DC: Group Convenes Stakeholders to Reform Alzheimer's Trials

21 December 2010. Follow the coverage, on Alzforum and in the general media, of clinical trial failure after failure in recent years, and you'll come away thinking that nothing works in Alzheimer's disease. But while public awareness of the disease's looming public health threat rises in parallel with an anguished recognition of a federal research funding crisis, one piece is getting lost amid the noise: Between scientific discovery and new drugs for the patient, there lies an important, if obscure, area of coordination and regulatory work to improve a fledgling drug program's chance at success. While this area is difficult to communicate, it is where some of the perhaps most pressing—some say most promising—innovation is happening in the AD field at this point.

By this measure, the field is not stuck at all; rather, it's gearing up to test candidate drugs faster and to freely share data from negative trials across companies so everyone in industry and academia can learn from them. The catchwords are data standardization, simulation model, and biomarker qualification—stuff too dry for nightly television, not fit for print in the nation's flagship newspapers. And yet, anyone who cares about better treatment for AD may want to take note. A neutral group called Coalition Against Major Diseases (CAMD) is driving a large-scale effort at reforming the drug trial and drug approval process, and doing it all hand-in-hand with the regulatory authorities in the U.S. and Europe. On 30 November 2010, the group met in Washington, DC, for a daylong powwow on what they achieved in 2010 and what to do in 2011. Here is a summary of its parallel projects; the who, the why, and the when.

This CAMD meeting clearly illustrated that none of the stakeholders in AD drug development—individual pharma companies, academic trialists, a regulatory agency, or a patient group—can break the current logjam on their own. Together, perhaps they can. This means data sharing. Not in a casual "sure, let's collaborate" sort of way, but by doing the hard, sustained work of standardizing and pooling large clinical datasets for everyone's benefit. **Marc Cantillon**, CAMD's executive director, summarized it like this: "Our original vision was the sharing of knowledge for faster and safer drug development. We wanted to develop tools to innovate the processes. This cooperation in the pre-competitive space, developing tools for all, is game changing. Sharing of data has been talked about for decades, but never done in this way."

Companies, perhaps humbled by their setbacks, are cooperating. Said a director at Pfizer, "Continued investment in Alzheimer's requires success, and success requires pre-competitive teamwork across organizations. CAMD provides the team framework. We do not want AD to be like stroke." Due to its history of failure, stroke is often called a "graveyard for drug development." An executive from Bristol-Myers Squibb added this: "Drug development is getting harder. CAMD is innovative, and a huge opportunity for us." [Editor's note: This news story does not cite most company officials by name to avoid delays from corporate communications policies.] Former Food and Drug Administration commissioner **Marc McClellan**, who now directs the Engelberg Center for Health Care Reform at the Brookings Institution, said, "New drugs are not made just by putting more funds into labs. Collaborative efforts like CAMD are indispensable. There is no alternative out there to what they do." Other

speakers agreed that a shrinking pharma industry would be well advised to participate in CAMD's projects.

What, then, is CAMD? Led jointly by Cantillon, formerly of Schering-Plough (Merck), and **Frank Casty** of AstraZeneca, CAMD is an industry-government collaboration with patient organizations and academic consultants. Started in 2008, CAMD is one of the coalitions formed by the Critical Path Institute (C-Path, for short) based in Arizona and Maryland and founded in 2005 by **Ray Woosley**. This independent nonprofit institute serves as a third party that brings scientists from academia, industry, and the FDA and the European Medicines Agency (EMA) together on pre-competitive projects. Funded by the government and philanthropy, the institute was inspired by the FDA's 2004 Critical Path Initiative developed by then-commissioner McClellan and FDA official **Janet Woodcock**. That initiative grew out the painful recognition that, despite growing NIH expenditures for biomedical research funding, few innovative medical products were coming online. The initiative called for applied science to plug this alarming hole in the product development pipeline. C-Path formed with the charge to develop enabling tools and processes, and CAMD is C-Path's Alzheimer's and Parkinson's group. (CAMD just expanded its efforts to include Huntington's by including the Cure Huntington's Disease Initiative as a member.)

The problem CAMD is addressing is intensifying. Since the approval of the current Alzheimer's drugs in the 1990s and early 2000s, not a single drug program has succeeded, even though research has flourished. This includes most prominently a handful of anti-amyloid treatments, but also others, from Dimebon, valproate, DHA, statins, to rosiglitazone, NSAIDs, estrogen, vitamins E and B, homocysteine, and prevention with gingko biloba extract, for example. Not mentioned are countless lesser-known pharmaceutical compounds that died for various reasons without much public notice. In the last six years, Alzheimer's disease has seen a 46 percent increase in mortality, where some other big diseases have had a modest decrease, said Cantillon. "This reflects our absolute frustration of not coming up with better treatments," he said.

The litany of failure has created worry that senior executives in pharma companies won't commit funds to AD programs anymore because they view them as too risky. Regardless of pharma's popularity in the eye of the individual, this concern matters hugely. Despite some public misperception to the contrary, academic scientists or practicing doctors do not develop new drugs; biopharma companies do, and AD scientists there are finding their disease an increasingly hard sell. One pharma scientist summarized the present situation this way: "We compete internally for resources with other indications. For example, we compete with anti-infectives, where a study runs for weeks, not years. We do that with a success rate that gets calculated. We go to our governance and ask for money. They want to know why AD is a good area to invest in. Yes, the medical need is huge, but the risk is huge, too. Our primary product has been dead compounds. We need arguments that the success rate can go up."

"The trial failures have marked the AD story for the past five years, and we don't know why," Cantillon said. "Thousands of patients have gone into trials, and we can't even say if the trials had worked if some aspect had been done differently." One

reason lies in "wasted" data. There may well be drugs on shelves that could be helpful, but no one knows it because the data are not being used. Each drug sponsor, public or private, recruits and assesses patients in its own way, and when a trial fails, the data move into storage. As a result, the FDA has "warehouses" of data in separate formats that do not speak to each other and can't be used. CAMD is working on a set of interconnected projects to change that. The coalition is proposing a data standard by which data from many trials can be analyzed together in a shared database. This is useful to see, for example, if failed drugs actually worked for some subgroup of patients. Moreover, the database enables the building of a quantitative model of disease progression and drug response—blessed by the regulators—that trial designers can query to design trials in the future. Finally, it is working to get biomarkers FDA validated (aka "qualified" in preferred regulatory lingo) for use in those trials. For more on these projects, see Part 2, Part 3, and upcoming Part 4 of this series.—Gabrielle Strobel.

DC: Standard Data—Music to Regulators' Ears

22 December 2010. The Coalition Against Major Diseases started one and a half years ago to develop tools that could improve drug development. These tools are to be pre-competitive, i.e., open to all; hence, CAMD forms a consortia to build them. The idea is that everyone has much at stake, but no single player can build these tools or get the field at large to embrace them. Importantly, no single company can elicit nearly the same degree of regulatory engagement that a neutral coalition enjoys. So despite a certain "consortia fatigue" that can set in with large collective efforts, collaborative work is CAMD's bread and butter. "Consortia are the model to effect outcomes in the pre-competitive area. You can't do it with any one group," **Rick Myers** of C-Path said at a CAMD conference held 30 November 2010 in Washington, DC. For its projects, CAMD has recruited representatives of seven patient groups and foundations, 12 biopharma companies, leading academic scientists, scientists at the Food and Drug Administration (FDA) and the European Medicines Association (EMA), as well as the National Institute on Aging (NIA) and the National Institute of Neurological Disorders and Stroke (NINDS). More companies will soon join, said CAMD's executive director **Marc Cantillon**.

Besides herding these cats, what is CAMD doing, exactly? The coalition has five working groups: on data standards, a disease model, on biomarkers, statistics, and on government submissions. To start with number one, a clinical data standard for all AD trials is the "rock on which all this is built," said **Marc Cantillon**, who co-leads CAMD. [Editor's note: Yes, dear reader, here now a few graphs on standardization. Read on, it's not so bad!] Standardization is key to getting information to reviewers at the FDA/EMA and to ensure they digest it efficiently. Even though about half of submissions these days come to the agencies electronically, that does not mean they are standardized. Even banal things like age and sex vary from one submission to the next, slowing down the reviewers as they try to make sense of the material.

Data standards are soporific to most people, but speakers insisted they deserve an image makeover. "Standards are far and away the most important goal with respect to savings and understanding AD clinical trial data," a Pfizer scientist said. "Data standards allow for collecting and interchanging data across programs. Our field is an

intellectual power of Babel. Each investigator has a few trials and speaks from that. The variability seems huge. Everybody is coming to the table with a little piece of the truth. If we can come to the table with standard data, CAMD has been a victory already." **Marc McClellan**, former head of the FDA and now at the Brookings Institution, weighed in with this: "Data standards in Alzheimer's and Parkinson's are really really—and I'll add another really here—important for the efficiency of the regulatory process itself. We have to create momentum behind these standards."

CAMD has developed a data standard for AD trials together with the Clinical Data Interchange Standards Consortium. With its more than 250 member organizations, this global nonprofit establishes freely downloadable industry standards in many areas of technology and science. **Bron Kisler** of CDISC showed a slide of five different global outlet plugs to symbolize the problem of disparate datasets that connect only when each is hooked up to a universal adaptor plug. CDISC and CAMD scientists have developed such a universal adaptor, i.e., an AD clinical data standard. They will publish this standard, along with a guide on how to implement it, for free download and comment on the CDISC website in January 2011. These standards use defined terminology and data structure (for more on these, read up on STMD and CDASH on CDISC's website. The CDISC website lists a series of data standard training workshops, too.

This voluntary standard is useful in several ways, scientists said. Existing clinical trial data can be mapped to this standard and in this form flow into a pooled database (see below). Going forward, trialists can opt to use the CDISC data standard from the get-go for new trials. This is preferable, speakers agreed, because aligning existing data from old trials to a new standard is difficult. Leading the pack, the Alzheimer's Prevention Initiative, which intends to start pre-symptomatic trials in high-risk populations as early as 2011, has indicated it will adopt the CDISC data standard, said **Klaus Romero** of CAMD.

Kisler emphasized that a disease-specific data standard improves collaboration in many ways. It makes it easier to collect data, to exchange data, and to aggregate it so scientists can analyze much larger datasets. "CDISC's open-access philosophy made it our key partner on standards," Cantillon added. "With them, we are developing downloadable Alzheimer's and Parkinson's case report forms in this new standard for download by fall 2011."

As a neutral convener, CDISC has become the FDA's partner on standards, as well, said **Josh Benner** of the Brookings Institution. The agency not only welcomes submissions in CDISC standards to speed internal review, it also calls for their use in one of the main FDA projects launched with stimulus funding from the Recovery Act. The Partnership in Applied Comparative Effectiveness Science (PACES) aims to facilitate meta-analysis across studies to pinpoint subgroup-level differences in effectiveness. This goal echoes in the mind of AD clinicians, who at times spotted tantalizing hints for promising subgroup effects (i.e., in the less advanced, in ApoE4-negative patients), but those hints generally lacked sufficient power to inform next steps. For PACES, the FDA needs a clinical trial repository of datasets collected using common CDISC standards. "This project is now underway," said Benner, adding that PACES serves as an example of how CAMD is aligning its work with that of the FDA.

For its part, the NINDS has begun its own initiative to develop common clinical data elements that the institute's grant recipients can use in their clinical research. **Petra Kaufmann** from NINDS noted that this effort currently covers traumatic brain injury, spinal cord injury, epilepsy, stroke, frontotemporal dementia, and other conditions. Standards for Parkinson's are currently out for public review at the agency's website. In discussion, **Steve Broadbent** of C-Path cautioned that having separate standards—a CDISC standard, a NINDS standard—might confuse investigators. Kaufmann said that NINDS will ensure that its data elements are compatible with CDISC's standards so extensive remapping for data-sharing hopefully won't be necessary down the road.

Scientists at the conference debated how best to get individual researchers to adopt these standards. Science is enough like art that investigators, given their druthers, tend to work like individualists, pursuing their own ideas and methods. Some attendees urged NIA and NINDS to use its power of the purse to mandate use of standards so individual investigators stop spending scarce federal dollars on developing yet more separate data collection instruments. Other preferred the gentler power of persuasion. "We want the standards to be really good so people will want to use them," Kaufmann said. Others cautioned that experience has shown individual investigators to resist using even excellent common standards, and that years might be lost until investigators adopted them "organically." Short of a mandate, adoption will require at least teaching effort, scientists agreed. "We all love our own way of doing things," said **Dan Van Kammen** of the Cure Huntington's Disease Initiative. "Our task is to bring people together to see that the standard is better for them."

For its part, the CAMD-CDISC data standard is already being put to work in a pooled clinical trials database for all researchers to peruse. For the latest on that, see Part 3.—Gabrielle Strobel.

DC: Shared Pain Is Lessened—Open-Trial Data Gain AD Model

23 December 2010. When a clinical trial comes up short, typically the data gets parked at the pharmaceutical company and the FDA. No one else uses it; no one learns from the other's misfortune. Over the course of the past year, the Coalition Against Major Diseases (CAMD), a collaborative initiative of the Critical Path Institute, has developed an open tool to connect those silos of information. Last June, CAMD announced the launch of the C-Path Online Data Repository (CODR). CODR is the first database in which pharmaceutical companies share Alzheimer's disease placebo and some treatment data for researchers in academia and industry worldwide to use freely.

The database uses a standard format, favored by the Food and Drug Administration, which was developed with the nonprofit standard setting organization CDISC (see Part 2 of this series). CDISC helped CAMD develop the data standard, and scientists at each company then mapped their own dataset to it so the data could be plugged into CODR. In turn, CODR forms the basis for the building of a quantitative drug and disease simulation model of human Alzheimer's disease. This model—another CAMD project—will give researchers a stronger empirical basis to simulate therapeutic trials. Pharma, academic, and government scientists who gathered at a CAMD conference held 30 November 2010 in Washington, DC, widely agreed that

such a simulation model would go a long way toward reducing the risk of failure in those trials.

How far along is this plan? "Last year at this meeting, I said we had interest from six companies in data sharing. The question hung in the room: will they really do the work required to share?" said **Steve Broadbent** from C-Path. "Now we have that database. More than 200 researchers from all over the world have applied for access and received it; we get some 20 new applications per week."

What do those researchers find in the database? As of now, placebo and some therapeutic data on 3,600 patients from nine trials by six CAMD member companies, i.e., Abbott, AstraZeneca, GSK, Johnson & Johnson, Pfizer, Sanofi-Aventis, **Stephen Kopko** of CDISC told the audience. One trial promised by Novartis is yet to come, and a second Pfizer trial is currently being transferred. Eli Lilly and Company has promised to contribute its semagacestat data (see ARF related news story), said **Marc Cantillon**, who directs CAMD.

At present, Kopko and colleagues are translating their first non-industry trial into the CDISC data standard. It is the homocysteine trial by the Alzheimer's Disease Cooperative Study group. Next on the list is ADNI, which would add invaluable biomarker and disease progression data to the repository. At this point, the database contains mostly older trials of symptomatic drugs in mild to moderate AD. CAMD wants to expand it with trials that are newer, use biomarkers, and are done at milder/MCI stages. "We were limited so far because companies were not always willing to give us datasets. For NIH-funded trials, we hope that will be easier," Cantillon said.

Kopko hopes that the January publication of CDISC's AD data standard will encourage more trial sponsors to align their existing data with this standard and contribute them to CODR. New trials being planned now and in the future can adopt this voluntary standard.

CODR could be a bounty for all, scientists said. To pick a hypothetical example around the latest high-profile setback, Eli Lilly could have theoretically decided not to spend millions of dollars on semagacestat, or design the program differently, had it been able to analyze data by other companies that had been testing γ-secretase inhibitors before. It was common knowledge that Merck and Bristol-Myers Squibb, for example, had been discontinuing compounds with this activity after clinical tests. "As it is, each company has access to only their own, limited AD clinical trial experience," Cantillon said. Often, poor drugs for various reasons are kept alive too long only to fail in late stages, EMA regulator Cristina Sampaio said at a meeting earlier this year (see ARF Springfield story).

A Pfizer scientist noted that CODR could help companies recruit because it enables them to make a commitment to their trial participants that they will share data equitably and create value from otherwise unsuccessful trials. "We can say to patient groups and patients: The compound we are testing here may die. But your effort is not lost because we give the placebo data back to the community. Enrolling in AD trials is benefiting all AD research, not just this sponsor," he said. Patients and relatives are

frequently dismayed if information gleaned from their research participation is not shared.

A further boon lies in better understanding placebo responses. When a treatment trial falls flat, sponsors sometimes blame insufficient placebo decline, but research has shown that a given trial's placebo group is often too small to support such claims (see ARF related news story). The CODR shows how placebo groups truly behave.

The database will continue growing for the research community's use. However, Kopko said, at some point the CAMD disease model group will cut the existing data to build a simulation model of Alzheimer's disease and ask the FDA and the European Medicines Agency (EMA) to formally qualify that. This model is a central piece of CAMD's vision.

Why qualify a model? The idea is that a model of the progression of Alzheimer's would enable all drug developers to optimize a slew of how-to questions about their next planned trial. This is not to replace actual trials with some sort of virtual version, said **Klaus Romero** of CAMD. Rather, it is to simulate specific questions of trial design—staggered start, when to take samples, to name just two examples—and see how tweaking those would likely affect the outcome. Most importantly, perhaps, a simulation model can help scientists pick the right endpoints to measure.

"The groundbreaking thing here is that we have the regulators along every step of the way," Romero said. Indeed, Romero and his colleagues presented a draft research plan on how to build the model to the FDA in April and to the EMA earlier this fall. "It was very exciting to have this be a multi-company meeting," said a scientist at AstraZeneca who helps CAMD with all regulatory aspects. "It was a different feeling. It was collegial." Working independently, each pharma company would not get this kind of input from the agencies.

"By developing disease models using a broader range of data than any company can generate on its own, research will be able to design more effective treatments and diagnostics," said **Mark McClellan**, who co-developed the Critical Path Initiative in 2004 when he headed the FDA. McClellan is now at the Brookings Institution.

Regulators strongly support publicly shared simulation models for trial design, said **Jogarao Gobburu** of the FDA. He cited one example of a model for non-small cell lung cancer that helps researchers simulate how their drug will behave in trials. Another such model, in pulmonary hypertension, helped FDA scientists to determine what the right endpoint would be in pediatric trials testing drugs originally made for adults. Those sorts of goals are why the FDA qualifies disease simulation models.

The day's discussion briefly touched on whether such a model could serve as a control in lieu of placebo. In general, regulators prefer placebo controls, but some speakers noted that it can be difficult in late-stage trials to find participants who will honestly stay on placebo and not find a way to get drug. This issue came up at a recent EMA conference on clinical trials in preclinical neurodegenerative disease, and has generated scientific commentary (see Spiegel).

The CAMD disease models group is currently implementing the FDA and EMA's feedback on their draft research plan for how to build the model. For example, regulators requested that an external review panel add clinical expertise to the model; **Lon Schneider** of the University of Southern California will lead this panel. Much work remains to execute the plan, and the group will need to consult the agencies again, but CAMD hopes to submit the model for qualification by end of spring 2011, Cantillon said. Pfizer has committed its regulatory staff to write and submit the qualification documents for this model, which will be freely available to all drug sponsors in industry and academia.

The simulation model provides a quantitative description of the disease. It would be a combined drug and progression model, because it draws on CODR placebo data, the published literature of older drug trials in nearly 20,000 patients, and the ADNI database. The last contains biomarker and psychometric data on the natural history of pre-AD and AD, and has led to a staging model of preclinical AD (see ARF Live Discussion). The model should give investigators a range of outcomes depending on how they tweak features of their intended trial, Romero said. Members of the CAMD modeling group published a paper about their collaborative approach this past September in the Journal of Clinical Pharmacology (Romero et al., 2010). Read upcoming Part 4 on biomarkers, Parkinson's, and growing pains.—Gabrielle Strobel.

DC: Biomarkers, Parkinson's—CAMD Needs All Hands on Deck

24 December 2010. At a meeting of the Coalition Against Major Diseases on 30 November 2010 in Washington, DC, speakers focused on this group's goal of garnering the official seal of approval by the U.S. and European drug regulatory agencies for biomarkers in AD drug development. **Holly Soares**, formerly of Pfizer and now at of Bristol-Myers Squibb, heads this working group, which has been split into five subgroups because the task is so complex. Each of them is working on three things: to pinpoint biomarkers in AD that can advance clinical trials within a specific context of use, to reanalyze the available data on the performance of those markers, and submit a qualification (aka approval) package to the agencies.

This ongoing effort echoes what the FDA requests in a draft guidance called Qualification Process for Drug Development Tools that the agency issued to all industry in October 2010. In this document, the FDA calls for companies to collaborate on the work needed to gain biomarker qualification. "It is in the interest of companies to work with CAMD," said former FDA commissioner **Mark McClellan**, who is now at the Brookings Institution.

Initially, the CAMD biomarker group's work was slowed by the confusing terminology used to describe earlier stages of Alzheimer's disease, Soares noted. In the spirit of Bruno Dubois and colleagues' redefinition of the lexicon (Dubois et al., 2007; Dubois et al., 2010), the CAMD group now calls this stage "symptomatic pre-dementia AD," Soares said. These are people who complain about a memory problem, show a decrement on a test, and have an abnormal biomarker reading. The CAMD workgroup decided against considering cognition a biomarker, in part because they did not want to settle on a particular test.

For fluid biomarkers, the group heard from the agencies that ADNI data would be insufficient; hence, it is including data from U.S. studies done at Washington University, St. Louis, and a European consortium study analyzed at Sahlgrenska Hospital in Göteborg, Sweden, as well. Of all biomarkers, fluid analytes are furthest along on the road to qualification, Soares said. However, even though findings of CSF Aβ reduction and tau increase are robust, work remains to bring down variability in the assays and collection methods (see ARF related news story on worldwide quality control). On MRI, standardization remains a challenge, and other imaging markers at present remain underrepresented in the CAMD effort.

The CAMD biomarkers group has fielded feedback on its draft research plan from the FDA and the EMA, and is aiming to submit a formal package in summer 2011. The stakes are high for biomarker qualification, some scientists noted. Because their use will drive up the cost of a trial in AD, they had better prove their worth by boosting its chance of success, or at least making it shorter. Unlike the disease model group, the biomarkers group has not yet found a champion who has volunteered to prepare the regulatory package. "We need more industry folks actively involved and committed to these large tasks," said an AstraZeneca scientist.

This is true of all of CAMD's efforts in Parkinson's disease. PD is high on the agenda with similar goals as AD—a data standard, a trials database, a disease model, biomarker qualification—but most lag behind AD at this point. Partly, it's just a question of doing the work, but partly, the lag results from more tepid industry interest, some attendees said. Existing PD drugs are more effective than AD drugs, raising the bar in the argument for urgent medical need, and biomarker research is less developed. However, early detection and disease modification of Parkinson's are badly needed, **Marc Cantillon**, CAMD's executive director, said. CAMD recently signed on the Michael J. Fox Foundation and Orion Pharmaceuticals, which makes entacapone for PD, in hopes that these partners will galvanize support for PD projects.

On almost all its projects, CAMD scientists need more help. Of the 12 member companies, about half last year provided some in-kind help, but only a quarter of the more than 100 industry scientists who are nominally involved in CAMD participate actively. This small group shouldered most of the work that led to CAMD's tangible successes in 2010—the standards, the database, and the research plans for the model and biomarkers. "How can we engage more of you?" asked **Frank Casty** of AstraZeneca, who co-directs CAMD. The scientists cited reasons ranging from overwork of remaining employees as pharma lays off to the fact that pre-competitive collaboration works best if it is formally included in a scientist's day job so (s)he can allocate time, get credit for this work, and need not fit it in on Saturday nights. CAMD does not pay industry scientists for their time. Like all distributed collaborations, CAMD work requires intense project management, communicating clearly who does what and by when, and keeping all partners up to date. This, too, is difficult when everybody piles collaborative work onto an already overflowing plate.

In addition, CAMD faces a communication challenge. Applied science and regulatory lingo do not lend themselves to snappy stories on the evening news shows or pithy sound bites to Congress, though Cantillon did testify on the Hill on 9 December 2010 in advance of last week's passing of NAPA (download from CAMD website; see ARF brief on NAPA). At this early juncture, **Louis Kirby** of C-Path said, CAMD's

primary audience is clinical scientists in academia and pharma. Once they learn about its work and decide to adopt the Clinical Data Interchange Standards Consortium (CDISC) data standard and to offer their trials to the C-Path Online Data Repository (CODR), the coalition will achieve its other goals. "You need a tangible success to get more support, not just in-kind, but also financial. Biomarker qualification would go a long way," said McClellan. Other attendees recalled that ADNI for the first two years struggled to maintain interest in the research community until data started rolling in.

The crunch in the current fiscal environment does not help matters, as the FDA is unlikely to receive a much-needed infusion of funding to expand its work on Critical Path initiatives. "Given current budgetary limitations, CAMD's work is now more urgent than ever," McClellan told the assembled coalition scientists. Said a senior executive at Bristol-Myers Squibb, "I encourage industry to redouble their efforts to support this initiative."—Gabrielle Strobel.