

## ISSUE BACKGROUND

### Orphan Drug Exclusion from the Annual Pharmaceutical Fee

**Issue:** The orphan drug exclusion from the annual pharmaceutical fee fails to serve the policy goal of rewarding past and encouraging future innovation in developing therapeutic interventions for the treatment of rare diseases, disorders, and conditions because it is hinged on whether the manufacturer took a tax credit rather than strictly on disease prevalence.

**Current Law:** Beginning in 2011, the Internal Revenue Service (“IRS”) will assess an excise tax, known as the “annual pharmaceutical fee,” on the sales volume of most branded pharmaceuticals sold into several government channels: Medicaid, Medicare Part B, Medicare Part D, the Department of Veterans’ Affairs, the Department of Defense, and the TRICARE retail pharmacy program.<sup>1</sup> In calculating one’s market share in these government channels for the purpose of the annual fee, manufacturers are to exclude sales of any “orphan drugs,” which the statute defines as those that qualified for the Orphan Drug Act (“ODA”) tax credit.<sup>2</sup> Guidance from the IRS expressly requires the manufacturer to actually have taken the ODA tax credit to be eligible for the orphan drug sales exclusion.<sup>3</sup> A manufacturer will not be permitted to exclude orphan drug sales from its tax liability if the U.S. Food and Drug Administration (“FDA”) approves the orphan drug “for any indication other than the treatment of the rare disease or condition” that secured the tax credit.<sup>4</sup>

**What is the purpose of the annual pharmaceutical fee?** Congress created this revenue stream as another mechanism to help fund health reform under the belief that those industries that are “benefitting” from the “new business” provided by the 32 million previously uninsured Americans receiving insurance coverage should have a financial stake.<sup>5</sup> The annual revenue raised by the fee – initially \$2.5 billion, escalating each year to 2018, when it reaches \$4.1 billion, before retreating to \$2.8 billion in 2019 – will be placed in the trust fund used to pay for items and services covered under Medicare Part B.<sup>6</sup>

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<sup>1</sup> See Section 9008 of the Patient Protection and Affordable Care Act of 2010 (Pub. L. No. 111-148) (“PPACA”), as modified by section 1404 of the Health Care and Education Reconciliation Act of 2010 (Pub. L. No. 111-152).

<sup>2</sup> See § 9008(e)(3) of the PPACA. The tax credit, seven years of market exclusivity, and federal appropriations for grants and contracts for orphan development are the three key incentives provided by the ODA to encourage drug manufacturers to develop medicines for the treatment of rare diseases, disorders, and conditions. See 26 U.S.C. § 45C; 21 U.S.C. § 360cc(a); 21 U.S.C. § 360ee.

<sup>3</sup> See Internal Revenue Service, Notice 2011-9, <http://www.irs.gov/pub/irs-drop/n-11-09.pdf> (last visited March 30, 2011).

<sup>4</sup> See § 9008(e)(3) of the PPACA. This limitation on the exclusion is intended to prevent “blockbuster drugs” originally approved as an orphan drug from inadvertently benefitting from the provision.

<sup>5</sup> See, e.g., Lauren Smith, *Pharma’s Reform Bounce: How Big a Boost Will \$80 Bil. Buy?*, THE RPM REPORT (Sept. 21, 2009), [http://therpmreport.com/Free/db79ab7c-1c40-4fe6-bb90-9b3ee1f65b9b.aspx?utm\\_source=RPMel](http://therpmreport.com/Free/db79ab7c-1c40-4fe6-bb90-9b3ee1f65b9b.aspx?utm_source=RPMel) (last visited Dec. 14, 2010); see also Rick Newman, *How Big Pharma Wins from Healthcare Reform*, U.S. NEWS & WORLD REPORT (Sept. 25, 2009), <http://money.usnews.com/money/blogs/flowchart/2009/9/25/how-big-pharma-wins-from-healthcare-reform> (last visited Dec. 14, 2010).

<sup>6</sup> See § 1404(a)(2) of the HCERA; § 9008(c) of the PPACA.

**What is the ODA tax credit?** The ODA tax credit allows manufacturers to claim a tax credit of up to 50% for the expenses paid or incurred by the manufacturer or the sponsor in the taxable year on human clinical trials necessary to obtain FDA marketing approval of the drug or biological for the rare disease or condition for which it received an “orphan” designation.<sup>7</sup>

**What is an orphan designated drug?** Drugs or biologicals used to treat rare diseases, disorders, and conditions may be eligible to receive an orphan drug designation from FDA. In order to be designated by FDA as an “orphan drug,” the manufacturer or the sponsor of a drug may request FDA to designate it as a drug for a rare disease or condition.<sup>8</sup> Such designation must be sought prior to submission of a new drug application (“NDA”) or a biologics license application (“BLA”) for that disease or condition and that drug or biological must meet the rare disease threshold of treating less than 200,000 patients in the U.S. for the disease or condition for which it is seeking FDA marketing approval.<sup>9</sup>

**Why does the requirement that manufacturers take the ODA tax credit to qualify for the orphan drug exclusion from the annual pharmaceutical fee undercut the policy goal of the exclusion?** Many manufacturers were either unable to take the credit, or made the business decision to take a different tax credit that precluded a claim for the ODA tax credit in the same year or with respect to the same research and development expenses.

- **The ODA tax credit was not available for an 18 month period.** Prior to June 1, 1997,<sup>10</sup> the ODA tax credit was not permanent. Between January 1, 1995 and June 30, 1996, Congress had failed to reauthorize this provision, making it impossible for manufacturers to claim the credit for clinical testing expenses incurred during that period.<sup>11</sup>
- **During the first 12 years of the ODA, new market entrants were unlikely to claim the ODA tax credit.** For clinical testing expenses incurred from the effective date of the ODA on January 1, 1983 until December 31, 1994, manufacturers could not carry unused credits forward or backward;<sup>12</sup> thus, initially under the law, manufacturers had to

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<sup>7</sup> See 26 U.S.C. § 45C. The qualifying testing expenses must have occurred after the drug received “orphan designation” by the FDA, but before the agency’s approval of the new drug application (“NDA”) or biologics license application (“BLA”). See 26 U.S.C. § 45C(b)(2)(a).

<sup>8</sup> See 21 U.S.C. § 360bb.

<sup>9</sup> See 21 U.S.C. § 360bb(a)(2). The drug may treat more than 200,000 patients if there is no “reasonable expectation” that it will be profitable. *Id.*

<sup>10</sup> See Section 604 of the Taxpayers Relief Act of 1997, Pub L. No. 105-34, 111 Stat. 788, 863.

<sup>11</sup> See Section 1205(b) of the Small Business Job Protection Act of 1996, Pub. L. No. 104-188, 110 Stat. 1755, 1775.

<sup>12</sup> See Marvin S. Lieber and Richard R. Tarantine, *Federal Tax Developments Affecting Individuals, Corporations, and Other Organizations*, 68 PA. B. ASSN. Q. 68, 70 (1997). Beginning July 1, 1996, Congress reauthorized the ODA tax credit for 11 months through May 31, 1997 and reclassified it as a business credit. See Section 1205 of the Small Business Job Protection Act of 1996, Pub. L. No. 104-188, 110 Stat. 1755, 1775. This reclassification resulted in manufacturers finally having the ability to carry back and carry forward unused portions of the credit. See 26 U.S.C. § 39. Initially manufacturers could carry it back three years, or carry it forward 15 years. See Lieber, *supra* note 3. Since 1998, manufacturers are able to carry it back just one year, but carry it forward 20 years. See Section 1083(a) of the Taxpayers Relief Act of 1997, Pub L. No. 105-34, 111 Stat. 788, 951, *codified* at 26 U.S.C. § 39(a).

have income and high enough tax liability to take the ODA tax credit, which was difficult for newer market entrants that lacked revenue.<sup>13</sup>

- **Most drug manufacturers did not claim the ODA tax credit during the 1980s and early 1990s because they were receiving special tax breaks for having established manufacturing operations in Puerto Rico.** More than 40 of the world's largest drug manufacturers created thousands of jobs in Puerto Rico during this period in return for a tax exemption for all income derived from the specified facility.<sup>14</sup> Manufacturers that elected the section 936 credit in a given year could not also claim the ODA tax credit for any qualifying clinical testing expenses incurred during that same year.<sup>15</sup>
- **Some manufacturers may choose to claim the R&D tax credit, rather than the ODA tax credit for its clinical testing expenses.** Manufacturers may not claim both the ODA tax credit and the R&D tax credit under 26 U.S.C. § 41 for the same qualifying clinical testing expenses.<sup>16</sup>
- **Generally, foreign testing expenses are not eligible for the ODA tax credit.** Manufacturers may not claim the ODA tax credit with respect to any clinical testing conducted outside the U.S. unless there is an insufficient U.S. testing population due to the rarity of the disease.<sup>17</sup>
- **Because of the existing U.S. regulatory framework, some manufacturers have not been able to obtain orphan designation for drugs and biologicals exclusively FDA indicated for the treatment of rare diseases, disorders, or conditions, so have not been eligible for the ODA tax credit.**<sup>18</sup> According to Dobson DaVanzo & Associates, LLC, a health economics and consulting firm, 41 drugs and biologicals are solely indicated by FDA for the treatment of rare diseases, disorders, or conditions, but lack an orphan designation from FDA.<sup>19</sup> Thirty-three of these 41 therapies are plasma protein therapies, therefore, the annual fee in its current structure disproportionately affects the plasma protein industry.

**How does the existing U.S. regulatory framework impede some drugs and biologicals that are exclusively FDA indicated for the treatment of rare diseases, disorders, or conditions from receiving an orphan designation for that rare disease or condition from FDA?** As discussed above, a drug or biological must obtain "orphan designation" from FDA in order for the manufacturer or sponsor to claim the ODA tax credit for the drug. A manufacturer

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<sup>13</sup> See Li-Hsien Rin-Laures and Diane Janofsky, *Note: Recent Developments Concerning the Orphan Drug Act*, 4 HARV. J.L. & TECH. 269, 295 (1991).

<sup>14</sup> See U.S. GEN. ACCOUNTING OFFICE, GAO/GGD-92-72BR, PHARMACEUTICAL INDUSTRY: TAX BENEFITS OF OPERATING IN PUERTO RICO 1, 13, 16-17 (1992).

<sup>15</sup> See 26 U.S.C. § 45C(d)(2)(B).

<sup>16</sup> See 26 U.S.C. § 45C(c).

<sup>17</sup> See 26 U.S.C. § 45C(d)(2)(A). The section 936 tax credit was completely phased out by December 31, 2005.

<sup>18</sup> See 26 U.S.C. § 45C(b)(2)(A)(ii)(I).

<sup>19</sup> See JOAN E. DAVANZO ET AL., DOBSON DAVANZO, LLC, IDENTIFYING THERAPIES SOLELY INDICATED FOR TREATING ORPHAN DISEASES THAT DO NOT MEET THE ORPHAN DRUG EXCLUSION CRITERIA OF THE ANNUAL PHARMACEUTICAL FEE 2 (2010).

or sponsor may request orphan drug designation of: (1) a previously unapproved drug; (2) a new orphan indication for an already marketed drug; or (3) a drug that is otherwise the “same” drug as an already approved orphan drug and is for the same rare disease or condition as that already approved drug. For all three types of orphan drug designation applications, the applicable FDA regulations governing the content and format of such requests call for a substantial application that requires, among other things, the submission of evidence demonstrating a rare disease patient population of less than 200,000 for the orphan indication being sought. It is important to note that the third category of applications must satisfy an additional — and extraordinarily difficult — requirement. Specifically, for a drug or biological that is “otherwise the same drug as an already approved orphan drug,” an orphan drug designation can be obtained only if the drug sponsor presents a plausible hypothesis of “clinical superiority” to the already approved orphan drug. This requirement has created a scenario where, generally, only the product that is first to market in a particular therapeutic class can qualify for such designation. It should be further noted that even if FDA grants orphan drug designation for a product, it can be—and, indeed, nearly always is—a long, complex (and frequently unsuccessful) process to thereafter obtain FDA approval to market the orphan designated indication as a safe and effective treatment for the orphan condition.

- ***The clinically superior threshold acutely affects the plasma protein therapeutics industry because there are multiple brands in most therapeutic classes.*** The brands within each respective therapeutic class of plasma protein therapies are non-interchangeable, unique biologicals despite having the same active agent,<sup>20</sup> these therapies would meet the definition of “same drug” for the purpose of orphan designation found in the ODA regulations.<sup>21</sup> Ironically, this regulatory definition and its resulting effects are inconsistent with policy goals of the ODA. Plasma protein therapies represent 33 of the 41 drugs and biologicals that are solely indicated by FDA for the treatment of rare diseases, disorders, or conditions, but lack an orphan designation from FDA.<sup>22</sup>
- ***FDA has consistently denied orphan drug designation requests by second to market drugs because the clinically superior threshold is difficult to satisfy.***<sup>23</sup> According to the ODA regulations, in order to satisfy the clinically superior requirement, the manufacturer or sponsor of the subsequent NDA or BLA must present a plausible hypothesis that the brand exhibits greater safety or greater effectiveness than the first to market brand.<sup>24</sup> FDA would require comparative clinical trials to make such an assessment in some cases of “safety” claims and in most cases of “effectiveness” claims.<sup>25</sup> If unable to demonstrate greater safety or effectiveness, subsequent drugs coming to market for the same indication in the same therapeutic class can also qualify

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<sup>20</sup> See, e.g., Letter from Jordan Orange, M.D. and Kathleen Sullivan, M.D., to Anne Jacques, Dir. Clinical Pharmacy Servs., Highmark (Feb. 28, 2011) (describing the clinical differences among the brands of immune globulin) (on file with author).

<sup>21</sup> See 21 C.F.R. § 316.3(13)(ii)(A) (illustrating the impediment faced by manufacturers of subsequent market entrant plasma protein therapies in obtaining orphan designation).

<sup>22</sup> See DAVANZO, *supra* note 19.

<sup>23</sup> See, e.g., Baker Norton Pharmaceuticals, Inc. v. FDA, 132 F. Supp.2d 30 (D. D.C. 2001).

<sup>24</sup> See 21 C.F.R. § 316.3(3).

<sup>25</sup> *Id.*

as “clinically superior” to the original brand by demonstrating that the subsequent drug makes “a major contribution to patient care.”<sup>26</sup>

- ***Some drugs and biologicals used to treat rare diseases, disorders, and conditions received FDA approval prior to the ODA, so have been unable to receive orphan designation.*** The ODA went into effect January 1, 1983. FDA first approved immune globulin therapies for treating primary immune deficiency diseases (“PIDDs”) in 1981. While new formulations of immune globulin that came to market after enactment of the ODA could certainly have sought orphan designation for PIDDs, there was no incentive for the manufacturer to do so because obtaining the seven years of market exclusivity under 21 U.S.C. § 360cc(a) would have been impossible because there is not an unlimited supply of this therapy since it is a derivative of human plasma.<sup>27</sup>

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<sup>26</sup> *Id.*

<sup>27</sup> See 21 U.S.C. § 360cc(b)(1) (highlighting that the FDA will not grant orphan drug market exclusivity to products that are unable to meet patient access needs by themselves).