THE CANCER LETTER

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GAO Calls For Stronger FDA Enforcement Of Accelerated Approval Followup Studies

By Paul Goldberg

Has the FDA approach to accelerated approval of oncology drugs become dysfunctional?

—It has, says Sen. Chuck Grassley (R-Iowa). A report he requested from the Government Accountability Office tells the agency to force sponsors to conduct studies to demonstrate that drugs approved on surrogate endpoints provide clinical benefits.

—It has, agree the authors of a paper published in the Sept. 10 issue of the Journal of Clinical Oncology. According to the paper, by Elizabeth Richey *et al.*, the proportion of accelerated approvals has dipped by more than

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Interview:

Accelerated Approval In Oncology Shaves A Year Off Development Time, FDA Data Show

The Cancer Letter asked Richard Pazdur, director of the FDA Office of Oncology Drug Products, to respond to recent criticism of the use of accelerated approval in oncology.

The interview questions were submitted by editor Paul Goldberg and responses were received via email.

TCL: *A paper by Richey* et al. *in the Sept. 10 JCO states that the period required for an accelerated approval in oncology is roughly equivalent to the period required for a regular approval. Is this correct? The authors of the JCO paper didn't have the IND dates for about 25 percent of oncology drugs. This information is not public for each drug—but you have it.*

Has the agency attempted a complete analysis of median processing times for all drugs to derive an accurate comparison of times required for an accelerated vs. regular approval in oncology? (Such analysis could be carried out in the aggregate and would not require disclosure of filing dates for each drug.)

What is the actual difference in development times for drugs going through regular vs. accelerated approval in oncology? Is there a way to break it down further, producing the same comparison for biologics?

PAZDUR: FDA submitted a Letter to the Editor responding to the publication by Richie *et al.*, who reported the median development time from IND approval to drug approval for accelerated approval) drugs was similar to that for drugs receiving regular approval. The median development time in

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Changing Endpoints Make Approval A Moving Target

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half since the beginning of the decade. The authors also contend that the time required to process an accelerated approval drug in oncology is roughly the same as the time required for a regular approval.

Is FDA too generous to sponsors of drugs approved based on their impact on surrogate endpoints, as Grassley states? And is it, in fact, decelerating the accelerated approval process, as per the JCO paper?

Responding to critics, the agency says that it has no plans to crack down on sponsors whose drugs have not been confirmed following accelerated approval, and would continue its enforcement efforts on a case-by-case basis.

This is particularly significant, because the 2007 FDA Amendments Act gives the agency a new authority to impose civil, criminal, and financial penalties on sponsors who fail to live up to commitments under accelerated approval.

The GAO report is posted at http://cancerletter.com/special-reports.

Addressing the JCO paper, the agency says that the authors made several miscalculations and that accelerated approval still offers a substantial time advantage. The authors of the JCO paper didn't have access to about a quarter of all Investigational New Drug filing dates since such information cannot be legally divulged by the agency.

The JCO paper estimates that the median development time required for a regular approval for a new molecular entity in oncology was at 7.2 years, compared to 7.3 years for an accelerated approval.

Richard Pazdur, director of the FDA Office of Oncology Drug Products, said FDA's internal data show that the median development time for an accelerated approval was a year shorter than a regular approval, or 6.1 years for accelerated approval vs. 7.1 years for regular.

Besides, the criteria for accelerated approval in oncology have changed in recent years.

"Our changes in acceptance of endpoints for regular approval that were previously considered for accelerated approval and the increasing number of approved indications renders comparisons and conclusions regarding of accelerated approvals difficult," Pazdur said.

An interview with Pazdur appears on page 1.

"Difficult, If Not Impossible," To State Enforcement Criteria

The GAO audit requested by Grassley found that over the years FDA has issued more accelerated approvals in oncology than in any other therapeutic area and that oncology has the highest number of post-approval studies that remain unfinished.

Overall, between 1992—the year the accelerated approval program was created—and 2008, FDA issued 90 accelerated approvals covering 64 different molecular entities. Oncology accounted for 38 of these approvals. It was trailed by HIV/AIDS, with 30 approvals.

Throughout the agency, sponsors have completed two-thirds of required post-approval studies, the report states. But in oncology, the number of outstanding commitments from sponsors was far above the agency-wide average. As of the end of 2008, FDA classified 52 studies of accelerated approval drugs as "open," or not complete. Of those studies, 34 were in oncology.

Unfinished studies are less common in HIV/AIDS, because in that area a typical drug development schema requires two randomized trials, which support both an accelerated and a regular approval. The accelerated approval is granted based on an interim analysis while the studies continue to generate data that lead to the full approval.

Cancer is different. In oncology, sponsors often have obtained accelerated approvals based on large phase II studies, then started over to launch phase III trials.

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Following accelerated approval, the sponsor would be expected to start a confirmatory randomized trial. Sometimes this would be difficult to complete, particularly in the U.S., since the accelerated approval often changes the standard of care.

In recent years, the approval criteria in oncology have changed substantially. As the agency has moved away from demanding survival data for an increasing number of indications, endpoints measuring the delay in progression, which in the past could at best qualify for an accelerated approval, increasingly result in regular approval.

The GAO report makes a single recommendation: FDA should prospectively specify the circumstances under which it would seek to pull drugs off the market.

The agency should "clarify the conditions under which the agency would utilize its authority to expedite the withdrawal of drugs approved based on surrogate endpoints under the accelerated approval process if sponsors either fail to complete required confirmatory studies with due diligence, or if studies are completed, but fail to demonstrate the clinical effectiveness of the drugs," the report states.

Grassley, ranking minority member of the Senate Finance Committee, agreed that the agency should get tough on procrastinators.

"Approvals based on surrogate endpoints can help to get new drugs and treatment possibilities on the market more quickly," he said in a statement. "Once those drugs are on the market, the FDA also needs to monitor the outcomes, and this GAO report indicates that the follow-up hasn't been happening as it needs to be. The report should serve as an impetus for the FDA to improve the post-market surveillance of these drugs, giving patients and their doctors' meaningful information and necessary safeguards."

Though the 2007 legislation gives FDA authority to punish sponsors who are not making good-faith efforts to learn whether their drugs confer benefits, the agency's response to GAO suggests that it will continue to practice regulatory restraint.

"Outside of a situation where a confirmatory trial clearly demonstrates harm to patients (e.g. decreased survival for patients with the accelerated approval drug), FDA believes that each case must be considered on its merits and that the criteria in the existing regulations and Title IX of the FDAAA that authorize civil, criminal and monetary penalties for failure to conduct a postmarketing confirmatory trial) provide FDA with sufficient authority and flexibility to make balanced decisions that protect the program from abuse by sponsors and ensure that patients will continue to have access to needed treatments," the agency said in a response to the GAO report.

Disagreeing with the GAO recommendation to spell out the criteria for enforcement, FDA officials wrote:

"In light of the complexities… and the need for case-by-case assessment, FDA believes it would be difficult, if not impossible, to provide further clarification as to when it might utilize its authority to expedite withdrawal of drugs approved on the basis of surrogate endpoints."

The Case of Iressa: An Example of Restraint

In its response to GAO, FDA focused on its handling of Iressa (gefitinib), an AstraZeneca drug, as an example of restraint.

The agency decided to restrict access to Iressa only because another drug with a similar mechanism of action—Genentech's and OSI's Tarceva (erlotinib)—had been shown to improve survival in non-small cell lung cancer.

The agency noted that Iressa's sponsor pursued confirmatory studies with due diligence.

Also, FDA noted that there were cases where patients appeared to have benefited, and that there was "a suggestion, though not yet proven by controlled clinical trials, that certain patients might be responsive to Iressa due to the genetic markers on their tumor cells while other patients might not respond.

"This was thought to possibly explain the dramatic individual responses seen in some patients and the lack of response seen in others," the FDA response states. "This could also explain the failure to see clinical benefit in a mixed population of patients, many of whom might not be responsive to Iressa due to the genetic makeup of their tumors."

Placing Iressa in a restricted access program is an illustration of a "balanced approach" to handling the drug, the agency said.

"The sponsor of Iressa has continued to investigate the factors that might predict response to the drug, and it is possible that the future clinical trials in properly selected patients will demonstrate clinical benefit," the agency said.

Earlier this year, the European drug approval authorities granted a marketing authorization for Iressa. The decision was based on two non-inferiority trials, one of which was conducted primarily in populations known to respond to Iressa (The Cancer Letter, July 31).

Interview:

Confirmatory Trials Should Be Part Of Drug Development Plan

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their publication for AA drugs was 7.3 years compared to 7.2 years for RA.

The authors acknowledged that 25% of the IND filing dates was missing in their analysis. We noted several inaccuracies in the categorization of drugs (*e.g.,* drugs incorrectly designated as AA or RA).

FDA provided the missing IND development times and corrected inaccuracies noted above. In our analysis, we found the median development times for new molecular entities for novel drugs and biologics receiving AA and RA were 6.1 (range: 3.1 -12.4 years) and 7.1 years (range 3.0 -33.4 years), respectively.

For non-biologic NMEs (82% of the drugs in the dataset and 75% of the AA), the median development time for AA was 5.5 versus 7.3 years for NDAs that received RA. The data set for the biologic NMEs was relatively small comprised of only 9 BLAs (5 AA and 4 RA); therefore, not allowing us to make any meaningful comparisons.

Although the FDA analysis was performed in response to the article by Richie *et al.*, we caution that comparisons of development times are problematic in attempting to evaluate the success of individual factors. The effect of accelerated approval affects only the time to complete a registration trial—this is a limited portion of the total development timeline.

Differences in drug development timelines (filing an IND to drug approval) can be impacted by multiple factors—some more influential than whether an application has received AA.

For example, sponsors may initiate human studies in other countries and open an IND in the US years later. The size, number, and patient accrual rates of clinical trials and completion of manufacturing and other nonclinical requirements may differ between drugs.

Resources allocated by sponsors to specific drugs may vary considerably between sponsors and drugs. Emerging safety issues encountered during any of the phases of drug development can markedly influence the development timeline. Restrictions imposed by other regulatory authorities may also impact drug development.

TCL: *Surrogate endpoints seem to be a moving target. The delay in progression endpoints that would have supported an accelerated approval a decade ago in some indications now support a regular approval. The designs of studies supporting accelerated approval have changed over the past decade as well. Given all this, is there a more accurate way to measure the state of affairs in accelerated approval? Has this been attempted?*

PAZDUR: As noted in your question, the agency's thinking has evolved and we have increasingly accepted PFS (of a meaningful duration) in selected settings as a clinical benefit endpoint, therefore, leading to regular approval.

An example is that five of the six renal cell cancer drugs approvals since 2005 were based on a PFS improvement and received RA. This change in regulatory endpoints supporting RA confounds attempts to derive conclusions such as those purported by Richie *et al.*

Ideally, the impact of accelerated approval on a drug development timeline would be measured by the difference in time between accelerated approval (based on a surrogate endpoint) and completion of the confirmatory trial (demonstration of clinical benefit). This assumes that sponsors would allocate the same resources and commitment to the completion of confirmatory trials as the initial registration trial. We are presently completing an analysis examining this difference.

For the past few years, a number of oncology indications, including supplements, have been approved. We recently reported that between July 2005 (Office of Oncology Drug Products inception) and December 2007 (Food and Drug Administration Amendments Act of 2007 implementation), 53 new indications (including 18 new molecular entities) were approved by our office.

Since drugs approved under AA must demonstrate an improvement over available therapy, sponsors may elect RA development strategies where this requirement does not exist, especially with increasing number of approved indications.

Our changes in acceptance of endpoints for RA that were previously considered for AA and the increasing number of approved indications renders comparisons and conclusions regarding of accelerated approvals difficult.

TCL: *Not much has been said by the agency in public on the subject of monitoring the sponsors' conduct of studies justifying accelerated approval since the Nov. 8, 2005, ODAC. What is the current thinking on getting companies to perform these studies? How does the FDA experience—or its authority to mandate studies under accelerated approval—compare with the European experience?*

PAZDUR: Under AA, sponsors must complete the

post-approval confirmatory trials to demonstrate clinical benefit with "due diligence." There is no specified time period to complete these trials stipulated in the regulations.

FDA assumes the responsibility to monitor that these trials are completed in a timely fashion. This is in contrast to the EMEA conditional approval regulations where the conditional marketing authorization is of one year duration and must be renewed annually.

Financial penalties may be imposed for non-compliance with post-approval studies. This is a relatively new program compared to the US accelerated approval program.

As you note, we have had ODAC meetings to discuss the timely completion of AA confirmatory trials. At other ODAC meetings, I have drawn attention to confirmatory trials that have not been completed, especially when supplemental indications are being sought for the drug. The oncology divisions have had multiple non-public meetings with sponsors to address the timeliness of completion of these studies.

FDA has published articles on approaches to accelerated approval including the importance of initiation of confirmatory trials prior to drug approval. Realizing that once a drug is approved, completion of a confirmatory trial in the approved indication may be difficult, FDA has allowed confirmatory trials to be completed in earlier stages of the disease or in related diseases.

TCL: *The GAO report states that most of the studies that remain to be completed under accelerated approval are in oncology. Why is this the case?*

PAZDUR: The majority of AA applications are reviewed in either Oncology or Anti-Viral divisions. The clinical trial paradigm for AA in AIDS (Anti-Viral Division) differs from oncology.

With the AIDS AA paradigm, two randomized trials with several hundred patients in each arm are submitted for AA consideration. AA is granted on reduction in viral load at 24 weeks and conversion to RA is based on viral load at 48 weeks in the same trial.

We have smaller patient numbers enrolled in AA oncology trials. Many AAs are in disease settings with very limited patient numbers. Frequently, AA is granted on a single arm trial using response rate as the regulatory endpoint. New randomized trials are subsequently performed examining a clinical benefit endpoint, such as overall survival.

These different approaches to confirmatory trials probably explains the GAO findings.

In our public discussions and publications, we have emphasized that confirmatory trials should be part of a comprehensive drug development plan and discussed early with the Agency prior to AA. These trials should preferentially be initiated and enrolling patients prior to AA.

We have also suggested that trials similar to the AIDS AA paradigm be used in oncology. For example, AA could be granted on the findings of an interim analysis of a randomized trial using a surrogate endpoint (*e.g.*, response rate) and conversion to RA be made when an overall survival improvement is determined at the final analysis.

TCL: *I understand FDA has greater leverage in mandating studies for animal drugs approved under the conditional approval mechanism. Is this correct?*

PAZDUR: Conditional approval in FDA veterinary medicine is an interesting program, especially with the regulatory restrictions placed on sponsors and drugs while "effectiveness" studies are being completed. The veterinary medicine conditional approval program effectiveness standard is "a reasonable *expectation* of effectiveness."

In the veterinary medicine program, conditional approval must be renewed annually and sponsors have up to five years to complete effectiveness studies to full NADA (New Animal Drug Application) standards. There is no "extra label" (off-label) use permitted while the drug has conditional approval. There are also labeling restrictions.

The drug name is altered by having "CA" (conditional approval) added after the product name ("Name—CA"). A statement is added to labeling that "extra-label use of this drug is prohibited" and all labeling components have the statement that the drug is "conditionally approved by FDA pending a full demonstration of effectiveness under application number XXX."

These labeling restrictions are removed when effectiveness standards for a full NADA are achieved.

TCL: *Under the FDA Amendments Act of 2007, the agency has the authority to impose fines on drug sponsors or limit drug distribution when postmarketing commitments are not completed. What is the status of implementation of these new authorities? Under what circumstances would FDA consider applying sanctions against sponsors who don't live up to their commitments under accelerated approval?*

PAZDUR: The Food and Drug Administration Amendments Act of 2007 provided the FDA the ability to impose fines for failure of Sponsors to conduct certain post-marketing studies and clinical trials, including those

clinical trials that would be considered confirmatory studies to demonstrate clinical benefit under AA. FDA is presently working on the implementation of this new authority.

FDA News:

Arzerra Approved For Chronic Lymphocytic Leukemia

FDA approved Arzerra (ofatumumab, GlaxoSmithKline) for patients with chronic lymphocytic leukemia whose cancer is no longer being controlled by other forms of chemotherapy.

Arzerra is a monoclonal antibody that binds to a specific protein found on the surface of both normal and malignant B cells, making the cells more susceptible to immune system attack.

The product was approved under the FDA's accelerated approval process, which allows earlier approval of drugs that meet unmet medical needs. Products may receive accelerated approval based on a surrogate endpoint, such as a reduction in the size of the tumor or decrease in the number of cancerous white cells or in an enlarged spleen or lymph nodes. These indirect measures for clinical outcomes are considered reasonably likely to predict that the drug will allow patients to live longer or with fewer side effects of a disease.

"The approval of Arzerra illustrates FDA's commitment to using the accelerated approval process to approve drugs for patients who have limited therapeutic options," said Richard Pazdur, director of the Office of Oncology Drug Products in the FDA's Center for Drug Evaluation and Research.

The accelerated approval process requires further study of the drug. The manufacturer is currently conducting a clinical trial in CLL patients to confirm that the addition of Arzerra to standard chemotherapy delays the progression of the disease.

Arzerra's effectiveness was evaluated in 59 patients with CLL whose disease no longer responded to the available therapies. The product's safety was evaluated in 181 patients in two studies in patients with cancer. Common side effects included a decrease in normal white blood cells, pneumonia, fever, cough, diarrhea, lower red blood cell counts, fatigue, shortness of breath, rash, nausea, bronchitis and upper respiratory tract infections.

The most serious side effects of Arzerra are increased chance of infections, including progressive multifocal leukoencephalopathy.

NCI News:

Centralized Review Expedites Trial Approval, Study Finds

A Central Institutional Review Board for cancer clinical trials that was created by NCI in 2001 helps trials start more quickly by shaving about a month off of local review times, according to a study published in the Oct. 19 Journal of Clinical Oncology.

The study was performed by scientists at the Veterans Affairs Palo Alto Health Care System and Stanford University School of Medicine, with assistance from NCI.

Over the past 40 years, more than 1,700 institutions in the U.S. have enrolled up to 20,000 patients annually in phase III clinical trials coordinated by NCI and have used separate IRBs to monitor research involving patients. Federal regulations require that most NIH-funded clinical trials be monitored by an IRB.

To determine whether a new treatment is safe and more effective than current treatments using clinical trials is a lengthy process that can take up to 10 years and cost more than $1 billion, in some cases. Many researchers have complained that administrative requirements, including IRB oversight, are delaying the release of new treatments. One solution NCI proposed was to form a CIRB to conduct IRB review of large, multi-site oncology trials.

"Mounting a CIRB that is nationwide in scope has been challenging for NCI due to the complexity involved in assuring high-quality protection for study participants while attempting to speed the process," said Jeffrey Abrams, associate director of NCI's Cancer Therapy Evaluation Program. "For all the volunteer reviewers and participating sites, this study provides objective confirmation that a centralized approach significantly improves the overall process for participants in multi-site trials."

The study assessed whether use of NCI's CIRB was associated with lower effort, time, and cost in processing adult phase III oncology trials, which are the gold-standard of trials for validating whether a therapy becomes a new standard of care. Early phase trials (phase I and II) and pediatric trials were not included in the analysis due to the lower patient enrollment populations required.

Clinical trial sites that are not enrolled with the CIRB must have their local IRB conduct a full board review as they would with any research study. Sites enrolled with the CIRB have their local IRB conduct a facilitated review, which is a review category requiring

only that the local IRB chairman or designee signal acceptance of the CIRB's review.

To determine whether the CIRB was achieving the hoped-for efficiencies, researchers compared clinical trial review at sites affiliated with the NCI CIRB with the review at unaffiliated sites that used their local IRB. Oncology research staff and IRB staff were surveyed to understand differences in effort, timing and costs of clinical trial review.

CIRB affiliation was associated with faster local review (about 34 days) and about six hours less research staff effort. Many clinical trials sponsors value faster and more predictable reviews and often pay commercial, fee-for-service, central IRBs to perform reviews.

Affiliation with NCI's CIRB was also associated with a savings of $717 per initial review, of which about half was associated with time savings for research staff and the remainder was associated with savings for the IRB staff.

Overall, the program resulted in a net cost of $55,000 per month for NCI, but the CIRB could actually save costs if more sites were to use the CIRB. Moreover, this net cost estimate does not include the benefits of bringing new cancer therapeutics to market more quickly.

"Efforts are underway to expand enrollment in the CIRB and to encourage sites to use the CIRB to minimize administrative inefficiencies," said lead researcher Todd Wagner, health economist, VAPAHCS and Stanford University. "Based on our research, increased efficiencies and net savings are likely."

Cancer Screening:

M.D. Anderson Posts Its Own Risk-Based Screening Guide

M. D. Anderson Cancer Center released risk-based screening guidelines for breast, cervical, and colorectal cancers.

Available on M. D. Anderson's Web site, the recommendations translate best practices in cancer prevention employed at M. D. Anderson into accessible guidelines the public can follow, with risk categories identified and information about when to begin and discontinue screening exams.

"Cancer screening is not one-size-fits-all," said Therese Bevers, medical director of M. D. Anderson's Cancer Prevention Center. "Our new risk-based recommendations are markedly more personalized and precise, offering detailed guidance than what has previously been made available to the public here or by other cancer organizations."

Cancer screening recommendations have been targeted largely to individuals at average risk for developing cancer based on characteristics such as age, family history, or genetic predisposition. However, average risk was not previously defined and recommendations for individuals at increased or high risk were not outlined.

The cancer center's screening guidelines define risk and offer recommendations for those at increased and high risk of developing cancer. For example, there are five different sets of screening recommendations for those at increased risk for breast cancer; four categories of age-based risk recommendations for cervical cancer; and for colorectal cancer, there are three categories defining those at increased risk and three categories defining those at high risk.

The risk categories and related guidelines were developed by multidisciplinary panels of M. D. Anderson disease site experts across several areas, including: medical oncology, surgical oncology, cancer prevention, imaging and others. Risk-based screening guidelines for prostate, liver, skin, endometrial and ovarian cancers are currently in development and a new online risk assessment tool integrating the new screening guidelines will be launched on the M. D. Anderson Web site in early 2010.

The guidelines offer the following recommendations:

—**Breast Cancer:** Starting at age 20, women at all risk levels should practice breast self-awareness by being familiar with how their breasts look and feel and immediately reporting any changes to their doctor. Women aged 40 years and older at average risk should get annual mammograms and breast exams.

For women at increased risk, the type and frequency of exams—including clinical breast exams, mammograms and breast MRI—depend on factors putting them at increased risk, including: history of radiation treatment to the chest; genetic predisposition; diagnosis of lobular carcinoma in situ; Gail Model score of greater than 1.7 percent; or family history.

—Cervical Cancer: For women at average risk, M.D. Anderson recommends that women under age 21 get a liquid-based Pap test within three years of initiating vaginal intercourse. She should continue to have Pap tests annually until she has had three consecutive negative test results. After that, M. D. Anderson recommends screening every two years unless she is at increased risk of cervical cancer based on risk factors, including: history of cervical cancer or severe cervical dysplasia;

persistently testing positive for HPV; exposure to diethylstilbestrol before birth; HIV infection; or an immune system that does not function properly.

Beginning at age 30, adding HPV testing is a preferred option to the Pap test, and if both are negative, a woman may go to every three years unless she is at increased risk based on the risk factors cited above or unless the optional HPV test was not done.

—Colorectal Cancer: M. D. Anderson recommends a colonoscopy every 10 years (preferred screening), a virtual colonoscopy every five years, or a yearly fecal occult blood test for men and women aged 50 years and older who are at average risk. For men and women at increased or high risk, the type and frequency of exams—including colonoscopy and flexible sigmoidoscopy—depend on the following factors: personal history of precancerous (adenomatous) polyps; personal history of colorectal cancer; family history of colorectal cancer or precancerous (adenomatous) polyps; genetic diagnosis of Familial Adenomatous Polyposis; genetic history of Hereditary Nonpolyposis Colorectal Cancer or a clinical history suggesting such; or inflammatory bowel disease (ulcerative colitis or Crohn's disease).

In the Cancer Centers:

CANCER THERAPY & RESEARCH CENTER at The University of Texas Health Science Center at San Antonio said **Tyler Curiel** has stepped down as executive director and three cancer specialists have been chosen to lead the center. The changes were announced by **William Henrich**, president of the Health Science Center. Curiel, a professor of hematology and medical oncology, expressed a desire to devote full attention to laboratory and clinical research. Henrich commended Curiel for his leadership in securing three-year renewal of CTRC's designation as an NCI cancer center, which came with $5.4 million in funding through 2012.

Ian Thompson will serve as CTRC's interim executive director. He is chairman of the Department of Urology and leads the Genitourinary Cancer Clinic, as well as three major NCI grants. Serving as the interim deputy director will be **Thomas Slaga**, professor of pharmacology, co-leader of the CTRC's Cancer Progression and Development program and director for research for the Health Science Center's Regional Academic Health Center in Edinburg, Texas. **Susan Mooberry** was named interim director of the Institute for Drug Development. She is a professor with cross-appointments in pharmacology, medicine and biochemistry, and is co-leader of the Experimental Therapeutics Program. Mooberry succeeds **Francis Giles**, professor of hematology and medical oncology, who stepped down from his dual role as director of the IDD and deputy director of the CTRC. He will continue his clinical and research work. . . . **FRED HUTCHINSON CANCER RESEARCH CENTER** received a $500,000 grant from the U.S. Agency for International Development to aid in the construction of the first American cancer clinic and medical-training facility in Africa. Additional federal and private funding is being sought to complete the $1.4 million project and to construct an adjacent clinical and laboratory research building. Hutchinson physician-scientist **Corey Casper** is the scientific co-director of the Uganda Program on Cancer and Infectious Diseases, a research effort begun in 2004 between Hutchinson and the Uganda Cancer Institute in Kampala. The goals of the collaboration, co-led by **Jackson Orem**, director of the Uganda Cancer Institute, are to better understand the link between infectious disease and cancer; improve access and delivery of clinical care to patients with infection-related cancers in the U.S. and Uganda; and train American and Ugandan physicians and scientists to combat these cancers. . . . **CITY OF HOPE** received two grants totaling a $32.5 million from the California Institute for Regenerative Medicine for research into tumor targeting stem cells to deliver cancer killing agents specifically to brain tumors and research into an AIDS-related lymphoma therapy that may provide patients with permanent immunity to HIV. **Karen Aboody**, associate professor in the departments of neurosciences and hematology and hematopoietic cell transplantation, will lead a four-year study supported by an $18 million grant to research a novel treatment for high-grade glioma. City of Hope will collaborate with Childrens Hospital Los Angeles on the study. Co-PIs are **Larry Couture** and **Jana Portnow**. A $14.5 million grant will support AIDS research by a multidisciplinary team of investigators led by **John Zaia**, the Aaron D. and Edith Miller Chair in Gene Therapy, and chairman of virology, City of Hope. His grant submission received the highest evaluation score among all of the submissions CIRM received for this round of funding. . . . **UNIVERSITY OF ARKANSAS FOR MEDICAL SCIENCES'** Myeloma Institute for Research and Therapy received competitive renewal of a program project grant amounting to $19.5 million over five years. **Bart Barlogie** is the principal investigator. Project leaders include **Frits van Rhee**, **John Shaughnessy**, **Shmuel Yaccoby**, **Joshua Epstein**, and **William Bellamy**.

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