European Union Creates Its Own “Critical Path”

By Gunjan Sinha

To lure the biomedical industry to Europe, the European Commission (EC) is throwing out some bait. A proposed initiative under the EC’s 7th Framework Programme (FP7), the European Union’s primary science funding mechanism, would allocate 1 billion euros over the next 7 years to boost research on therapeutic drugs.

Called the Innovative Medicines Initiative (IMI), the proposal recommends using the funds to establish a committee that will dole out grant money to Europe-based public–private collaborations. The grants will go specifically to research that addresses bottlenecks in the drug development pipeline and will ultimately increase the flow of new drugs hitting the market. The EC is presently discussing details of the initiative internally, and the European Council is expected to vote on it by the end of this year.

IMI is similar to FDA’s Critical Path Initiative, launched in 2004 in that they both aim to boost drug development. However, they rely on different paths to reach that goal. “Critical Path was initiated by the Food and Drug Administration, but they are not taking leadership in implementing it,” explained Karen Strandgaard, manager of the research director’s group at the European Federation of Pharmaceutical Industry and Associations. “IMI was written by industry in partnership with the European Commission. We plan to implement it together.”

But perhaps the biggest difference between the two initiatives is funding. While the FDA’s proposed 2008 budget includes $6.7 million for Critical Path and a pending congressional bill would devote an extra $20 million a year toward a new institute to focus research on drug development (see JNCI, vol. 99, no. 6, p. 426–7), the numbers are paltry compared with the initial annual 100 million euros proposed for IMI.

“It’s amazing what the commission is willing to put on the table to foster this area,” said Jacky Vonderscher, Ph.D., vice president and global head of biomarker development at Novartis. IMI would require industry partners to at least match EC funding, so the actual funds spent on the program could be much larger.

The EC’s willingness to support such an initiative is part of its new science strategy. In the face of flagging scientific prowess, one of FP7’s stated goals is to transform Europe “into a competitive knowledge-based economy.” Consequently, IMI’s goals are broader than Critical Path’s, Vonderscher said.

Critical Path attempts to facilitate projects that validate existing technologies to ease the regulatory process. IMI, on the other hand, is focusing on more basic discovery. “We want to achieve synergies,” Strandgaard said. “We want to make sure that we do projects complementary to those carried out in the U.S.” A common thread between the two, however, is that both strive to drive traditionally competitive foes to collaborate—an effort that is already paying off.

The Proposal

While both IMI and Critical Path aim to widen a narrow pipeline of new medicines, IMI has a second goal: to promote and support European biomedical science. Not only does the EU invest less than the U.S. and Japan on research and development as a percentage of gross domestic product, the status of European research has been declining. A 2004 study in Nature found that while U.S.-based scientists garnered almost 50% of all scientific citations between 1997 and 2001, scientists based in the EU member countries received only about 40%. The EU fared even worse in the top 1% of most frequently cited publications—only 37.3% of citations went to EU researchers, while 62.8% went to U.S. scientists (some studies may include authors from both the U.S. and the EU).

IMI is a small piece of FP7’s overall science funding scheme, but it specifically draws attention to biomedical investment. In a recent report, the European pharmaceutical research group detailed four key bottlenecks in biomedical R&D that IMI is intended to address: predicting drug safety; predicting drug efficacy; data interpretation and sharing; and education and training of all biomedical professionals, including those involved in regulating medicines.

Once the governing body and scientific committee are established, IMI will accept proposals that address those bottlenecks. In its research agenda, IMI placed a high priority on biomarkers that predict drug safety and efficacy for various types of disease. Any group can apply for funds, provided that they collaborate with industrial partners, which can include pharmaceutical and small- to medium-sized biotechnology companies. The industry partners must match the government funding, either in cash or in kind.

While EU science will certainly benefit from more investment, so too will the biomedical industry and patients as research is translated into better and safer medicines, experts said. As evidence of how collaboration can benefit drug research, they pointed to several successful projects in the U.S.

Collaborators Reap Rewards

Responding to FDA’s Critical Path Initiative, Novartis spearheaded three cooperative research projects in 2004, one of which aimed to validate biomarkers to assess drug-induced toxicity and carcinogenicity of the kidney, liver, and vascular system. While other members concentrated on the liver and vascular systems, Novartis and Merck focused on drug-induced kidney toxicity. The goal was to identify biomarkers that can flag early insult to the kidney—before the organ’s pathology has changed. Company scientists were also looking for markers that would specifically identify which kidney part—glomerular, tubular, etc.—was affected.

Both companies had already identified nephrotoxicity biomarkers, but they needed
to validate them. Ultimately both companies ran antibody-based assays on two different platforms to correlate and confirm each other’s results. The results were later folded into the Critical Path Institute’s Predictive Safety Testing Consortium, which was officially established in 2006. Critical Path scientists acted as neutral arbiters so that other consortium members, which include 16 companies in total, could cross-validate Novartis’ and Merck’s results. To ensure that the project met goals outlined in Critical Path, the consortium consulted FDA scientists throughout. This July, the Predictive Safety Consortium plans to present the data to both European and U.S. regulators.

“It sounds pretty simple, but it was extremely complicated,” Vonderscher said, and it was not just the science. Sorting out intellectual property and data sharing issues ate up a lot of time. At one point there were 35 lawyers sitting around a table to negotiate the consortium contract, Vonderscher recalled—and this was regarding research that wasn’t yet competitive.

Nevertheless, “we learned a lot from the process and we are extremely happy with the first results,” Vonderscher added.

Regulators in the Process
Besides the industry cooperation, what makes this example different is that now companies are voluntarily presenting their early data to regulators. Sharing such information ensures that once a company applies to market a drug, reviewers will be familiar with the technologies and biomarkers being used, said William Potter, M.D., Ph.D., vice president for neuroscience translational research at Merck.

“People used to think, ‘If I measure a biomarker and I’m not sure what it means, maybe FDA will start asking questions about safety and not approve a drug,’” Potter explained. But what Critical Path is saying is that “you don’t have to explain it away. They’ve created a free space for us to do more exploratory work without having to define every value and every outcome measure.”

Potter is enthusiastic about both Critical Path and IMI. But because IMI forces the private and academic sectors to collaborate, it may prove even more valuable than Critical Path, he said. For evidence he points to Merck’s involvement in a neuroimaging consortium that, while not initiated by the Critical Path, does illustrate the power of public–private teamwork. Launched by the National Institute on Aging in 2000, the Alzheimer Disease Neuroimaging Initiative (ADNI) was a 5-year, $40 million project that prospectively studied biomarkers associated with Alzheimer progression. Patients came from the Alzheimer collaborative study group, a network of 50 academic centers partly funded by the institute. It invited industry to get involved, and the industry scientists who pushed centers to systematically collect cerebrospinal fluid, which is routine among some European Alzheimer research groups, Potter said, “and now everyone is thrilled that it was done.”

“We’ve more than captured the value of every penny we’ve contributed simply by ADNI working out how to get good measures across multiple sites,” Potter added.

ADNI is a strictly U.S.-based project. But researchers in Europe are already working on a complementary neuroimaging project. In late 2005, European researchers launched an IMI pilot project that was funded by the EC and industry collaborators. Called AddNeuroMed, it aimed to identify new biomarkers associated with Alzheimer disease progression. While ADNI is largely about validation of known biomarkers, AddNeuroMed is geared toward discovery of biomarkers through animal studies and human clinical research, explained Simon Lovestone, Ph.D., principal investigator at King’s College in London. “We purposefully set up AddNeuroMed to be ADNI compatible,” Lovestone commented. He has already published research on a set of new potential biomarkers that can be measured in plasma. Funding for AddNeuroMed will run out in 2008. If IMI is approved, however, the consortium will probably apply for further funding.

While many people anticipate that Critical Path and IMI will spur more mutually beneficial collaborative projects in the future, the real difficulty may be creativity.

“It will be a real challenge to come up with projects that are precompetitive and of sufficient magnitude to take advantage of the funding the commission intends to put on the table. We have to come up with good ideas, projects and proposals that lend themselves to this [collaborative] approach.”

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