BIG BIOTECH SAVINGS

NEW FDA RULES FOR FOODS AND DRUGS

WASHINGTON, D.C.—November saw the U.S. Food and Drug Administration (FDA, Bethesda, MD) moving energetically into a regulatory reform mode—announcing proposals to revamp the drug-review process as well as to make sweeping changes in food-labeling regulations. Of the two developments, the drug reform proposals could bring significant savings to biotechnology companies, enabling products to be marketed sooner because data-gathering requirements would become less burdensome.

"We're encouraged. The proposals are a step in the right direction," says Alan Goldhammer of the Industrial Biotechnology Association (IBA, Washington, DC). "It's a win-win situation," says Bruce Mackler, general counsel of the Association of Biotechnology Companies (Washington, DC). "Anything that will move products along more rapidly through the agency—especially in the absence of new resources—is welcomed."

Among its proposals, FDA plans to move towards accepting a greater number of "surrogate end points" when assessing prospective drugs. Thus, instead of basing judgments solely on how a drug affects mortality or cure rates among patients, other signs of clinical improvements—chosen to reflect the nature of the disease and drug being studied—will be used to help establish whether a new drug is effective. This approach already has been used on a limited basis for evaluating new AIDS drugs. The approach promises to shorten and simplify the clinical-trial phase of a drug's evaluation—changes that are bound to reduce costs.

Another potentially key change for the biotechnology industry is an FDA recommendation calling for deregulation of phase-I safety studies in drug clinical trials. Thus, instead of FDA officials poring over results from this stage of clinical studies—which are intended to establish gross toxicities and relative dose ranges for new products—such tests and evaluations are to be done under the supervision of institutional review boards (IRBs) or other locally established advisory boards. Here again, time and cost savings could be significant, particularly for smaller companies, since they have fewer resources. Moreover, because the changed rules also would apply to investigators proposing initial clinical tests of gene-therapy procedures, the FDA may effectively be removed as an added regulatory hurdle for such research.

Some observers are skeptical whether IRBs or their equivalent will have the know-how or confidence to take full advantage of this proposal for FDA to stop reviewing Phase-I clinical trials. "Companies may still want to go to FDA out of liability fears," IBA's Goldhammer points out. Meanwhile, other observers fear that such changes could lead to a lowering of safety standards.

Other changes proposed by FDA could help biotechnology companies indirectly. For instance, one proposal calls for shifting the review of certain categories of drugs, such as antihistamines and analgesics, to private-sector contractors. Although few biotechnology-derived drugs will likely be part of this switch, the overall change could provide agency reviewers with more time than now is available, thus expediting their examination of biotech products still under their jurisdiction.

By contrast to these proposed reforms for regulating drugs, FDA's recently recommended food-labeling changes are unlikely to have much impact on biotechnology companies, most observers say. The labeling proposals are intended to provide nutritional information in a uniform format that is readily accessible to consumers. If genetically engineered traits in foods were treated as "additives," though, they would qualify for inclusion on product labels. However, although the agency's biotechnology-related food policies still are not formulated, insiders say there is little likelihood that engineered traits in whole foods will be construed as additives. **—Jeffrey L. Fox**

CONTINUED UNCERTAINTY

XOMA TOPS CENTOCOR

NEW YORK—The verdict was "guilty" when the eight-member jury emerged recently in Xoma's (Berkeley, CA) patent infringement case against rival Centocor (Malvern, PA). Jurors in the U.S. District Court for the Northern District of California found that Centocor's anti-endotoxin monoclonal antibody, Centoxin, infringed the patent Xoma had licensed from the University of California (Berkeley) for its E5 antibody.

Xoma has won a round in the courtroom, but Centocor has caught up at the Patent & Trademark Office (Alexandria, VA), which awarded a patent for Centoxin over a week before the jury started deliberating. So what does the verdict mean? "A continued uncertainty for about two years," says biotech analyst David Stone of Cowen & Co (Boston, MA). He notes that neither side is showing signs of moving toward a settlement.

What magnifies the legal uncertainty is the regulatory uncertainty. Neither company has won approval where it counts most, with the U.S. Food and Drug Administration (FDA, Bethesda, MD). In September, an FDA advisory panel recommended marketing approval of Centoxin for septic patients with Gram-negative bacteremia. At the same time, FDA told the advisory panel it would not take a recommendation yet on E5.

If E5 is not approved, the "Xoma patent won't have really sharp teeth," says Alex. Brown & Sons' (New York) David Webber, a biotech analyst. Under that scenario, Webber says, Xoma would get a royalty, at most.

But Webber, who is one of Xoma's few remaining champions on Wall Street, looks for other outcomes if E5 wins approval and if the verdict withstands appeals. These are big ifs, though, since Webber himself notes that "the appeals process defies analysis." The best case for Xoma, he says, would be to gain the entire U.S. market, while the worst case would be a cross-licensing arrangement with Centocor. A cross-license would be the best possible outcome for Centocor, while the worst case would be exclusion from the U.S. market.

That's a minority view. "It's probably unlikely that a judge would grant an injunction" against selling Centoxin now that Centocor has a patent, says Cowen's Stone. Assuming U.S. approval for Centoxin, "Centocor will get to market," says Robert Kupor, a biotech analyst at Kidder Peabody (New York). "There's no precedent" in the U.S. for keeping a lifesaving drug off the market, he adds.

Because an appeal is likely, Kupor expects the judge, Robert Schnacke, to require Centocor to set up an escrow account if and when U.S. sales of Centoxin begin. Kupor thinks this reserve fund would be no more than 10 percent of sales, assuming that E5 will not be approved and that, therefore, Xoma could not claim punitive damages.

Ultimately, Centocor has "a good chance of overturning Xoma's patent," Kupor says. "But that takes us into 1993." **—Mimi Bluestone**