MARCH 10, 2010

**Push to Cure Rare Diseases**

*FDA Officials Go to New Lengths to Encourage Applications for Orphan-Drug Status*

By AMY DOCKSER MARCUS

CLAREMONT, Calif.—Staff members at the Food and Drug Administration are doing something unusual. They are leaving Washington to help drug makers take a crucial step in developing drugs for rare diseases.

The staffers help administer the Orphan Drug Act, which provides incentives to create therapies for so-called orphan diseases—those that affect fewer than 200,000 Americans. There are about 7,000 such maladies, most of them serious, that have few or no drugs to treat them, from adenoid cystic carcinoma, a rare head and neck cancer, to Zollinger-Ellison syndrome, which is associated with a tumor that causes the production of high levels of stomach acid.

As a result, doctors may end up prescribing drugs developed for other diseases off-label, but not all insurers will cover this kind of use.

Getting an orphan-drug designation opens the door to incentives once the FDA approves a medicine for sale in the U.S., including seven years' marketing exclusivity and tax breaks. Last year, just 250 requests for orphan-drug designation were filed, and 160 received it.

"We're barely scratching the surface," says Timothy Coté, director of the FDA's Office of Orphan Products Development, the workshop's sponsor. He says there are roughly 350 orphan drugs approved, covering about 150 rare diseases.

Tim Cunniff, vice president of global regulatory affairs at Lundbeck Inc., which has a number of approved orphan drugs, says most companies developing orphan drugs are small.

Big companies are starting to get more interested in rare diseases, but the key issue is the high cost of developing a drug and the typically long time it takes to move it from a lab into a clinic as a treatment that gets prescribed. Before starting down this arduous path, a company needs to feel there is a reasonable chance of making a profit.

To help get more applications, Dr. Coté's office put out the word: Help is available, in two workshops with on-the-spot regulatory advice. The first workshop, held last month at the Keck Graduate Institute here, drew 29 potential sponsors, from major drug companies to academic centers, small biotechs and even some patient advocates. In a follow-up survey, 74% said they had never before filed an application for orphan drug designation.

M. Ian Phillips, director of Keck's Center for Rare Disease Therapies, said he knew ensuring confidentiality would be critical, as the drug industry is extremely competitive. So participants' name badges didn't include company names. The rooms where the teams worked to fill out the applications were labeled only by number, such as "Team 1" or "Team 2."
At the introductory meetings, participants were admonished to be friendly at lunches and receptions but not push anyone to reveal more than he or she wanted. "I remember someone introducing himself as 'Ralph' at one of the receptions and that's all I ever found out about him," Dr. Phillips said.

Dr. Coté said he wanted participants to understand that the workshop wasn't providing an alternative pathway to orphan-drug designation, just regulatory advice. He said it was very important that the FDA avoid the "perception of favoritism" and even stressed that in the cover letter to an application, the sponsors shouldn't say they had been at the workshop.

Each team met four times over the course of two days with FDA staffers who offered advice on nine critical issues in filling out an application. A key one is providing evidence—preferably either trial data or published reports of animal studies—that a drug exists and holds promise for treating a rare disease. Sometimes statistics on very rare diseases are hard to obtain.

Barbara Fant, president and chief executive of Clinical Research Consultants Inc., attended the workshop to prepare an application for a drug-company client, and said this was her first time filing for an orphan drug designation.

An FDA staffer pointed out issues in her application that "would have come back to me as questions and delayed the designation process" if she had filed before the workshop. "I learned some nuances that I didn't know," said Dr. Fant, who declined to provide details about her client or the drug.

An orphan-drug designation is no guarantee a medicine will ultimately be approved for marketing. A different FDA division reviews safety and efficacy data for approval. Upon further testing, a drug may turn out to be too dangerous or not effective. Companies may decide a product is too expensive to make, change direction, or go out of business. But Dr. Phillips and Dr. Coté hope that by increasing the pool of applicants for designation, they will increase the chances of getting more approvals.

The resolution of the first workshop suggests the orphan-products office has a ways to go to reach the goal of doubling the number of yearly applications. In the end, 14 of the 29 submitted applications at the end of the two-day workshop, though they can still submit any time, and more could do so in ensuing months. It usually takes the FDA 60 days to determine whether the designation will be given.

Dr. Coté said he considered the workshop a success but was disappointed that not every group submitted. "It's not 'War and Peace,'" he said in a meeting at the close. "The applications are six or seven pages."

Up to 50 more organizations can attend the second workshop, to be held at the University of Minnesota in August. Dr. Coté said he was considering a workshop in Europe. Next time, he wants to weed out applicants who can't file at the end of two days; a number of participants said they couldn't file the finished product without approval from their companies.

The FDA is reaching out aggressively, but resources are still limited. "Don't come if you're not going to submit," he said.

Write to Amy Dockser Marcus at amy.marcus@wsj.com