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Client Alert

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FDA Leaves an Orphan Out in the Cold

In what appears to be a first, the Food and Drug Administration (FDA) recently rescinded an orphan drug exclusivity it granted two years ago to a drug company, claiming it made a mistake. In its decision[1], made in response to a Citizen Petition, FDA made a strong distinction between orphan drug designation, which it continued to recognize for the affected product, and orphan drug exclusivity, which it took away in this case.

This bulletin highlights what we believe are the key FDA points and issues for orphan drug companies to consider as they either defend their exclusivity or develop orphan drugs. We also note how, nearly thirty years since the passage of the Orphan Drug Act, the agency's views continue to emerge. We will not detail the facts of the particular case, nor will we review the basic provisions of the Orphan Drug Act.

Overview of Important Facts

- In 2009, Octapharma USA Inc. obtained orphan drug exclusivity after demonstrating to FDA that its biological product, Wilate (von Willebrand Factor/Coagulation Factor VIII Complex (Human)), was clinically superior to CSL Behring LLC's Humate-P product.

- In 2011, CSL Behring submitted a Citizen Petition, questioning the evidentiary support for superiority and asking FDA to rescind Wilate's orphan drug designation and exclusivity (CSL made other requests, which FDA rejected, and that are not discussed in this bulletin).

- On August 8, 2012, FDA granted CSL's Citizen Petition in part and denied it in part. See Docket No. FDA-2011-P-0213.

Key FDA Findings

- FDA rescinded orphan drug exclusivity for Wilate, thereby revoking Octapharma's seven-year exclusivity that started in 2009. FDA concluded that Octapharma's Wilate was not clinically superior to CSL's Humate-P, despite a different decision two years earlier. The law allows that a competitor drug can be granted orphan drug designation and exclusivity, despite another's orphan drug exclusivity, if it demonstrates clinical superiority to the first drug approved for the orphan indication. See e.g., 21 C.F.R. §§ 316.3 and 316.20(b)(5). One can show superiority

1 FDA, Response to CSL Behring Citizen Petition (Aug. 8, 2012), available at: http://www.regulations.gov/#!documentDetail;D=FDA-2011-P-0213-0017

in terms of safety, efficacy, or a major contribution to patient care. See 21 C.F.R. § 316.3(b)(3). Demonstration of clinical superiority is not common. After FDA re-reviewed Wilate, it concluded that the data did not "support a conclusion that Wilate has been demonstrated to 'provide a significant therapeutic advantage over and above that provided by' Humate."[2] As such, the agency found it had erred in granting exclusivity and was, therefore, revoking the exclusivity.

- FDA allowed Octapharma to keep its orphan designation. The agency said a plausible hypothesis of superiority is sufficient to obtain orphan drug designation. See 21 C.F.R. §§ 316.20(a) and 316.25(a)(3). However, this hypothesis must be proven to secure exclusivity. Thus, Octapharma demonstrated a plausible hypothesis in 2009 that Wilate was clinically superior to CSL's product, sufficient for designation, which it can keep.

- FDA rejected CSL's request that the agency require head-to-head comparative clinical evidence of superiority in future orphan designation and exclusivity reviews. The agency said it did not want to limit "the precise type and amount of evidence necessary."[3] Rather, FDA will evaluate each case individually as to what information is required to demonstrate clinical superiority.

Sign of Things to Come?

FDA's decision is significant in its attempt to further explain its position on orphan drug-related issues. It appears to be a continuum of events, as FDA's views continue to evolve, even nearly thirty years since Congress enacted the law. In 2011, FDA issued proposed amendments to its regulations, which we described in a prior bulletin which can be accessed by clicking here. In addition, this year, FDA has argued in court that it is under no legal obligation to take enforcement action against those that might undermine a drug company's orphan drug exclusivity; it has enforcement discretion, but no obligation. *K-V Pharmaceutical Company v. United States Food and Drug Administration*, filed July 5, 2012, D.D.C., Case Number 1:2012cv01105 (FDA Memorandum in Support of Motion to Dismiss). In this case, which AGG is following for clients, FDA said that, despite K-V Pharmaceutical's orphan drug exclusivity for its Makena drug product, the agency is not required to take enforcement against pharmacies that compound the active ingredient. Based on FDA's inaction, the compounders' actions undermined K-V's exclusivity, even though the compounding might violate FDA's policies. Id. (case pending – no decision at this time).

While the Octapharma/CSL case is unusual and fact-specific, this case, along with the agency's proposed amendments and the K-V example, demonstrate a continued evaluation and evolution of FDA's policies, views, and interpretations of orphan drug law. Any company with orphan drug designation, exclusivity, or both, or those considering the orphan drug approach, should continue to monitor developments, as we certainly will for clients.

2 See Response, p. 2.
3 FDA Response, p. 13.