THE CANCER LETTER

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*Bioinformatics*

## How NCI's Plans for Software Giveaway Sank In Scientific and Legal Disputes

*By Paul Goldberg*

*This is the second article of a series examining the NCI efforts to create a single biomedical informatics system for all its clinical trials.*

NCI Director Andrew von Eschenbach was a man with a plan: eliminate "suffering and death due to cancer" by the year 2015.

To accomplish this, he started development of a weapons system so massive, and so ambitious, so expensive that it fully warranted the acronym that vaguely evoked the sound of heavy impact you might find in comic book: caBIG!

caBIG was going to make data available to cancer researchers regardless of their place in the war effort.

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*The Duke Scandal:*

## "We Deeply Regret" The Effect on Science; Authors—Including Potti—Retract NEJM Paper

*By Paul Goldberg*

Duke University scientists retracted a paper in the New England Journal of Medicine in which they claimed to have developed a methodology for predicting the course of disease in lung cancer patients.

The retraction, published by NEJM online March 2, reads:

"We would like to retract our article, 'A Genomic Strategy to Refine Prognosis in Early-Stage Non–Small-Cell Lung Cancer,' which was published in the Journal on Aug. 10, 2006.

"Using a sample set from a study by the American College of Surgeons Oncology Group (ACOSOG) and a collection of samples from a study by the Cancer and Leukemia Group B (CALGB), we have tried and failed to reproduce results supporting the validation of the lung metagene model described in the article.

"We deeply regret the effect of this action on the work of other investigators."

The retraction was signed by all authors—including lead author Anil Potti, who resigned from Duke in the midst of probes into his science and credentials (The Cancer Letter, July 16, 2010).

The controversy began when two biostatisticians—Keith Baggerly and Kevin Coombes, both of MD Anderson Cancer Center attempted to

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## caBIG Cost $350 Mil, Not $200 Mil., BSA Committee Review Determines

(Continued from page 1)

No expense was spared. Recently, officials who run caBIG said to The Cancer Letter that over six years, the institute poured $200 million into the informatics venture (The Cancer Letter, Feb. 25).

Though staggering, this figure turns out to have been too low. Actual expenditures exceeded $350 million from fiscal year 2004 to 2010, a subcommittee of the NCI Board of Scientific Advisors said in a report presented at a meeting March 1.

Averaging $50 million a year, this is enough to cover the annual costs of 100 R01 grants. Alternatively, you could support three clinical trials cooperative groups at current funding levels.

caBIG money wasn't spent entirely on research and development. According to the BSA report, management costs added up to $60 million. A big share of these funds went to NCI contractors, including SAIC and Booz Allen Hamilton.

If the caBIG products worked, that could have been almost justifiable, but after interviewing 59 individuals at 46 institutions, the BSA subcommittee found that the tools were typically not functional.

BSA unanimously accepted the subcommittee's report, which included the recommendation to conduct "a thorough audit of all aspects of caBIG budget and expenditures to identify unspent funds." The executive summary of the report and the group's recommendations appear on page 8. A copy of the report is posted at http://www.cancerletter.com/categories/documents.

A story about the document and the board's discussion of future directions in informatics will appear in The Cancer Letter next week.

**Focusing on Data Capture**

Unlike the BSA subcommittee's investigation, which reviewed the caBIG program comprehensively, The Cancer Letter's investigation focused on the program's key element: the effort to adopt a single data capture system for all NCI-supported clinical trials.

The objective of the investigation was to examine the scientific challenges facing this effort and to understand how it got bogged down in a contracting dispute.

• The scientific challenge is fundamental. Critics say that the institute should have focused on developing data standards instead of focusing on selecting and purchasing common data capture software.

• The legal challenge comes from software developer Velos Inc., of Fremont, Calif., which argues that NCI had wrongly decided to award a $24.3 million contract to New York-based Medidata Solutions Inc. Twice, the General Accounting Office overruled NCI's award, and in January Velos filed a third complaint. The agency's decision is expected in May.

In legal filings, Velos contends that its system was selected by a review panel convened to guide selection of available technologies. However, the company argues that it was passed over because its software competes head-on with the NCI-developed products called the caBIG Clinical Trials Suite.

GAO's rulings in the contract dispute are posted at http://www.cancerletter.com/categories/documents.

NCI's pick—Medidata Rave—has been used primarily by pharmaceutical companies and contract research organizations. It focuses on capturing data and doesn't compete with the products caBIG spent millions to develop, informatics experts say.

NCI's vision was to provide free data capture and supporting software to everyone involved in clinical trials. Critics argue that the NCI software development venture has led government scientists, bureaucrats and contractors into the software development business, where they aren't equipped to compete. Critics say that many of caBIG's programs aren't usable.

"Sometimes we are asked 'Who is using everything in caBIG?'" Kenneth Buetow, director of the NCI Center for Biomedical Informatics and Information Technology and chief architect of the institute's informatics systems,

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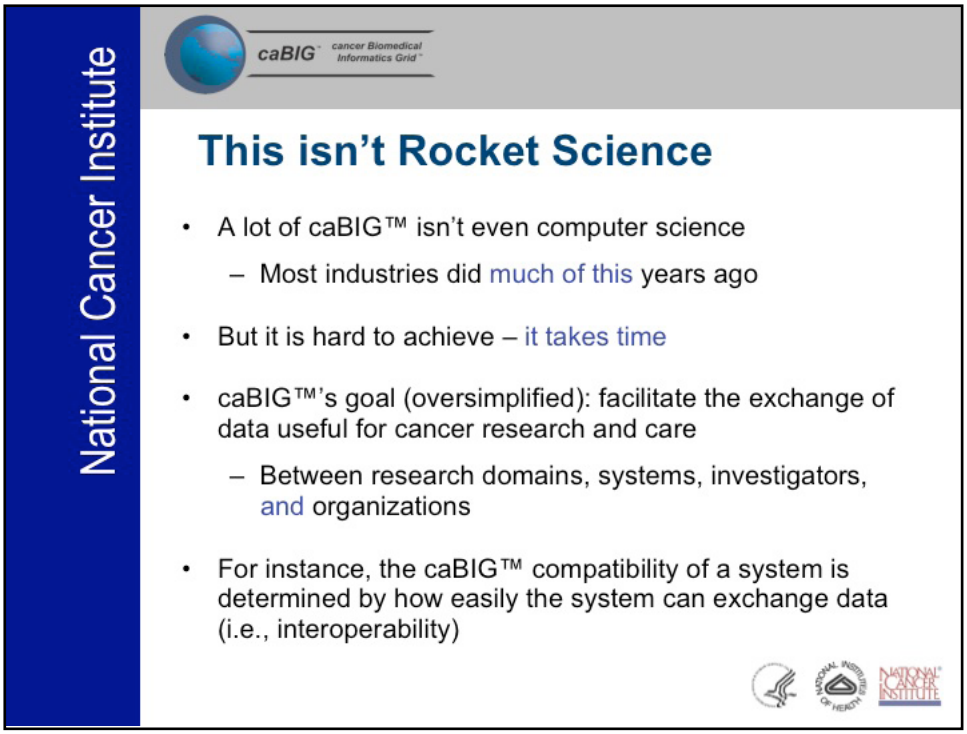
said in an email to The Cancer Letter before the March 1 meeting of the BSA. "While there may be institutions that have a need for the total 'menu,' caBIG capabilities are modularly designed to meet the needs of a diverse community.

"For example, caBIG capabilities are being used by 56 of the 65 NCI-designated Cancer Centers; no two of those centers have had precisely the same needs or use precisely the same set of caBIG resources," Buetow wrote in the email. "Similarly, 30 of the NCI Community Cancer Center Program participants use caBIG (in 30 different configurations of usage.) Similarly, organizations in fifteen different countries use some aspects of caBIG—again, in customized ways that address their particular needs."




**The $350 million program produced many glossy slides to describe future harmonization of all cancer research efforts.**

Sources at cancer centers say that many of them are indeed using the caTissue Suite, a caBIG tool for biospecimen inventory management, tracking, and annotation.

However, commercial applications are rapidly expanding into this market, sources said.

Overall, Buetow said he stands by the NCI's original bioinformatics plan.

"An underlying premise of caBIG was that individual research functions along the biomedical continuum from discovery through clinical development of products through clinical care and back to discovery research needed to be connected, in order for the data/results of one step to inform/drive the subsequent step (a "virtuous circle" that is known by the Institute of Medicine and others as the Rapid Learning Healthcare System.)," he wrote. "There are countless functions that must therefore be enabled (all based on a set of common standards), plus a vast (and growing daily) number of diverse data sets that researchers need tools to use productively."

**A User's Experience**

Only one cancer center in the U.S. uses the entire caBIG clinical trials suite, and the anatomy of that center's decision to use NCI-promulgated tools illustrates the initial appeal of the institute's software development effort and the logistical obstacles it created.

The University of Arkansas for Medical Sciences Winthrop P. Rockefeller Cancer Institute was the perfect adapter.

The institution isn't enormous, and it had the luxury of starting from scratch. In 2006, the center had only two electronic medical record systems for inpatient and outpatient services.

"We had nothing," said Cheryl Lane, director of Information Technology Research and Development Systems. "We had individual investigators keeping patient information spreadsheets, keeping data information on their laptop computers, no standardization."

Also, the institution had no budget to explore available technologies and no money for initial investment in data systems.

In 2006, Lane and Laura Hutchins, director of the hematology/oncology division, went to a caBIG annual meeting to examine software available to support clinical trials.

"It wasn't an overwhelming up-front millions and millions of dollars investment to get started," Lane said. "It evolved from a small tool to a group of tools.

"There is no cost for the tools period because they are open source. The cost to our institution is the

personnel to do the customization and maintenance. But you are going to have some of that with any vendor system."

Each tool required up to a year of work, and on top of this, the center has developed a program that connected research tools to billing. Though the institution's systems function well, they require a staff of 15.

Reflecting on the experience, Lane says the NCI's plan was logical: have some institutions develop open-source tools and share them with any institution that wants them.

"If you have your own tools, as long as you can match to the standards that we are designing, you can use those tools," Lane said. "But we are also offering those to you even if you don't have any of your own. Just like in our case, we had nothing when we started."

Lane said her center was anxious to use the caBIG products.

"But then the problem for us was that what would be released was not really ready," she said. "It just wasn't up to the standards that vendor products would normally be." This work was done with minimal financial support from NCI, officials say.

The Arkansas cancer center will face a new challenge if NCI goes through with its plans to deploy the Medidata system. Along with the UAMS, the cancer center uses another data capture system, OpenClinica, and officials say that they would be unable to make the unilateral decision to switch from this open-source tool.

This means that the center would have to operate two data capture systems—or develop a way for OpenClinica to work with Medidata.

The center's IT experts say they are up to the challenge of integrating the systems, but others in the field say that this would be no small task (The Cancer Letter, Feb. 25).

**Initial Focus: Cooperative Groups**

NCI's efforts to institute a single data capture system initially focused on cooperative groups.

Yet, cooperative groups differ fundamentally from cancer centers. Centers run more trials than groups and they need to integrate data capture with a variety of other functions.

NCI's selection of Medidata—or, for that matter, selection of any other single data capture system—would create a major new challenge to their operations.

Some centers argue that the choice of Medidata is more disruptive than other potential choices. The Medidata system hasn't been used by centers, which have mosty relied on Velos, OnCore and homegrown systems. Velos said it serves 55 cancer centers, including 18 NCI-designated cancer centers.

Before vying for the caBIG contract, Medidata was used mostly by drug companies, pharmaceutical contract research organizations and industry consultants. Now, its customers also include City of Hope and the Mayo Clinic.

The Velos-Medidata dispute can be traced back to October 2007, when NCI issued a request for proposals for off-the-shelf data capture and management systems to support all NCI clinical trials.

The purchasing was handled by the National Business Center of the U.S. Department of the Interior on behalf of NCI. Though the difference between cancer and management of federal lands is vast, it is legal for government agencies to award each other's contracts.

In the evaluation, both Velos and Medidata received "Very Good" scores, and in May 2008, Velos was notified that it had won the award based on technical evaluation and price. The company and officials at Interior needed to work out some technical provisions on licensure. However, these negotiations ended, and in August 2008, Interior awarded the contract to Medidata.

Velos callenged the award by petitioning the U.S. Government Accountability Office, an arm of Congress that adjudicates contract disputes. The GAO conducted a two-day hearing and in a decision in November 2008, it recommended that the Request for Proposals be reconsidered and Velos reimbursed for pursuing the protest.

GAO determined that the Interior and NCI "conducted prejudicially misleading discussions," creating the impression of accepting a Velos postion on licensing provisions of the agreement, then shifting its position.

NCI and the Interior complied, but in August 2009 they once again awarded the contract to Medidata. Again, Velos protested, and GAO held another two-day hearing. In February 2010, the agency once more ruled in favor of Velos.

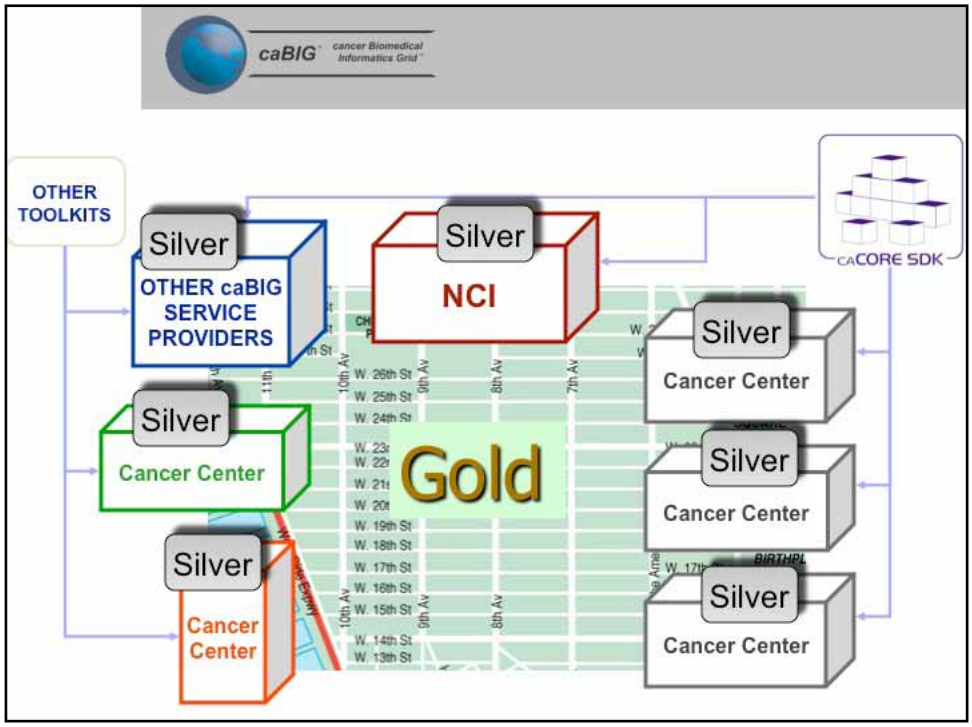
This time, GAO challenged the technical assessment of the two systems. Instead of using an evaluation panel, NCI used the evaluation of a consultant who was not a panel member.

Also, the interior dinged Velos for failing to provide a more current Dun & Broadstreet report on its credit. In GAO's view, this was unreasonable, because the contracting officer had no reasons to question financial viability of Velos.

In November 2010, the Interior notified Velos

that for the third time the contract would be awarded to Medidata. This time, the letter stated that Velos received an overall rating of "Very Good," while Medidata's rating was "Excellent." It's not clear whether another technical evaluation was held, because in two earlier efforts, both products were rated "Very Good."

"Although the Velos price was less expensive than Medidata, the government found in its tradeoff analysis and best value determination that Medidata represented the best overall value to the government," states the Nov. 4, 2010, letter from the Interior to Velos president and CEO McIlwain.




**caBIG officials said their strategy was inspired by development of New York: "from an ad hoc series of neighborhoods to an increasingly ordered grid. "**

The documents are posted at http://www.cancerletter.com/categories/documents.

In a third appeal to GAO, Velos argued that Interior has now subjected Velos to technical requirements not stated in the RFP. "By steering the contract away from Velos and to Medidata, caBIG leadership has sought to bolster the position of caBIG Clinical Trial Suite," McIlwain wrote in a letter to Varmus. "Conversely, had Velos been selected, the need for caBIG Clinical Trials Suite, would be greatly diminished."

**Appeal Goes On**

Last December, the Interior asked GAO to dismiss the third protest by Velos because "the agency has decided to cancel the underlying procurement, thereby rendering the protest academic."

The Cancer Letter asked NCI officials to explain whether they had abandoned plans to switch all trials to a unique system.

In an interview at the time, Buetow said the plans to adopt Medidata were still on. He said the institute had obtained a license to use the data capture system, and suggested that the focus would now be on its installation and support.

"The mechanism by which we received the licenses was the original procurement," he said in a three-way on-record conversation that included an NCI spokesman. "The way the procurement played out—it had to do with the sequence and timing of protests—the government received particular goods and services that we have the right to use.

"So we plan to move forward with the use of those goods and services that were procured," Buetow continued. "But because of subsequent protest, we decided to move forward with different mechanisms to support the use of those licenses and other infrastructure."

Buetow confirmed that the contract or procurement would be done through NIH. "We want to move this activity within the NIH and HHS," he said. "One of the reasons I don't want to give a single answer is there may be multiple answers to this question."

Responding to follow-up questions from The Cancer Letter in writing, NCI officials said that the Cancer Therapy Evaluation Program "is planning to support the use of this software as part of a centralized IT network for the Clinical Trials Cooperative Groups."

The document, dated Jan. 17, contained no attribution. It continued:

"At this time, NCI is not supplying software maintenance, technical support or local installation support broadly across the NCI clinical research enterprise. However, as noted above, NCI CTEP is planning to support the use of this software as part of a centralized IT network for the NCI Clinical Trials Cooperative Groups. Organizations that do not want

to wait for NCI deployment support should make private arrangements for deployment, maintenance and technical support at their own expense directly with Medidata."

The Cancer Letter provided these responses to Velos officials. The documents were forwarded for the purpose of obtaining on-record responses in order to obtain their comments for this story.

Velos officials responded by filing another protest to GAO.

"The statements from the NCI make it clear that the NCI and the Department of Interior personnel misrepresented the facts to the Government Accountability Office to get around the protest," Velos President and CEO McIlwain said to The Cancer Letter. "The GAO was told the Department of Interior 'decided to cancel the underlying procurement, thereby rendering the protest academic.'

"This, in turn, prompted the GAO to dismiss the latest Velos protest. Based on NCI statements given to The Cancer Letter, the truth is that the underlying procurement is very much proceeding. The correct statement to the GAO would have been 'to get around the Velos protest and the GAO rulings in favor of Velos, we're going to cancel the procurement through Department of the Interior and fulfill the underlying procurement through other channels.' The GAO's recommendations were essentially ignored."

Velos filed its third GAO protest Jan. 31.

After the filing of the latest protest, NCI resubmitted an updated version of written responses to questions from The Cancer Letter. The newer version didn't mention the CTEP plans. Both versions of the document are posted at http://www.cancerletter.com/categories/documents

**Redesigning Silos?**

For cancer centers, the adoption of Medidata would create the need to type in the data that needs to be used in both the research system and the housekeeping systems.

As battles over the data capture systems intensified, many IT experts at cancer centers wondered whether institute officials fully understood the implications of their actions—and whether they were knowingly painting themselves into a corner.

Did NCI really expect cancer centers to abandon their multi-million-dollar investments in fully functional data capture systems?

This controversy baffles Roy Jones, professor at the Department of Stem Cell Transplantation at MD Anderson Cancer Center.

Jones said Medidata makes sense in the context of cooperative groups, which may initiate 15 or 20 trials a year. But it doesn't work as well at a gigantic center like MD Anderson, which initiates about 1,000 clinical studies a year.

"In addition to electronic data capture, we need a trial management system that takes a protocol from the time of conception through data collection through reporting, the entire protocol life cycle," said Jones, who headed the committee that chose Velos for MD Anderson. Jones is also a member of the oversight board for the clinical trials management system workspace of caBIG.

MD Anderson's evaluation of possible bioinformatics systems took two years to complete.

"Cooperative groups manage a small number of trials, and they are totally about electronic data capture," Jones said in an interview. "They want discreet information from each center about the patients that get put on studies, but they don't have to do a lot of trial management, because they don't have a lot of trials to manage.

"A cooperative group may have a trial of 4,000 patients comparing two breast cancer therapies. Here at MD Anderson, such trials are only 10 to 15 percent of all our trial entrants. Here we have 1,000 new trials every year. And most of our trials involve 15 to 50 patients who are being treated with a novel therapy. And since we have 1,000 of them we have a problem that is much more fundamental than electronic data capture."

A cooperative group may need 20 sets of forms to collect information for the trials. MD Anderson needs 1,000 sets of forms.

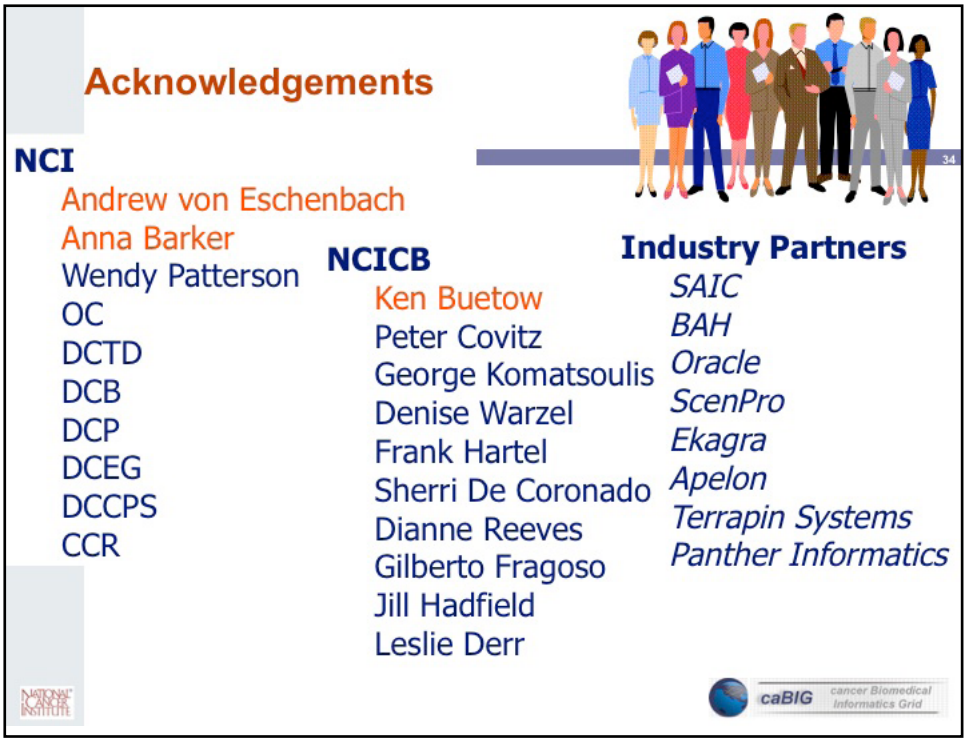
"We need a system that can handle the writing of the trial, submitting it to the IRB, submitting it to grants and contracts to work out the financial aspects of it, the auditing of the information," Jones said. "We need all of that to do the total job at MD Anderson. Medidata not only can't do the kinds of things we talk about, but it has a greater degree of inflexibility. We looked, we did a two-year-long RFP to identify a product that would work for us, and Medidata was one of the finalists. But we realized that when we found out that it took often several months to design the forms for a given trial, if we have 1,000 trials a year, we can't do that. We have to design the forms in less than a week."

Jones said the institution chose Velos and will continue using it even if NCI successfully awards a grant to Medidata.

"My solution is to stop all the arguing," Jones

said. "Get these groups to cooperate, make both their products available, let the customers decide what they want, and make each comport to the caBIG data standards concepts so that if you put data in one it's freely viewable in the other. But let interoperability drive this. We simply have to move forward in this area. We can't continue to have siloed data streams.

"The big picture issue is way beyond Velos and Medidata. The issue is not application. It's interoperability. We have to be able to exchange data. And to exchange data is to describe data in a uniform way.




**A caBIG slide acknowledges contributions of NCI officials--and contractors.**

Daniel Sargent, a biostatistician at the Mayo clinic and Cancer and Leukemia Group B, said that, with customization, Medidata meets his institution's needs for both data capture and management of trials.

"We are installing Medidata Rave for all research clinical trials at Mayo Clinic," he said. "That's oncology, cardiovascular, neurology, everything. Mayo felt that this was the best tool and met our needs for both data collection and data management. We evaluated it comprehensively for both and we went ahead and signed an institutional agreement with Medidata in that regard."

Until signing a deal with Medidata, Mayo used homegrown computer systems, which are now being rebuilt around the Medidata system.

"There is no software that's just pure plug-and-play that is going to interact with every existing institutional system," Sargent said. "We are building integrations with multiple internal systems, but our belief was that we would have to do that no matter what product we ended up buying. We are building many interfaces, but that was expected and would have been the case for whatever software we would have chosen."

The need to build interfaces is not unique to Mayo.

"Until medical institutions constrain their number of systems with the number of different EMRs that are out there, with the number of different billing systems that are out there, the number of biospecimen tracking systems that are out there, these are integrations that you are going to have to build," Sargent said. "It's hard work to do that, but it's most of the time out of the research community's purviews. Those are clinical applications that are not standardized right now."

Mayo's situation was simpler than some, Sargent said.

Until signing with Medidata, the hospital didn't use a commercial informatics system.

"I certainly understand the challenges of an institution that's already using Velos for a number of components of their activity and having to integrate that with another system is certainly a challenge," Sargent said.

**A Bet on Medidata**

City of Hope is similarly integrating the Medidata data-capture capability with the centralized database.

The system was developed by Joyce Niland, chair of the Department of Information Sciences at City of Hope Cancer Center, when she first came to the institution 22 years ago.One of the first systems of its kind, it has withstood the test of time and is still used today.

However, with the emergence of robust commercially available systems, three years ago, the biostatistics groups at City of Hope initiated an evaluation of off-the-shelf systems, focusing on capability to handle case reports for clinical trials.

City of Hope looked at about 20 vendors, narrowed it to five or six, and ultimately accepted a free pilot from one of them. In that round, the committee was impressed by Medidata, but ruled it out based on cost.

"Since Medidata had worked primarily with the biopharmaceutical industry, they didn't initially have a pricing model that met the needs of academic cancer centers like us. We worked closely with them to come up with a pricing model that made sense for City of Hope, and potentially other cancer centers. We plan to mount 20 studies in the first two years of using the system."

"Our Informatics group has mounted six trials to date, and we have seven more in the queue," Niland said. "We have people knocking on the door." She is pleased with the prospect of NCI's deal with Medidata. "Next year, we will have two years of experience under our belt that most other cancer centers don't have, and would look forward to an NCI-sponsored licensing agreement," she said.

City of Hope runs about 400 clinical trials at any given time, and a third of those involve the center's own intellectual property.

"Those are the ones we will put into Medidata," she said. "Also, if cooperative cooperative groups continue to move to Medidata, these trials, too, will be entered into the system."

"If" is the key word now that NCI's grand plan to deploy a single data-capture system to harmonize the enterprise of cancer research faces the prospect of being scaled back or dispatched to the shredder.

*BSA Report:*

## BSA Call For "Moratorium" on Development of caBIG Tools

The NCI Board of Scientific Advisors March 1 unanimously approved a subcommittee report on the caBIG program.

The review was commissioned by NCI Director Harold Varmus (The Cancer Letter, Nov. 12, 2010). The BSA subcommittee that conducted the review was headed by Andrea Califano, professor of systems biology at Columbia University and associate director for informatics at the Herbert Irving Comprehensive Cancer Center.

The full document is posted at http://www.cancerletter.com/categories/documents. It will be posted on the NCI website next week.

*The text of the report's executive summary and recommendations follow.*

**Executive Summary**

Since his appointment in July 2010, the NCI Director has undertaken a review of NCI's largest programs.

Over the last seven years, the Cancer Biomedical Informatics Grid (caBIG), supervised by the NCI's Center for Bioinformatics and Information Technology (CBIIT), has been one of NCI's most far-reaching programs, dedicated to designing and developing the next generation of collaborative IT infrastructure for biomedical research. Such an infrastructure would be capable of handling data collection, integration, analysis, and dissemination challenges across the grid of NCI designated cancer centers, collaborating institutions, cooperative groups, and other NCI programs to accelerate the discovery of new approaches for the detection, diagnosis, treatment, and prevention of cancer.

The caBIG budget has grown annually, from approximately $15 million in fiscal year 2004 to more than $47 million of appropriated money in fiscal year 2010.

An additional $87-100 million from the American Reinvestment and Recovery Act (ARRA) in fiscal years 2009 and 2010 brings the total cost of the caBIG program to at least $350 million for fiscal years 2004 to 2010. Future plans, including electronic health records (EHR), cloud computing, and other far-reaching activities related to personalized molecular medicine, are likely to continue the trend of escalating expenses. Therefore, a thorough and objective review of this important NCI program is warranted at this time.

To undertake the assessment, the WG requested information from the caBIG leadership on caBIG program activities in four areas: Life Sciences/ Integrative Research tools; Clinical Trials Management tools; Infrastructure/Data Sharing tools; and Budget, Program Administration and Contracts Management.

The WG conducted an interview-based assessment of the caBIG program, interviewing 59 individuals with a wide variety of caBIG-relevant experiences and perspectives from 46 institutions.

The interviews focused on the impact of the caBIG program on the NCI-designated Cancer Centers, the cooperative clinical trials groups, and other NCI research initiatives which caBIG was expected to support, such as The Cancer Genome Atlas project, and industry.

The results of this 4-month assessment have been surprisingly uniform and far less polarized than was

originally expected. There was complete agreement that caBIG's original goals were worthy and remain highly relevant to the future of cancer research in the United States (U.S.).

However, there was also strong consensus among those interviewed that caBIG has expanded far beyond those goals to implement an overly complex and ambitious software enterprise of NCI-branded tools, especially in the Clinical Trial Management System (CTMS) space.

These have produced limited traction in the cancer community, compete against established commercial vendors, and create financially untenable long-term maintenance and support commitments for the NCI.

Furthermore, creating this all-inclusive software enterprise has required the support of a vast management network of external contractors that consumed at least $60M in overhead costs in the past seven fiscal years and continues to grow.

There appears to be only a few NCI-Designated Cancer Centers that have adopted the full caBIG CTMS solution, while adoption of individual components was relegated to small pilot projects, with little impact on the Centers' mainstream operation.

Progress on the caBIG Life Science tools has been somewhat better, with a handful of tools being broadly adopted by several research lab and large projects. However, the level of impact for most of the tools has not been commensurate with the level of investment.

For example, many tools, such as caArray ($9.3M), have been developed at significant expense and without a clear justification, particularly since a number of similar commercial and open software tools already existed.

It is indeed noteworthy and a lesson for the future that the more widely adopted Life Sciences tools have their roots in projects that were already fairly successfully developed by academic research institutions, whereas most of the caBIG-initiated projects have been less successful and, ironically, much more expensive.

Similarly, enormous effort was devoted to the development of caGRID ($9.8M), an environment for grid-based cloud computing, but the WG did not find evidence that it has empowered a new class of tools to "accelerate the discovery of new approaches for the detection, diagnosis, treatment, and prevention of cancer" as envisioned.

The WG's analysis also revealed problems in the approaches used by the program for implementing the highly valuable vision it had helped define. In particular, the interviews suggest that the strategic goals of the program were determined by technological advances rather than by key, pre-determined scientific and clinical requirements.

Thus, caBIG ended up developing powerful and far-reaching technology, such as caGRID, without clear applications to demonstrate what these technologies could and would do for cancer research. While some large projects, such as the I-SPY Breast Cancer study, have been built around caBIG tools, the WG struggled to find projects that could not have been implemented with alternative less expensive or existing technologies and software tools.

Perhaps the greatest impact of the caBIG program on cancer research has been to gather several communities around a virtual table to help create and manage community-driven standards for data exchange and application interoperability.

The development of a semantic infrastructure that allows data to be harmonized across cancer centers is widely perceived to be one of the most important contributions of the caBIG program.

Importantly, caBIG helped to move the cancer research community beyond messaging systems and limited structured vocabularies and ontologies to push for semantic standards that have achieved significant penetration in the cancer clinical research community.

The program has also had impact by supporting the development, maintenance, enhancement, and dissemination of software tools developed by the academic research community.

The WG was surprised to discover that caBIG projects and initiatives have not undergone the usual NCI concept review and approval process, depriving the program of the opportunity to receive valuable guidance in shaping its strategies, approaches andgriorities as it grew.

Despite the obvious qualifications, technical vision, and integrity of caBIG 's NCI management team, the lack of independent external oversight and the non-peer-review based funding decisions have significantly compromised the ability of the caBIG program to achieve its initial goals.

The WG would like to stress that, going forward, the creation of an infrastructure for data collection, management, analysis, and dissemination remains a critical and only partially addressed problem.

It is thus critical that the WG's findings about the caBIG program's progress and traction does not

diminish NCI's enthusiasm for and commitment to supporting this critical area of development.

Specifically, we recommend that caBIG return to its original mission and premises and that NCI focus separately on informatics tools for clinical and basic research components.

The former should become more driven by the requirements of the organizations that run clinical studies. The latter should be better integrated with NCI's existing portfolio of programs that support the development of highly innovative analytical tools, which currently lack any but the most basic form of support for community-based software development, maintenance, and dissemination.

The WG also recommends certain immediate actions aimed at reducing expenditures while the program is reorganized, and at creating a critically needed mitigation plan to support the labs and organizations that have become dependent on caBIG tools and that may suffer from the reorganization process.

**Immediate Tactical Recommendations**

1. Institute an immediate moratorium on all ongoing software development projects, both internally within caBIG and through commercial contracts, (such as enhancement and development of tools in the CTMS suite, the caGRID, cloud computing, EHR, and caBIG 2.0) while initiating a mitigation plan to lessen the adverse impact of this moratorium on the cancer research community. Support for maintenance of caARRAY, caTissue, the imaging tools and ongoing multi-site clinical trials dependent on caBIG tools should be exempt from this moratorium.

2. Institute a one-year moratorium on the initiation of all new projects, contracts and subcontracts through caBIG pending their review by the independent oversight committee described in Recommendation 4.

3. Provide a one-year extension of caBIG supported academic efforts for development, dissemination, and maintenance of new and existing community-developed software tools.

4. Establish an independent oversight committee, representing academic, industrial, and government (NCI, NIH) perspectives to review ongoing and planned initiatives for scientific merit and to recommend effective transition options to current users of caBIG tools.

5. Conduct a thorough audit of all aspects of caBIG budget and expenditures to identify unspent funds that can be reprogrammed for use in implementing the WG's other recommendations and for other NCI priorities.

**Longer Term Strategic Recommendations**

6. Create a Scientific Advisory Group (SAG) that has an appropriate mix of scientific, technology and informatics expertise to advise NCI on its priorities, future initiatives, business model(s), and resource allocations in the area of biomedical informatics. The SAG should also facilitate abatement of barriers with similar efforts in other NIH Institutes, in the community and abroad. It might be appropriate for a subcommittee of the BSA to do this function.

7. Refocus caBIG on its original mission and discontinue all strategic efforts to develop and maintain its own brand of software tools, either directly or indirectly through commercial contractor efforts.

8. Separate the clinical informatics and bioinformatics components of the caBIG program.

9. Use the usual and established mechanisms for concept review through the NCI BSA and peer review of NCI biomedical informatics initiatives in the future.

10. Promote interoperability and data sharing by making them key review criteria for grant and cooperative agreement applications and R&D contracts and by including them as requirements for award.

## *Appropriations*

# Shutdown Averted As Congress Extends Deadline by Two Weeks

*By Conor Hale*

The federal government reset the clock on the budget debate, extending the deadline to pass an appropriations bill by another two weeks.

On March 2, President Barack Obama signed a mini continuing resolution, funding the government until March 18 and putting off the possibility of a shutdown.

The measure contains about $4 billion in spending cuts, and while NIH funding will not be affected. However, $20 million has been shaved off the budget of the Centers for Disease Control and Prevention.

The hastily assembled resolution passed the House and Senate over two days, mainly as a means to provide more time to negotiate a larger spending bill that would ultimately fund the government through the rest of the fiscal year.

Many of the focused cuts in the two-week resolution were already outlined in the president's budget proposal and were easy targets for both sides of the aisle helping to expedite its passage.

Last month, House Republicans offered H.R. 1, a sweeping measure to fund the government until October, while shrinking the current federal operating budget by

over $60 billion.

The House measure would trim dollars for many agencies and outright cancel funding for particular programs, making it difficult to pass muster with Senate Democrats. Specifically, the bill halts any funds set aside to implement the health care reform act passed last year. The White House has promised to veto the bill in its current form.

At the moment, it's difficult to see who has the next move.

Many observers predict that debate will continue until the last possible second.

The bill's chances of passing the Senate are slim-to-none. Senate Majority Whip Dick Durbin (D-Ill.) has already promised to filibuster the bill.

And while all new spending bills have to begin in the House, Speaker John Boehner (R-Ohio) has said it's the Senate's turn to make a move and come up with an alternative plan. Meanwhile, Obama said his budget staff would meet with Congressional leaders to help broker a deal.

The standoff over the budget hasn't ended, but the countdown has been halted, forcing the game to be replayed within the next two weeks.

## NEJM Retraction Was Expected, Follows Action by Three Journals

(Continued from page 1)

reproduce the work of the Duke group, but instead found an extraordinary number of errors.

However, the issue exploded after The Cancer Letter reported that Potti had stated falsely that he had been a Rhodes Scholar and claimed to have won other awards he hadn't, in fact, won. He resigned from Duke last November (The Cancer Letter, Nov. 19).

The retraction is his first public expression of regret over the scandal.

NEJM is the fourth journal to retract a paper by the Duke group. The Journal of Clinical Oncology, the Lancet Oncology, and Nature Medicine have done so before.

Questions about the NEJM paper were first discussed in a public forum last summer (The Cancer Letter, July 30, 2010). In a detailed statement to The Cancer Letter, David Beer, a genomic scientist and professor of surgery and radiation oncology at the University of Michigan and an investigator with the NCI Director's Challenge Consortium, said Potti had improperly obtained his group's data and conducted a highly suspect analysis of these data.

Beer said that he informed the NEJM editors, NCI officials, and Potti's mentor Joseph Nevins about these issues. Nonetheless, Nevins and NEJM declined to retract the paper, Beer said.

Duke had enrolled patients in three clinical trials that used genomic technology to assign patients to treatment. Altogether about 110 patients had been assigned to treatment.

The technology described in the NEJM paper wasn't used in these studies. However, it was being offered for licensing by the Duke technology transfer office. CALGB used the test as an add-on in a clinical trial, though not as a method for assigning patients to therapy (The Cancer Letter, Oct. 2, 2009).

Ultimately, NCI mandated that the use of the technology be stopped, because it was found to be useless (The Cancer Letter, Jan. 7, Jan. 14).

In a related development, the Institute of Medicine has announced the second meeting of a panel examining the issues stemming from the Duke case. The meeting will include a panel of editors of medical journals, who will address the role journals can play in investigating irregularities in science.

NCI used the committee as a way to release hundreds of pages of documents related to the controversy. The agenda is posted at http://www.iom.edu/~/media/Files/Activity%20Files/Research/OmicsBasedTests/WorkshopDrftAgendaPublic.pdf

*In the Cancer Centers:*

## Winners of Weintraub Award Announced by Fred Hutchinson

Twelve graduate students have been chosen to receive the 2011 Harold M. Weintraub Graduate Student Award sponsored by the **FRED HUTCHINSON CANCER RESEARCH CENTER**. The recipients will present at a symposium May 6 at the Hutchinson Center. They will each receive a certificate, travel expenses and an honorarium from the Weintraub and Groudine Fund.

Weintraub identified genes that instructed cells to differentiate into specific tissues. He died from brain cancer at age 49 in 1995.

The award recipients include: **Kevin Alby**, Brown Univ.; **Lacramioara Bintu**, UC Berkeley; **John Calarco**, Univ. of Toronto; **Kevin Esvelt**, Harvard Univ.; **Jason Gorman**, Columbia Univ.; **Harry Benjamin Larman**, Harvard Univ./MIT; **Paula Montero** Llopis, Yale Univ.; **Kellen Olszewski**, Princeton Univ.; **Lisa Rachel Racki**, UC San Francisco; **Justin Siegel**, Univ. of Washington; **Gabriel Victora**, NYU Medical School; and **Stephanie Weber**, Stanford Univ.