a gonadotropin-releasing hormone antagonist that lowers testosterone. Plenaxis is marketed by **Praecis Pharmaceuticals Inc.**, of Waltham, Mass.

The effectiveness of Plenaxis in lowering testosterone production was demonstrated in a study of 81 men who avoided surgical castration by undergoing at least 12 weeks of treatment, FDA said. Other benefits included decreased pain and relief from urinary problems. However, three of the 81 patients experienced serious allergic reactions, one of which included loss of consciousness.

Because of the risk of low blood pressure and fainting as part of the allergic reaction to the drug, patients who receive the drug are to be monitored for at least 30 minutes after receiving a dose, FDA said. The manufacturer will not be distributing the drug through retail pharmacies. The drug will be distributed directly to physicians and hospital pharmacies enrolled in the Plenaxis RMP.

Plenaxis is administered as an injection into the muscles of the buttocks every two weeks for the first month of therapy, followed by once every four weeks thereafter. Because the drug may stop working in certain patients, doctors should perform blood tests

about every two months to make sure Plenaxis is working by keeping the level of testosterone low.

The most common side effects seen in the clinical trial were hot flashes, sleep disturbances, pain, including back pain, breast enlargement or pain, and constipation, FDA said.

As part of the RMP program, the sponsor will only distribute Plenaxis to physicians who attest to certain qualifications and are enrolled in the Praecis Plenaxis PLUS (Plenaxis User Safety) Program, FDA said. The company is forming educational programs for physicians, patients, and hospital pharmacists about the risks and benefits of the drug. Patients will be asked to read and sign a patient information leaflet before receiving the drug. The company will also establish a system that collects and reports adverse events to FDA.

* * *

**ImClone Systems Inc**. (NASDAQ:IMCL) of New York and **Bristol-Myers Squibb Co.** (NYSE:BMY) of Princeton, N.J., said that ImClone Systems has filed a new drug submission to use Erbitux (cetuximab) in combination with irinotecan for Epidermal Growth Factor Receptor -expressing, irinotecan-refractory metastatic colorectal cancer with the Biologics and Genetic Therapies Directorate of Health Canada.

The companies said the NDS is being reviewed under priority review.

"This filing represents a significant step forward in our global regulatory strategy, including our goal of reaching the greatest number of patients with colorectal cancer that may benefit from the use of Erbitux," Daniel Lynch, acting chief executive officer of ImClone Systems. "We are pleased to be able to file the NDS under Priority Review with Health Canada following similar Erbitux submissions in the U.S., Europe and Australia."

Erbitux is an investigational IgG1 monoclonal antibody designed that targets and blocks the EGFR, which is expressed on the surface of cancer cells in multiple tumor types, the companies said. The drug binds to and internalize EGFR and prevent natural ligands called growth factors from binding to the receptor and activating signaling to the tumor.

Erbitux is also being studied in earlier stages of colorectal cancer, as well as in other types of cancer that express the EGF receptor, including lung, pancreatic, ovarian and head and neck cancers, the companies said.

In another development, ImClone said **Swissmedic** pre-notified **Merck KGaA** of its intent to authorize the marketing of Erbitux in Switzerland:

The final approval is expected within thirty days, said Merck KgaA.

Once approved, Erbitux could be administered in combination with the standard chemotherapy irinotecan, the companies said.

Erbitux is an investigational IgG1 monoclonal antibody targets and blocks the Epidermal Growth Factor Receptor, the company said.

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**Eastman Kodak Co.** of Rochester, N.Y., said it has received an approval letter from FDA for a mammography computer-aided detection device.

Kodak said it would offer CAD software as a stand-alone product and as a component of its digital capture and image-and-information management systems.

The software uses algorithms to highlight areas on digitized images, signaling examination for disease, the company said.

The CAD system uses technology acquired from MiraMedica Inc., of Los Gatos, Calif.

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**Fischer Imaging Corp**. (Nasdaq:FIMG) of Denver, Colo., and **R2 Technology, Inc.** of Sunnyvale, Calif., said FDA has approved the R2 proprietary mammography CAD technology with the Fischer SenoScan TrueView Digital Scanning Mammography system.

CAD technology detects findings, such as calcifications, that might otherwise be overlooked during the review process of mammography, the companies said.

Under a development and marketing agreement, Fischer will integrate the R2 CAD technology into its SenoScan TrueView Digital Scanning Mammography System and have distribution rights to the integrated system. The R2 Technology ImageChecker DM system, which received FDA approval last September, also will support CAD analysis of digital images acquired on the SenoScan system. The ImageChecker DM System will be distributed directly by R2 and by Fischer in conjunction with its traditional film-based mammography products, the companies said.

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**Maxim Pharmaceuticals** (Nasdaq: MAXM) of San Diego, Calif., said it has filed a European centralized procedure marketing authorization application for Ceplene (histamine dihydrochloride),

in combination with interleukin-2, for advanced malignant melanoma.

Clinical results supporting the European application include multiple phase III and phase II trials demonstrating survival improvement, the company said.

"We believe in the approvability of our eCTD application based upon the most recent 36-month follow-up data from the MP-US-M01 phase III trial for advanced malignant melanoma coupled with the single-arm MP-MA-0103 phase II trial," said Richard Lowenthal, head, worldwide regulatory affairs and drug safety at Maxim.

After 36 months of follow-up of the 305-patient M01 phase III trial, the Ceplene/IL-2 combination demonstrated a statistically significant increase in survival (p=0.039, Log-Rank test, adjusted for multiple hypotheses) in the overall intent-to-treat population of advanced malignant melanoma patients compared to treatment with the same dose regimen of IL-2 alone, the company said.

The increase in survival duration for patients treated with the Ceplene/IL-2 combination in the patients that entered the study with liver metastases was also statistically significant after 36 months of follow-up (p=0.0062, Log-Rank test, adjusted for multiple hypotheses), the company said.

In the M01 trial, two-year survival rates for liver metastases were 18.2 percent for the group treated with the Ceplene/IL-2 combination versus 2.7 percent for the group treated with IL-2 alone, the company said.

The safety and side-effect profile of Ceplene combination therapy has allowed patients to administer treatment at home, the company said.

In the M01 trial, the incidences of treatment-emergent serious adverse events were comparable among patients treated with the Ceplene/IL-2 combination and those receiving IL-2 alone, the company said.

*Patents:*

## Curis Inc. Wins U.S. Patent For Hedgehog Proteins

**Curis Inc.** (Nasdaq: CRIS) of Cambridge, Mass., said it has been issued a patent for its hedgehog signaling proteins.

The Hedgehog signaling proteins in the compositions are characterized in terms of the DNA sequences that encode the proteins, as well as certain biological activities associated with the pathway, the company said.

Curis is using the Hedgehog signaling pathway as a technology platform to develop drug candidates for neurological disorders, cancer, cardiovascular disease, and hair growth disorders, the company said.

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**DRAXIMAGE Inc.,** the radiopharmaceutical subsidiary of **DRAXIS Health Inc.** (TSX: DAX, Nasdaq: DRAX) of Mississauga, Ontario, said it has been granted a U.S. patent for chelating compounds for the development of imaging and radiotherapeutic agents to diagnose and treat diseases, including cancerous tumors or metastases.

The invention is a synthesis and application of a new family of molecules known as high affinity bifunctional chelators containing hydroxamic acid residues, the company said. Chelators are organic molecules with the property to bind metals with high affinity. The proprietary chelators can be used to develop and commercialize adiopharmaceuticals based on metallic radioisotopes such as Gallium-67, Gallium-68, Indium-111 and others.

The chelating agents are bifunctional since their molecular structure also contains a reactive group that permits attachment to biologically active substances such as peptides, proteins or antibodies, the company said. This feature means that combining the agent with a biologically active molecule results in a compound that can be radiolabelled with an appropriate radioisotope to form a new diagnostic or therapeutic agent.

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**Xechem International Inc**. (OTCBB: XKEM) of New Brunswick, N.J., said it has received a patent from the Canadian Patent and Trade Mark Office on its proprietary technology for Isolation and Purification of paclitaxel from Yew tree (Taxus brevifolia and Taxus species).

The move would protect the technology, which also leads to nine next generation paclitaxel analogs, until 2016, the company said.

Xechem said it has U.S. and international patents on its proprietary technology.

FDA first approved Paclitaxel for ovarian cancer under the name of Taxol. Subsequently, Taxol was approved for breast cancer, small-cell lung and stomach cancers and AIDS related Kaposi Sarcoma. It then became available as a generic.

Xechem said is pursuing a superior proprietary paclitaxel formulation.

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