FDA transparency rules could hit small companies hardest

The US Food and Drug Administration (FDA) is considering changing how much information it discloses about product applications—news that biotechs have greeted with a mixture of trepidation and hope. The agency is proposing to make publicly available 'complete response' and 'refuse-to-file' letters for drugs and 'not approvable' letters for devices. From opinions gathered in advance of the final decision, it seems the smallest biotechs stand to lose the most.

The proposed changes are wide-reaching and include some things most experts agree are good. On the upside, they say, this is an opportunity to make more information about what FDA does available to the public and ensure that data sources are more user-friendly. The downside, however, is the proposal to disclose information early in the approval process, including Investigational New Drug (IND) applications, holds and IND withdrawals. Few can see how revealing more information at the product application stage can be reconciled with trade secrets protection.

The Biotechnology Industry Organization (BIO) wants more details about how these proposed regulations would be implemented. "They [FDA] define trade secrets [in the document], but oddly there is no definition of what constitutes competitive information," explains Andrew Emmett, director for science and regulatory affairs at BIO, based in Washington, DC. The organization also wants clarification around who will decide what remains secret. Under current Freedom of Information Act regulations, Emmett says, companies have five days to determine whether documents that are going to be made public contain trade secrets that should be redacted. "We need to know exactly what the role of the sponsor will be in deciding what information is going to be shared," he says. Otherwise, companies could be put at competitive disadvantage or become victims of wild speculation.

The confidentiality issue is particularly critical for small biotechs. "When a small public company has a clinical trial pending, hedge fund managers do everything they can to get a sense of what the outcome might be," says Alan Mendelson, senior partner at Los Angeles–headquartered law firm Latham and Watkins. If every pause in the clinical trial process gets announced to the public, it could lead to stock trading based on misleading or inadequate information. "It's bad enough today," he says, "But at least now people are commenting on definitive data, not just a signal that might prove to be nothing."

Wayne Kubick, a vice president in safety at Waltham, Massachusetts–based PhaseForward, says companies with "limited products" are also going to be at greatest risk of competitive disadvantage. Competitors will be able to use some types of information better than others. Says Gregory Conko, senior fellow at the Competitive Enterprise Institute in Washington, DC, "It's less important with complete response or rejection letters, but with a new drug application, a hold, or a withdrawal, that is where tipping off competitors is a much bigger concern." Smaller companies are already at a disadvantage in the review process. In comments it filed in April, BIO pointed out that a recent study from the law firm Booz Allen Hamilton found that small firms had only a 48% first-cycle approval rate for products in the priority review category, compared with a 78% rate for larger companies. In a survey of 168 of its members (http://www.bio.org/letters/20100412b.pdf), BIO also found that "early, frequent and explicit communication with the FDA" was felt to be the most helpful means for first-time filers to improve their success rates.

The transparency initiative could help shore up this communication weakness. "A variety of leaders have been pushing for more open and straightforward dialog with the agency for years," says J. Donald deBethizy, president and CEO of Winston-Salem, North Carolina–based Targacept. "This initiative could provide a means for that." Greater transparency could also put pressure on FDA to provide rationales for rejections, which critics charge are sometimes based on "petty" issues, according to Conko.

Overall, such changes may not necessarily translate to better decision making, Conko warns. "FDA's political incentives are still poorly aligned. Even when their rationale is weak, they still don't have to pay a price for it," he says.

On the other hand, transparency is not necessarily a bad thing. "The world is very different already in 2010" says Kubick. "We have clinicaltrials.gov and a lot of other information already available." But it means companies will face more instances where study data is used out of context. "You have to protect yourself against people who data mine and then hold up a little data nugget as the truth," deBethizy says.

Many are watching closely as the next phase of the initiative rolls out. "This is by no means a done deal," says Kubick. "Some [of the proposed] things are going to happen, but not everything will." Others are very skeptical, like Jack McLane,

IN brief

Supremes rule on Bilski

Lee Pettet/istockphoto

Biotech welcomes ruling.

The US Supreme Court has ruled on a long-awaited and controversial patent litigation case, a decision greeted with relief by the biotech industry but vague enough that both sides can claim victory. The *Bilski v. Kappos* case was closely watched by the biotech community after the US Court of Appeals for the Federal Circuit ruled in 2008 that only methods tied to a machine or transformed into a different state are patentable, a standard which appeared to exclude crucial aspects of medical diagnostics. Commentators feared a restrictive ruling could have severely limited the ability to obtain patents on methods that use genes, proteins and metabolites to diagnose disease. Instead, the Supreme Court struck down patent claims on narrow grounds. "The Court was clearly conscious of the potential negative and unforeseeable consequences of a broad and sweeping decision," stated Washington, DC–based Biotechnology Industry Organization president and CEO Jim Greenwood. The court ruled on two issues. First, it ruled against patenting only those inventions that are "tied to a particular machine" or those that transform "a particular article into a different state or thing." Second, the court held that the word "process" as used in the US Patent Act should be read broadly to include modern day inventions. The ruling does not address the eligibility of patents for diagnostic methods, however, which leaves a number of questions unanswered with regard to a string of pending cases, including the closely watched dispute against Myriad Genetics and its breast cancer gene patents. Dan Ravicher of the Public Patent Foundation, a co-plaintiff with the American Civil Liberties Union in the suit against Myriad Genetics, believes "the opinion reinforces the line of case law that Judge Sweet relied upon in his decision striking down gene patents [in the Myriad case]. It rejects the argument that 'anything' is patentable." Justices Stevens, Breyer, Ginsburg and Sotomayor would have struck down not only the specific Bilski business method claims, but all business method patents on historical grounds that this class of patents was never contemplated by the framers of the US Constitution. The same argument would be difficult to support in biotech-specific cases as there is ample evidence that Thomas Jefferson, who reformed the Patent Act of 1793, considered medicine a "useful art" as was originally stated, a language later changed to "process." *Kenneth Chahine & Javier Mixco*