US biotech prepares to fight generic biologics

As the US Congress debates a re-authorization of key US Food and Drug Administration (FDA; Rockville, MD) regulations, the biotechnology industry is preparing to fight an effort to permit the FDA to more readily approve knock-off versions of recombinant products.

Although the FDA can approve generic small-molecule drugs on the basis of bioequivalence data only, generic biologics are required to go through the expensive and painstaking clinical trial process. The generic drug industry, led by Barr Laboratories (Pomona, NY), is lobbying lawmakers to consider changes in the FDA's rules to bring the approval of generic biologics into line with that of small molecules.

At stake are billions: analyst Timothy Coan of ABN AMRO (New York) estimates recombinant products worth more than $10 billion in annual sales will lose patent protection by 2006, including blockbusters such as Amgen's anemia treatment Epogen and Biogen's multiple sclerosis drug Avonex. Without changes in the way the FDA operates, those billions will be safe from the quickly growing generic drug industry, which says the regulatory hurdles give biotech companies an unfair monopoly on their drugs, even after the patents expire. "It seems to me that any situation where there is a *de facto* monopoly set up, it has to be challenged," says Wayne Mulcahy, the senior director of scientific and professional affairs at Teva North America (North Wales, PA), a maker of generic drugs.

The biotechnology industry, however, is working to keep that effort from getting off the ground. The Biotechnology Industry Organization (BIO; Washington, DC) successfully fought attempts to add similar provisions to FDA-related bills last year by writing to influential members of Congress. This year, BIO expects to resume the fight, says Steve Lawton, the group's chief lobbyist on the issue.

For BIO, it is a matter of safety, says Lawton. Unlike traditional drugs, biologics are more than just pure chemical preparations: small changes to the manufacturing process can lead to clinical differences in the way products work. That makes it impossible to tell whether the same protein made by two different manufacturers will work in the same way, says Lawton. "As of now, the manufacturing is just too complex to support generic biologics," he says, echoing the group's pitch to lawmakers. Lawton cites the example of Johnson & Johnson's (New Brunswick, NJ) problems with Eprex, the version of erythropoietin the company sells in Europe. That drug has been linked to a rare cause of anemia known as pure red-cell aplasia in 40 patients, but Amgen (Thousand Oaks, CA) has seen a similar problem with its version Epogen only once. That suggests, says Lawton, that the two molecules made by two different companies, although same in name, do not have identical effects on the body.

Nevertheless, the FDA has already drafted a possible pathway for a few older recombinant products (such as recombinant insulin and human growth hormone) to win approval without a full complement of clinical testing. Although the generic drug industry says the scientific challenges in creating copies of more complex recombinant drugs can be overcome, the FDA proposal raised the hackles of industry and drew a sharp rebuke from Amgen, which wrote to the agency in December calling the effort "a direct threat to patient health and safety."

However, further regulatory changes concerning more complex generic biologics are inevitable, says Coan. Because biotechnology products are generally more expensive than drugs (with a year's supply of Avonex or of Immunex's rheumatoid arthritis treatment Enbrel, for example, each running more than $10,000), US legislators seeking to bring down health care spending may look to generic biologics. He says that although the FDA itself does not focus on drug pricing, legislators aware of the strain of rising medical spending on the government's insurance program are likely to push for the changes.

Brian Reid, Alexandria, VA

Nutraceuticals tread business tightrope in Europe

The nutraceuticals market in Europe could be worth some $300 billion within ten years, nearly two orders of magnitude larger than that in the United States, where definitions of what constitutes a nutraceutical are drawn much tighter. Whether that size will be reached depends in part on the success of nutraceutical producers in partnering with major food companies. It is also dependent on their ability to negotiate the gray area between food and drug regulations in Europe. These were the key messages to emerge from a discussion of nutraceuticals and functional foods at the BioSquare partnering conference held in Zurich at the end of February.

The best strategy for nutraceutical producers, according to Werner Badziong, vice president of quality and development at DGF Stoess (Eberbach, Germany), is to provide food marketing companies with value-added ingredients that have documentable health benefits. In DGF Stoess' case, the ingredient is gelatin, a product the company extracts from traditional animal sources and supplies for high-value end uses in the pharmaceutical, photographic, and food industries. Stoess also has an R&D relationship with Fibrogen (S. San Francisco, CA), a company with a strong intellectual property portfolio covering the production of recombinant gelatin. However, Stoess and its research collaborators are gathering evidence that consumption of a defined daily dose of gelatin has specific health benefits. According to Badziong, there is good evidence that daily gelatin strengthens hair and nails, and there are also strong indications that gelatin can reduce the incidence of bone fracture in osteoporosis and reduce joint inflammation in osteoarthritis. Working with Fibrogen, Stoess hopes to be able to establish claims related to specific gelatin fractions.

Armed with such health claims, Stoess aims to develop markets for gelatin using a business model that resembles the one Intel (Santa Clara, CA) developed for its chip sets. Intel promoted its chips directly to the purchasers of personal computers, allowing PC manufacturers to demand a premium for machines with "Intel inside." Similarly, Badziong believes that the claims nutraceutical manufacturers establish for their products will allow food manufacturers to promote new product lines containing those ingredients. To demonstrate proof of concept, DGF Stoess has developed a range of gelatin-containing products including drinks, confectionery, and a "Joint Food," a bar that displays the claim, "Collagen-Hydrolysates for healthier joints."

Claims from manufacturers will make or break the nutraceutical business. According to Christofer Eggers, a food law specialist with Mayer, Brown & Platt (Frankfurt am Main, Germany), nutraceuticals have to occupy a narrow stretch of legislative ground between pharmaceuticals and food. The gist of current regulations in Europe, which are largely nationally based, is that food may not be advertised with disease-related claims, says Eggers. "A claim that a food ingredient was effective against arthri-