IN brief

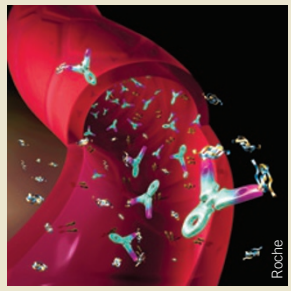
FDA inspections online

The US Food and Drug Administration (FDA) has released an online database of its final inspection classifications conducted in fiscal years 2009 and 2010. "We believe that disclosure of the compliance status of establishments will provide the public with a rationale for the agency's enforcement actions and may deter future violations and increase compliance with FDA regulations," says Howard Sklamberg, director of the FDA's Office of Enforcement. This includes inspections of clinical trial investigators, institutional review boards, and facilities that manufacture, process, pack or hold an FDA-regulated product that is currently marketed. The FDA will update the database every six months. In addition, the FDA is posting summaries of the most frequently cited regulations during inspections conducted by the FDA from fiscal years 2006 to 2010. "Disclosure of the inspection observations and number of times cited will provide industry with information that can be used to inform compliance efforts," adds Sklamberg. "The database information should be a reminder to all regulated industry that the FDA is out there, inspecting your facilities and that it is not a matter of if, but when, the agency will show up at your door. If this leads to a better understanding of how important it is to have solid systems and processes in place, then the database will have served a significant purpose," says Jack Garvey, founder and principal at Compliance Architects in Robbinsville, New Jersey. *Bethan Hughes*

Australian biotechs rejoice

The Australian Department of Innovation, Industry, Science & Research and The Treasury jointly announced an AUS $1.8 ($1.9) billion R&D tax credit last month aimed at boosting biotech companies and other innovation-oriented firms. In a bid to stimulate smaller businesses, companies with an aggregated turnover of less than AUS $20 ($21) million will benefit the most, with a 45% refundable tax credit on R&D expenditure. It is seen as being especially useful for startup biotech firms trading in loss. But larger companies exceeding the AUS $20 million benchmark will still enjoy a 40% nonrefundable offset. The reform, which is expected to pass the Senate in August and be backdated to July 1, has cross-party support and is the result of significant consultation and negotiation since at least 2008. Anna Lavelle, the CEO of AusBiotech, an industry organization representing more than 3,000 Australian biotech companies, said that the announcement represented the "most significant positive news" that the industry has had for a number of years. She predicts that the move will stimulate new investment and the production of more intellectual property, and will allow companies to begin their clinical trials earlier and reach their end goal of entering the market faster than before. She added, "All biotechnology companies will benefit from the reform to some degree and the majority will benefit dramatically." *Jennifer Rohn*

FDA panel votes to pull Avastin in breast cancer, again



The cancer treatment Avastin binds to VEGF secreted by the tumor.

For the second time in a year, a panel of US Food & Drug Administration (FDA) advisors has stated that Genentech's blockbuster cancer drug Avastin (bevacizumab) confers no meaningful clinical benefit when used with chemotherapy as an initial treatment for metastatic breast cancer and that its approval should therefore be rescinded. The forum for the current pronouncement was a two-day public hearing in late June requested by Genentech, the S. San Francisco, California, unit of Swiss pharmaceutical giant Roche. Avastin, a humanized monoclonal antibody that binds to vascular endothelial growth factor (VEGF), was approved in 2008 for use with chemotherapy in metastatic breast cancer under the agency's accelerated approval process. But last December, the FDA rescinded approval for the drug in that indication, prompting the drugmaker to request a hearing—the first time a drugmaker has ever contested such a move by the regulator (*Nat. Med.* **17**, 233, 2011).

Genentech claimed the confirmatory studies mandated for drugs receiving accelerated approval were positive and that in any case a decision should be tabled until the company obtains more data from a proposed new trial using a biomarker. Genentech also pointed to the high unmet medical need in first-line metastatic breast cancer as a rationale for continued use of its drug—a stance in agreement with the European Medicines Agency, which has approved Avastin for use in metastatic breast cancer, and oncology treatment guidelines outlined by the US National Comprehensive Cancer Network.

However, the advisory panel—a subset of the group that voted 12–1 last year against keeping Avastin on the market—voted unanimously against the drug on all of the questions put to it. These were: did the confirmatory trials verify the clinical benefit; did the available evidence show the drug to be effective; did the benefit justify the risks associated with its use; and should the FDA nevertheless continue the approval while additional studies are conducted? The advisors were most troubled by the failure of the two confirmatory studies to support the 5.5-month improvement in progression-free survival (PFS) seen in the original pivotal trial, called E2100. Compounded with ongoing safety concerns, including serious and life-threatening adverse events attributed to hypertension and kidney toxicity, they found the benefit–risk profile unacceptable. "The magnitude of PFS must be significant and outweigh the risks," Richard Pazdur, director of the FDA's Office of New Drugs within the Office of Oncology Drug Products, stated. Moreover, the accelerated approval process is "a two-way street," added Abigail Brandel of the FDA Office of the General Counsel. FDA may withdraw approval if post-approval studies fail to verify clinical benefit or other evidence demonstrates that the biological product is not safe and effective. "Both are shown here," she said.

Genentech contended that E2100 was a well-controlled trial and therefore the PFS data were not an outlier. Its assurances to the advisory panel—which did not contain a breast cancer specialist—that the safety issues could be effectively monitored, were also deemed unconvincing. What's more, the company had no data to support the notion that a proposed new study incorporating a biomarker test for high VEGF levels would be able to identify a patient subgroup that would benefit more from the drug. Nonetheless, it did establish at the hearing that FDA has discretion under the accelerated approval process to keep the breast cancer indication on the drug label.

A lot is at stake financially for Genentech/Roche. Avastin's approvals in other solid tumors, such as ovarian and small cell lung cancer, are not in issue, but moving the drug off-label in metastatic breast cancer may have a dramatic effect on sales. For the moment, payers announced they will continue to reimburse for the use of Avastin in metastatic breast cancer, but revenues for the drug have slipped since the advisory panel's original vote to withdraw in July 2010. In the first quarter of 2011, for example, sales were off 15% in the US compared with the first half of the previous year. Roche attributed the decline to regulatory and reimbursement uncertainty in the metastatic breast cancer indication.

FDA Commissioner Margaret Hamburg will make a final determination after the post-hearing comment period, which FDA extended for two weeks to July 28 to allow a full airing of public views. Mindful of strong public opinion in favor of giving patients a choice in this matter, shortly before the hearing, FDA decided to allow two hours of oral testimony from the public in addition to written comments into the record. **Mark Ratner** *Cambridge, Massachusetts*