THE CANCER LETTER

Vol. 29 No. 41
Nov. 7, 2003

Price $305 Per Year

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

FDA Examining Endpoints For Approval Of Cancer Therapies, Division Director Says

FDA is proceeding with a move to find alternative endpoints for approval of cancer therapies, including, potentially, a departure from survival as the gold standard, Richard Pazdur, director of the agency's Division of Oncology Drug Products, said in an interview with **The Cancer Letter**.

"We are concerned that a greater number of available therapies and the presence of crossover in randomized trials may confound the

(Continued to page 2)

In Brief:

NCCF, Ad Council Plan Public Service Ads Promoting Childhood Cancer Awareness

NATIONAL CHILDHOOD CANCER FOUNDATION and the Ad Council said they will develop a public service advertising campaign to help children with cancer and their families receive information about cancer treatment, resources, and support. The campaign, to be created at no charge by Young & Rubicam Inc., is scheduled to be made public in the third quarter of 2004. The NCCF represents the Children's Oncology Group. "We commend the Ad Council for its commitment to help us reach the day when every child with cancer can be offered a chance for a cure," said Gregory Reaman, COG chairman. . . . **NORKA RUIZ BRAVO** was appointed NIH deputy director for extramural research, said NIH Director **Elias Zerhouni**. Bravo was associate director for extramural activities at National Institute of General Medical Science, where she oversaw the $1.7 billion (FY 2003) research and research training grant programs from a policy, business, and scientific perspective. Prior to that, she served as program director of the NIGMS Division of Genetics and Developmental Biology, deputy director of the NCI Division of Cancer Biology, and acting director of the NCI Division of Cancer Biology. . . . **CLARA BLOOMFIELD** has been selected the winner of the 2003 John P. Minton Hero of Hope Research Champion Award for contributions to cancer. The award is given annually by the American Cancer Society Ohio Division. Bloomfield is the William G. Pace III Professor of Cancer Research at the Ohio State University. She is also senior advisor to the Ohio State University Comprehensive Cancer Center—Arthur G. James Cancer hospital and Richard J. Solove Research Institute. . . . **W. STRATFORD MAY JR** will receive the Leukemia & Lymphoma Society 2003 National Leadership Award. He is director of

(Continued to page 8)

Pazdur: Time-To-Progression May Be An Alternative Endpoint

(Continued from page 1)

demonstration and interpretation of a survival endpoint for some tumors," Pazdur said.

The agency, in collaboration with oncology professional societies and NCI, plans to conduct a review of the clinical trial endpoints in advanced colorectal cancer. The meeting will be held in Washington on Nov. 12.

Earlier this year, a similar panel reviewed the endpoints for approval of lung cancer therapies (**The Cancer Letter**, April 25). The findings of that panel will be presented to the Oncologic Drugs Advisory Committee next month.

"Endpoint guidelines need be disease-specific and must consider the risk-benefit relationship," Pazdur said. "Because of the toxicity of conventional cytotoxic chemotherapy agents, the ODAC recommendation in the early 1980's was that drug approval should be based on an improvement in survival or quality of life—improved patient functioning or improved tumor-related symptoms.

"This recommendation needs to be re-evaluated as less toxic therapies are developed."

The text of the interview follows.

CL: Is there a move at FDA to abandon survival as the gold standard for drug approval?

THE CANCER LETTER

Member, Newsletter and Electronic Publishers Association

World Wide Web: http://www.cancerletter.com

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
E-mail: info@cancerletter.com

Subscription $305 per year worldwide. ISSN 0096-3917. Published 46 times a year by The Cancer Letter Inc. Founded Dec. 21, 1973, by Jerry D. Boyd

PAZDUR: The demonstration of a survival advantage is the ultimate goal of any drug development program in oncology. Survival is an unambiguous endpoint that is not subject to investigator interpretation—especially important in oncology since most trials are unblinded.

Nevertheless, we are concerned that a greater number of available therapies and the presence of crossover in randomized trials may confound the demonstration and interpretation of a survival endpoint for some tumors.

There are examples where a survival advantage has been demonstrated despite a significant number of crossover patients (e.g., irinotecan in a second-line setting in colon cancer). However, the alternative situation—the failure to demonstrate a survival advantage because of crossover—is difficult to assess.

This failure could be due to under-powered trials or simply that the therapy lacks survival impact. A time-to-progression endpoint, although having methodological and interpretation difficulties, may be an alternative that will need further discussion with our disease panels selected in consultation with ASCO, AACR, and NCI, and, ultimately, recommendations from ODAC.

CL: Survival is unambiguous. Are other endpoints sufficiently reliable?

PAZDUR: We have experience with a variety endpoints and have discussed our experiences with these endpoints over a 13-year period (Johnson, Williams, Pazdur, JCO 21: 1404-1411, 2003).

Endpoints other than survival were the approval basis for 68% of oncology drug marketing applications granted regular approval and for most of the 14 applications granted accelerated approval during this period.

There are several issues to address with endpoints, such as TTP, response rates, or disease-free survival. First, are these endpoints surrogates for clinical benefit or do they represent clinical benefit per se?

Although the agency has considered the demonstration of a survival advantage or the delay or amelioration of symptoms as "clinical benefit," one could make a reasonable argument that a clinically relevant delay in disease progression could represent direct clinical benefit. Similarly, the complete disappearance or significant reduction in tumor size for a meaningful duration could be argued as a direct clinical benefit.

Alternatively, if these endpoints would be considered surrogate endpoints rather than direct clinical benefit, should we consider them *established* surrogates supporting full drug approval, *reasonably likely* surrogates used in accelerated approval in solid tumor applications or *exploratory* surrogates that may be useful to generate hypotheses or preliminary evidence of drug activity?

There are methological problems in assessing TTP that will need to be addressed—especially regarding the potential bias in the documentation and interpretation of this endpoint in unblinded trials.

Ultimately, we must have confidence that the effect on TTP is true, reliable, reproducible and not merely a chance finding. One could imagine the observation of a small impact only on a TTP endpoint measured in a few weeks associated with nominal statistical significance in a single trial.

This single finding could be due to chance and approval based on this one finding seems unlikely. Additional information that would increase our confidence of a true finding include statistical persuasiveness, consistent findings in secondary endpoints, similar effects noted in subgroups, and confirmation of results in additional clinical trials.

Endpoint guidelines need be disease-specific and must consider the risk-benefit relationship. Because of the toxicity of conventional cytotoxic chemotherapy agents, the ODAC recommendation in the early 1980's was that drug approval should be based on an improvement in survival or quality of life—improved patient functioning or improved tumor-related symptoms. This recommendation needs to be re-evaluated as less toxic therapies are developed.

If our guidelines change to accept TTP as the basis for approval where we have previously recommended survival, I would still recommend powering the trial for survival—although the actual approval would be based on TTP.

Why? First, if we don't ask the survival question, a drug's impact on survival will never be known. This lack of information will have a deleterious impact on the field of oncology in assessing our true gains. Secondly, trials with TTP as a primary endpoint have fewer patients than survival trials.

Even now, we have problems with trials under-powered for survival. I would be worried about a slippery slope with smaller and smaller trials that will be under-powered even for TTP.

TTP has problems. A technical problem is the lack of uniform methods of handling missing data, especially, patient visits and radiographic measurements. How much of an improvement in TTP constitutes a benefit? This is a clinical—not a statistical—decision.

In selected metastatic disease settings where death shortly follows disease progression—say by a few weeks or months—is the trade-off in uncertainty of TTP measurement and questionable surrogacy worth the potential compromise in regulatory decision-making? In this setting, one might argue that survival data would soon be available and that TTP offers no special advantage as a regulatory endpoint.

TTP assessment and interpretation can potentially be improved, and further discussion and research may be needed. For example, we would like to discuss a TTP analysis at a single pre-specified time point rather than a log rank analysis of the curve. This may minimize bias in TTP ascertainment, and reduce excessive radiological examinations. In addition, we will also discuss the concept of time-to-symptomatic progression.

There are many unanswered questions regarding these endpoints. I plan on asking for recommendations where further research needs to be performed.

This need for future research on endpoints may be a place to interact with the NCI and its external funding mechanisms via the inter-agency agreements that NCI Director Andrew von Eschenbach and FDA Commissioner Mark McClellan have initiated.

CL: It might be useful to discuss recent approvals to illustrate this. In colorectal cancer—your field—what would be the rationale for abandoning survival? How would this work?

PAZDUR: When I entered the field of colorectal cancer clinical research over 20 years ago, there was a single-agent—5-fluorouracil and, interestingly, we are still addressing its optimal schedule and delivery.

Because of the advent of multiple drugs that have demonstrated survival advantages in advanced colorectal cancer trials, regulatory agencies must address cross-over and subsequent therapies after disease progression.

These therapies may confound our interpretation of survival in randomized trials. TTP, with all its difficulties noted above, is an obvious alternative endpoint since cross-over and subsequent therapies are all prescribed after its measurement.

CL: What would it take to change the standards? Do you have the authority to do this administratively?

PAZDUR: In the 1970's, FDA usually approved cancer drugs based on objective response rates.

In the early 1980's, after discussion with ODAC, FDA determined that overall response rate was generally not sufficient evidence for approval because of the risk-benefit relationship observed with conventional cytotoxic drugs.

The regulatory basis for an NDA approval mandated by Congress does not stipulate endpoints. The agency has flexibility in accepting alternative endpoints. This is the reason we are having these discussions with the oncology community and the ODAC.

CL: Are you going to hold meetings and review the proposed changes indication by indication?

PAZDUR: The disease-specific meetings that we have organized with ASCO, AACR, and the NCI are aimed at identifying key issues that need discussion, pros and cons of issues, and areas that need further research as noted above.

Our division can take advice only from ODAC. We will have subsequent discussions with ODAC with selected participants from the disease-specific meetings presenting issues.

I doubt if we can independently review each disease. We have selected major diseases, especially those with pending applications or critical issues that need to be addressed. There will be common issues and advice that can be extrapolated to other diseases.

Our December ODAC meeting will have a general discussion of endpoints in a half-day session followed by a discussion of lung cancer endpoints that were discussed in March at an FDA/ASCO/NCI meeting.

The planning for these meetings required extensive time and effort. Grant Williams, our deputy director, took the lead on this important initiative. Dianne Spillman provided administrative support, and Pat Keegan and her colleagues in ODE 6 offered continuous discussion and input, as did our team leaders and medical review staff.

CL: I understand ODAC has a lot of time on its hands. Why do you think this is happening? Has the pace of drug discovery slowed down? Has the industry lost its touch? Is it something about the times we are in? Can you venture a hypothesis?

PAZDUR: The purpose of the ODAC meetings is to provide advice to the division. In indications where we have had significant past discussions, for example, the use of response rates of reasonable durations for accelerated approval, we have not taken recent applications to ODAC because of their clear prior advice.

With applications that are approved without an ODAC meeting, the division discusses each application with a variety of external consultants, including the ODAC chair and selected members, disease-specific experts, statisticians, and patient representatives prior to making a regulatory decision.

Another purpose of the ODAC is to allow transparency of the review process. I firmly believe that having well-defined endpoints and advice to sponsors and other stakeholders are the most important steps in a transparent process and trump any drug-by-drug discussion.

That is the reason that we devoted significant time to organize the disease-specific workshops to allow adequate discussion and external input. Our division has published detailed reviews of our regulatory decisions from a historical perspective and our regulatory basis of approval for specific drugs delineating the scientific and regulatory underpinnings of our decisions.

In addition, we have organized meetings for patient advocates and have a patient advocacy program to allow interaction throughout the drug development process.

Has industry lost its touch? I assume you are asking this question because I have a perspective as a drug regulator and medical oncologist with clinical trial experience. Oncology is an inherently risky business and we are aware of the problem.

Our traditional drugs are toxic with modest effects on clinically relevant endpoints. One major problem is the lack of predictive non-clinical models to guide drug development. This has been a problem with conventional cytotoxic drugs, and I hope that a greater understanding of the molecular mechanisms of diseases and drugs will reduce this uncertainty.

However, frequently, sponsors' decisions regarding drug development are made by chance observations of early activity in phase I trials, guided by registration strategies aimed at accelerated approval, or directed by commercial aspirations.

Industry's management of risk can impact drug development and regulation. Many sponsors seem reluctant to perform two trials in the same or similar indications. This decision-making process generally reflects the lack of preclinical guidance for future clinical development.

Where there exists a clear preclinical hypothesis, prior clinical experience, and hence, less risk, sponsors are willing to perform multiple, adequate trials. An example is the multiple trials usually performed for hormonal therapies in breast cancer NDAs.

Another risk reduction strategy is to perform only a limited phase II trial for accelerated approval and "see if the agency will bite."

We are comfortable with approving drugs for accelerated approval on the basis of a single-arm trial and believe that we have accelerated the delivery of important drugs to Americans via this approach. The delivery of new drugs with novel mechanisms can be expedited by limited activity in refractory patient populations.

In March, 2003 we had discussions with ODAC emphasizing the need for a comprehensive development plan for drugs being considered for accelerated approval. This plan would include subsequent trials demonstrating clinical benefit that preferably would be underway at the time of accelerated approval.

Fortunately, I believe as a result of this meeting, sponsors are proceeding with a dual strategy—a single-arm trial in a refractory population coupled with an ongoing randomized trial.

This plan can provide a second chance at accelerated approval using a surrogate endpoint interim analysis or can provide evidence of clinical benefit at the trial's conclusion. This strategy indicates a commitment to drug development allowing rapid approval of the drug if the single-arm trial is convincing and insurance if the single-arm trial is not acceptable.

We have also announced the flexibility of allowing multiple drugs to receive an accelerated approval indication until one demonstrates clinical benefit.

The management of risk can be observed by the appearances of drug "sequels." Improvements in toxicity, schedule, and convenience are laudable goals of drug development.

However, the demonstration of minor improvements with manipulated "legacy" drugs usually requires a large expenditure of resources, since these trials have non-inferiority endpoints.

In addition, the management of oncology drug development risk can be observed by several sponsors studying the same "target" and the same indication with very similar drugs.

CL: How can you and the division help the industry out of its predicament?

PAZDUR: The oncology community—which the FDA is a member of—has a common goal of providing to the American public safe and effective oncology drugs in an expeditious manner. Commercial sponsors must have clear advice from drug regulators.

In addition to scheduled meetings, such as end of phase II meetings, our division has actively requested sponsors to submit protocols for special protocol assessments—SPAs—to ensure binding agreement on important studies.

We must have flexibility in using clinical judgment.

We are not slaves to statistical "p" values. However, at the end of the day, we must have confidence in our decisions.

Regulatory leadership must inculcate a sense of urgency to the NDA review staff so Americans will have access to effective drugs as soon as possible.

Quality must not be sacrificed. Our division has taken regulatory actions on important drugs far sooner than our mandated six-month PDUFA deadlines.

CL: The FDA oncology portfolio was recently reorganized, split into three units. Will these standards be applied consistently through the three units? How would this be coordinated?

PAZDUR: There are advantages and disadvantages to separate review divisions. A greater degree of specialization allows greater expertise with regard to specific drug classes.

As you note, the review of biologics was recently divided into two groups, one which has joined CDER and one remaining in CBER. The review of drugs in our Division of Oncology Drug Products has not been changed.

Increasingly, applications will combine small molecules, biological agents, and conventional cytotoxic chemotherapy, questioning the regulatory jurisdiction of specific applications.

If an unapproved agent is studied with a commercially available agent, the primary review responsibility will usually be assumed by the division that holds the investigational agent, and there would be appropriate meetings and consultations with the other review unit.

A lead center generally would be designated on the predominant development issue. The Office of Combination Products in the Office of the Commissioner was recently established to facilitate inter-center product development.

Clinical Trials:

STAR Requires Only 2,000 More Women For Completion

The Study of Tamoxifen and Raloxifene to determine whether raloxifene can prevent breast cancer better and with fewer side effects than tamoxifen can be completed with fewer women than planned, researchers said last week.

The NCI-funded study began recruiting 22,000 postmenopausal women in July 1999. The clinical trials cooperative group leading the study, the National Surgical Adjuvant Breast and Bowel Project, said the study can be completed with 19,000 women.

The original estimate of the number of women needed for the study was based on volunteers having at least a 1.7 percent chance of developing invasive breast cancer within five years—about 17 women per 1,000. STAR enrollees have had about twice the minimum risk, or a 3.5 percent chance of developing cancer within that time period—35 per 1,000 women.

With the greater risk, fewer women are required to see the prevention effects from the drugs. NSABP officials said they hope to complete enrollment by next summer. Study results may be available by 2006.

"Because the participants are more likely to develop cancer than women at a lesser risk of the disease, the study will be able to get answers with fewer volunteers," said Norman Wolmark, chairman of NSABP and the Department of Human Oncology at Allegheny General Hospital in Pittsburgh.

"The other important factor is that so many of the women who have already volunteered are really committed to the trial," Wolmark said. "In any clinical trial, participants can withdraw at any time, for any reason. Fortunately, in STAR we have a strong core of dedicated volunteers, and we are certain we will be able to obtain our answers with 19,000 women."

STAR is the follow-up study to the Breast Cancer Prevention Trial, published in 1998, that led to the FDA approval of tamoxifen for risk reduction in women at increased risk of developing breast cancer. So far, more than 17,000 women have volunteered for STAR at more than 500 sites in the U.S., Canada, and Puerto Rico.

"NCI is pleased that STAR will be able to reach its conclusions with 3,000 fewer women than we originally planned," said Leslie Ford, associate director for clinical research in the NCI Division of Cancer Prevention. "We will do everything we can to make sure enrollment efforts continue at their current pace, so we can reach our goals on time or ahead of schedule."

STAR includes postmenopausal women who are at increased risk for breast cancer due to a combination of factors including age, family history of breast cancer, personal medical history, age at first menstrual period, and age at first live birth. Participants are randomly assigned to take either tamoxifen (Nolvadex) or raloxifene (Evista) daily for five years and will have regular follow-up examinations. The maker of tamoxifen, AstraZeneca, and the maker of raloxifene, Eli Lilly and Co., are providing the drugs without charge.

NSABP has established a Web site, www.breastcancerprevention.com, that includes information about the study, and a formula, the Gail model, that allows a woman to estimate her risk of developing breast cancer in the next five years and in her lifetime. The model, developed at NCI and NSABP, has been found to be reliable.

Further information about STAR and a list of participating sites is available from the NCI Cancer Information Service at 800-4-CANCER, or in Canada, the Canadian Cancer Society at 888-939-3333.

In the Cancer Centers:

Memorial Sloan-Kettering Begins $1 Billion Campaign

Memorial Sloan-Kettering Cancer Center has begun its first major capital campaign since the 1980s, with a goal of raising $1 billion over five years to expand the center's programs and facilities.

"We've set an ambitious financial goal so that we can expand our roster of talented scientists and clinicians and our pacesetting programs," said MSKCC President Harold Varmus. "We want to strengthen our technologically advanced research and cancer care facilities for the benefit of patients worldwide. This is happening at a pivotal moment in the institution's history, a time when developments both at Memorial Sloan-Kettering and in the broader scientific community have converged to set the stage for rapid and dramatic progress in the fight against cancer."

Serving as co-chairmen of the campaign are Douglas Warner III, chairman of the Boards of Overseers and Managers, and Louis Gerstner Jr., vice-chairman of the Boards and chairman of the Board of Managers of the Sloan-Kettering Institute.

About half of the funds to be raised will be earmarked for projects related to cancer treatment, such recruiting and training medical professionals and supporting the construction and renovation of patient-care facilities. The other half will help advance basic, translational, and clinical research, and fund a new research laboratory building on Memorial Sloan-Kettering's Upper East Side campus.

Among the projects included in the campaign:

—A new pediatric outpatient facility, connected to a renovated inpatient unit.

—21 new operating rooms with capabilities for imaging and robotic surgery.

—New pathology suites to allow the rapid examination of tumor samples taken during surgery.

—"Bridge" programs designed to connect laboratory investigations to studies involving patients.

—A new 420-foot research laboratory building that will enable the center to expand or develop programs in bioinformatics and computational biology; genetics and epidemiology; developmental biology and cell signaling; chemistry and structural biology; and genomic integrity.

Two years ago, the center began gathering support from board members and other contributors. So far, more than $457 million has been raised, the center said. Among the commitments recorded during the initial "quiet" phase are more than 70 gifts of $1 million and over, including:

—Pledges of $25 million from Dorothy and Jack Byrne and the Byrne Family Foundation to establish the Byrne Family Center for Cancer Biology; $25 million from Sidney Kimmel to establish The Sidney Kimmel Center for Prostate and Urologic Cancers and to support research in the field; and $25 million from The Starr Foundation toward the new surgical center at Memorial Hospital.

—$20 million from William and Alice Goodwin through the Commonwealth Foundation for Cancer Research for the Experimental Therapeutics Center.

—Commitments of $10 million from David Koch to establish an initiative on the immunologic control of cancer, and $10 million from Claire and Leonard Tow for the Claire Tow Pediatric Day Hospital and the Claire Tow Chair in Pediatric Oncology.

—Pledge of $7.5 million from Honorary Co-Chairman of the Boards Laurance Rockefeller, including funds to establish the Laurance S. Rockefeller Chair in Integrative Medicine, and $7 million from an anonymous donor for an initiative on lung cancer research.

* * *

FOX CHASE Cancer Center received $590,000 from Congress to support the American-Russian Cancer Alliance.

ARCA is a consortium of American and Russian cancer research institutes lead by Fox Chase, including University of Maryland-Greenebaum Cancer Center, N.N. Blokhin Cancer Center, and the Russian Research Centre-Kurchatov Institute.

The funds will support two research projects: a tobacco prevention and control program at the Blokhin Cancer Center in Moscow for cancer patients who continue to smoke, and laboratory research to explore the therapeutic use of radioactive isotopes supplied by the Kurchatov Institute in Moscow.

In June 2004, ARCA will be one of the sponsors for the first Russian National Conference on Cancer Prevention to be held in St. Petersburg, Russia. Later in 2004, ARCA will sponsor a conference in Moscow on colon and liver cancers.

Paul Engstrom, senior vice president of population science at Fox Chase, is chairman of the center's ARCA activities.

* * *

OHIO STATE University Comprehensive Cancer Center received an $8 million award from the Ohio Third Frontier program lung cancer research. The award is expected to attract an additional $13.5 million from the commercial partners of the project.

Mike Caligiuri, director of the OSUCCC, leads the project, which includes researchers at Ohio State, Battelle Memorial Institute, and Zivena Inc., of Columbus, and Siemens Medical Solutions, Germany.

Funding Opportunities:
Meeting For TTURC Applicants

NCI, National Institute on Drug Abuse, and National Institute on Alcohol Abuse and Alcoholism will hold an electronic meeting on Nov. 18 for applicants for RFA-CA-04-012:Transdisciplinary Tobacco Use Research Centers.

The meeting will be held via Web cast, from 1-3 pm Eastern. Instructions for viewing the video and a phone number for asking questions are posted at http://tobaccocontrol.cancer.gov/tturc/.

Registration is required with Ruth Stadius at rstadius@masimax.com. Transcript will be posted at http://dccps.nci.nih.gov/communicationcenters/index.html.

Inquiries: Glen Morgan, NCI Tobacco Control Research Branch, tel: 301-496-8585, email gmorgan@nih.gov.

In Brief:

NCI Scientist Wins Award From Thyroid Association

(Continued from page 1)

the University of Florida Shands Cancer Center and chief of the Division of Hematology/Oncology at the UF College of Medicine. He will receive the award Nov. 8 at the annual leadership conference of the society in Cleveland. . . . . **AMERICAN THYROID ASSOCIATION** announced the recipients of its 2003 distinguished awards. **Sheue-yann Cheng**, chief of the Gene Regulation Section, Laboratory of Molecular Biology at NCI, received the Sidney H. Ingbar Distinguished Lectureship. **Yaron Tomer**, associate professor of medicine, Endocrine Division at Mount Sinai, received the Van Meter Award; **E. Chester Ridgway**, head of the Division of Endocrinology, Metabolism and Diabetes, University of Colorado Health Sciences Center and senior associate dean of academic affairs in the School of Medicine, received the Paul Starr Award. **Paul Davis**, research endocrinologist and director of the Ordway Research Institute, a nonprofit biomedical research corporation affiliated with the Wadsworth Center/New York State Department of Health and Albany Medical College, received the Distinguished Service Award. **Lewis Braverman**, professor of medicine and chief of the Section of Endocrinology, Diabetes and Nutrition, Department of Medicine, Boston University School of Medicine and Boston Medical Center, received the Thyroid Pathophysiology Medal. . . . **RICHARD BOXER**, former member of the National Cancer Advisory Board and chairman of the National Health Policy Council, announced a Presidential Candidate Forum on National Health Policy, scheduled for Feb. 15, in Milwaukee. "Wisconsin and all American voters are entitled to hear directly from the Presidential candidates their vision for the future of health care in America," Boxer said. "The debate needs to begin early in 2004 so the electorate can decide who has the best plan to fix our broken system. We need to know how President Bush or his successor will provide an accessible, affordable, quality system. The Forum in Milwaukee will provide Republicans and Democratic candidates an opportunity to present their plan, unfiltered and directly to the voters of Wisconsin and the United States." All Democratic candidates have indicated they will attend.

Copying Policy for The Cancer Letter Interactive

The software that comes with your issue allows you to make a printout, intended for your own personal use. Because we cannot control what you do with the printout, we would like to remind you that routine cover-to-cover photocopying of The Cancer Letter Interactive is theft of intellectual property and is a crime under U.S. and international law.

Here are guidelines we advise our subscribers to follow regarding photocopying or distribution of the copyrighted material in The Cancer Letter Inc. publications in compliance with the U.S. Copyright Act:

What you can do:

--Route the printout of the newsletter to anyone in your office.

--Copy, on an occasional basis, a single story or article and send it to colleagues.

--Consider purchasing multiple subscriptions. Contact us for information on multiple subscription discounts.

What you can't do without prior permission:

--Make copies of an entire issue of the newsletter. The law forbids cover-to-cover photocopying.

--Routinely copy and distribute portions of the newsletter.

--Republish or repackage the contents of the newsletter.

We can provide reprints for nominal fees. If you have any questions or comments regarding photocopying, please contact Publisher Kirsten Boyd Goldberg, phone: 202-362-1809, email: kirsten@cancerletter.com

We welcome the opportunity to speak to you regarding your information needs.

Click Here for
Photocopying Guidelines