Drug Company Refuses to Take it Easy and Prevails in Court Case Against FDA Relating to Orphan Drug Exclusivity

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On March 13, 2020, Eagle Pharmaceuticals, Inc. refused to "take it easy" (yes song lyric pun included) against the Food and Drug Administration when it took a stand and prevailed in a court case against the agency concerning the then-clinically superior FDA regulatory requirement for orphan drug exclusivity determinations.[1] However, as will be discussed, the decision may have limited applicability.

The Court of Appeals for the D.C. Circuit found that the orphan drug exclusivity provisions in the Federal Food, Drug, and Cosmetic Act (namely, 21 U.S.C. § 360cc(a)) were clear and unambiguous in allowing orphan drug marketing exclusivity to a drug manufacturer when FDA granted orphan drug designation and, the company obtained new drug application approval. The court said the FDA cannot "add an after-the-fact requirement that a designated and approved drug prove clinical superiority before receiving that exclusive approval benefit." While the agency expressed concern about successive exclusivity periods, the court responded, "Nothing in the statute's text, structure or purpose limits this benefit to only one drug manufacturer."

In this Bulletin, we will not detail all of the statement of facts or FDA's failed arguments. In addition, we will not describe the orphan drug exclusivity regulatory framework in detail. However, we will try to provide an overview of the basic facts and those issues which we believe are most useful to provide context for the court's decision.

Regulatory Overview

- In 1983, Congress enacted the Orphan Drug Act to address the problem of "orphan drugs,"[2] i.e., drugs for rare diseases or conditions, at a time when pharmaceutical companies typically did not expend significant resources to develop treatments.
- The law allows FDA to designate a drug, at its development stage, as an orphan drug, which provides benefits designed to promote orphan drug development, such as tax credits and monetary grants to defray the costs of developing orphan drugs.[3]
- After a sponsor's drug has been designated as an orphan drug and approved for marketing, FDA provides the sponsor with a seven-year period of exclusive approval rights during which time the FDA may not approve another "such drug for such disease or condition" for marketing until the end of the seven-year exclusivity period.[4]
- The law does not define "such drug," which is an important term because it defines the scope of the exclusivity.
- FDA has interpreted "such drug" to mean the "same drug," [5], and has determined that a drug is the "same" as a previously approved drug if it shares the same "active moiety," i.e., the same active ingredient, and "is intended for the same use."[6]

1 *Eagle Pharmaceuticals, Inc. v. Azar,* 2020 WL 1222699 (D.C. Cir. March 13, 2020).
2 Pub. L. No. 97-414 (1983).
3 21 U.S.C. § 360bb.
4 21 U.S.C. § 360cc(a).
5 21 C.F.R. § 316.31(a).
6 21 C.F.R. § 316.3(b)(14)(i).

- The agency has determined, however, that, "if the subsequent drug can be shown to be clinically superior to the first drug," despite having the same active moiety, "it will not be considered to be the same drug."[7]
- A drug is clinically superior if it "is shown to provide a significant therapeutic advantage over and above that provided by an approved drug (that is otherwise the same drug) in one or more of the following ways: (1) [g]reater effectiveness … (ii) [g]reater safety … or (iii) [i]n unusual cases, … otherwise makes a major contribution to patient care."[8]
- In other words, the court noted:
  - FDA considers a drug the same as a previously-approved drug if it shares the same active moiety and is not otherwise clinically superior; it considers the drug to be different – and thus entitled to its own seven-year exclusivity period upon designation and approval – if it does not have the same active moiety or is clinically superior.
- The issue of clinical superiority comes up in two stages of the orphan drug process:
  1. At the designation stage, the sponsor of a drug that is otherwise the same (i.e., with the same active moiety as an already approved drug "may seek and obtain orphan-drug designation for the subsequent drug for the same rare disease or condition if it can present a plausible hypothesis that its drug may be clinically superior to the first drug."[9]
  2. After the drug has been approved for marketing, FDA requires the manufacturer to demonstrate that the drug is clinically superior to the previously approved drug" in order to receive the seven-year exclusivity period.[10]

Court Decision

- FDA granted orphan drug designation to Eagle's Bendeka cancer drug product, which contained the active ingredient bendamustine.
  - The agency had previously approved another drug product containing the same active ingredient and granted it orphan drug exclusivity (this product had a different formulation than Bendeka).
  - While the other company's orphan drug exclusivity period was running, FDA accepted Eagle's plausible hypothesis that its Bendeka product was clinically superior to the other product, thereby granting Bendeka orphan drug designation.
  - When FDA approved Bendeka, it did not grant the drug product orphan drug exclusivity, because FDA concluded Eagle had not met the post-approval clinical superiority requirement.
    - The agency also said that Eagle was not automatically entitled to exclusivity, despite the *Depomed* case, which rejected the clinical superiority requirement, because the FDA thought that decision was wrongly decided.[11]
- FDA made many arguments to support its position that Eagle was not entitled to orphan drug exclusivity, primarily concerned about successive or serial exclusivity periods.
- The court, in a 2-1 decision, rejected all of the arguments and affirmed the district court's decision, stating:
  - Based on this [statutory] language, the seven-year marketing exclusivity period applies automatically – the text leaves no room for the FDA to place additional requirements on a drug that has been designated and approved before granting its manufacturer the right to exclusivity.
- The court noted that some of FDA's concerns about serial exclusivity are "from the way the FDA had decided to regulate its definitions for designation and the scope of exclusivity."

7 21 C.F.R. § 316.3(b)(14)(i).
8 21 C.F.R. § 316.3(b)(3).
9 21 C.F.R. § 316.20(a).
10 21 C.F.R. § 316.34(c).
11 *Depomed, Inc. v. U.S. Dep't of Health & Human Services*, 66 F.Supp. 3d 217, 220 (D.D.C. 2014). We prepared a Bulletin on that decision: https://www.agg.com/news-insights/publications/orphan-drug-exclusivity-criteria-clarified-in-court-decision-10-28-2014/

Potential Effect of the Decision

- The decision may have limited applicability because, in 2017, while the Eagle case was pending, Congress amended the Orphan Drug Act to allow FDA to impose a clinical superiority requirement when evaluating exclusivity determinations.[12]
- The decision, though, may affect those cases that were pending before the 2017 Congressional amendments.

12 21 U.S.C. § 360cc(c).

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