



## Safety Net Hospitals for Pharmaceutical Access

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July 19, 2011

CDR Krista Pedley  
Director, Office of Pharmacy Affairs (OPA)  
Healthcare Systems Bureau (HSB)  
Health Resources and Services Administration (HRSA)  
5600 Fishers Lane  
Parklawn Building, Room 10C-03  
Rockville, Maryland 20857

**Re: Comments on Proposed Rule Regarding Exclusion of Orphan Drugs Under the 340B Program (RIN – 0906-AA94)**

Dear CDR Pedley:

Safety Net Hospitals for Pharmaceutical Access (SNHPA) respectfully submits these comments in response to the proposed rule to implement the exclusion of orphan drugs for certain covered entities under the 340B program, published by the Health Resources and Services Administration (HRSA) in the Federal Register on May 20, 2011 (RIN – 0906-AA94). SNHPA represents over 700 public and private non-profit hospitals enrolled in the 340B federal drug discount program, including over 100 rural and free-standing cancer hospitals that are affected by the orphan drug exclusion.

We applaud HRSA's decision to limit the orphan drug exclusion to situations when the orphan drugs are used for orphan indications. This proposed implementation policy represents legislative intent and is consistent with the purpose of the 340B program. The following comments (1) provide support for the proposed rule, (2) describe how hospitals can comply, (3) suggest alternative compliance opportunities, (4) confirm certain interpretations, and (5) urge HRSA to take additional steps to ensure access to orphan drugs during the period before this rule is finalized. Although we support HRSA's proposed implementation, we reiterate our longstanding opposition to the underlying statutory language excluding any orphan drugs from the 340B program. We urge HRSA to work with Congress and support the full repeal of the orphan drug exclusion. Finally, we recommend that HRSA incorporate long-standing guidance into the proposed definition of "covered outpatient drug."

### **I. Economic Impact of Proposed Rule on Affected Entities**

HRSA estimates that the proposed rule would have a net effect of reducing costs for affected covered entities.<sup>1</sup> HRSA also requested additional information from

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<sup>1</sup> Exclusion of Orphan Drugs for Certain Covered Entities under 340B Program, 76 FED. REG. 29183, 29187-88 (May 20, 2011).

stakeholders on this point.<sup>2</sup> SNHPA concurs with HRSA's estimate that the proposed rule would result in a net savings for affected covered entities. Since some manufacturers are currently interpreting the orphan drug exclusion as permitting them to refuse to offer 340B pricing on all orphan drugs regardless of use, the proposed rule would again permit affected hospitals to purchase 340B discounted orphan drugs from those manufacturers when the drugs are used for non-orphan indications.

SNHPA's comments on this matter are a result of multiple communications with our affected members, as well as careful review of a comprehensive analysis of a group of eighteen critical access hospitals (CAHs) recently prepared by the PRIME Institute.<sup>3</sup> Among our conclusions:

1. Rural hospitals routinely use drugs with an orphan designation.
2. The average cost of drugs with orphan designations is *nine* times higher than those without orphan designations.<sup>4</sup>
3. The top ten most expensive and most widely used orphan drugs are almost exclusively used in the outpatient setting.<sup>5</sup>
4. Use of orphan drugs is especially significant for hospitals with oncology/infusion clinics, as chemotherapy drugs often have an orphan designation.
5. Several hospitals reported to us that they would be able to save \$30,000 to \$40,000 per month if the proposed rule is finalized.

As discussed further below, hospitals have described to us their plans to comply with the proposed rule. Though all compliance proposals would require significant financial resources, most hospitals report that the benefits of 340B pricing under the proposed rule would outweigh the costs of compliance.<sup>6</sup> Therefore, we agree with HRSA's comments that the proposed rule will result in a net savings to affected covered entities when compared to the alternative of excluding all orphan drugs from 340B pricing regardless of indication.

## **II. SNHPA Supports HRSA's Proposed Interpretation of the Orphan Drug Exclusion**

We strongly support HRSA's proposed interpretation of the orphan drug exclusion. HRSA's position that 340B pricing is unavailable for orphan drugs only when the drugs

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<sup>2</sup> *Id.*

<sup>3</sup> Presentation at 15<sup>th</sup> Annual 340B Coalition Conference in Washington, D.C. by Madeline Carpinelli Wallack, PRIME Institute, University of Minnesota (July 13, 2011).

<sup>4</sup> *Id.* The PRIME Institute found that orphan drugs averaged \$760 per use compared to \$85 per use for non-orphan drugs.

<sup>5</sup> *Id.*

<sup>6</sup> There will be some hospitals for which the costs of compliance will outweigh the benefit of purchasing orphan drugs. As discussed elsewhere in these comments, we recommend that HRSA consider alternative compliance policies for such hospitals to allow them to access the 340B program.

are used for an orphan indication is consistent with the plain meaning of the statute and well within HRSA's legal authority.

The plain meaning of section 340B(e) of the Public Health Service Act (PHSA) is clear. It excludes from the definition of covered outpatient drug "a drug designated by the Secretary under section 526 of the Federal Food, Drug, and Cosmetic Act **for a rare disease or condition.**"<sup>7</sup> Appropriately, HRSA intends to implement the statute by excluding orphan drugs from 340B pricing only when they are used for the rare disease or condition for which they were designated. To do otherwise, and exclude all orphan drugs regardless of use, would ignore the language in the statute specifically referring to "a rare disease or condition." Principles of statutory construction require looking to every word of the statute to determine the law's meaning and to avoid rendering any words without meaning.<sup>8</sup> Thus, the word "drug" cannot be viewed in isolation and must be viewed in context of the entire phrase setting forth the exclusion, which includes "rare disease or condition" and not just the word "drug."

HRSA's interpretation is also consistent with the statute's reference to section 526 of the Food, Drug and Cosmetic Act (FDCA). The FDCA states that a "manufacturer or the sponsor of a drug may request the Secretary to designate the drug as *a drug for a rare disease or condition.*"<sup>9</sup> Designation under the FDCA applies only for purposes of specific diseases or conditions, and does not apply for just any use of the drug.

Thus, HRSA's interpretation gives meaning to all the words in the 340B statute and in the FDCA statute to which it refers, in conformance with long standing principles of statutory construction.<sup>10</sup> If the intent of Congress is clear in statutory language, then an agency's construction of the statute must match the express intent of Congress.<sup>11</sup> If an agency's statutory construction effectuates Congress' intent, a court must defer to the agency's regulation.<sup>12</sup> In this case, the law requires HRSA to implement the orphan drug exclusion to apply only to orphan drugs when they are used for their orphan indication.

Even if one could argue that Congress' intent was not clear, HRSA's interpretation is permissible, reasonable, and well within HRSA's legal authority. If Congress does not

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<sup>7</sup> 42 U.S.C. § 256b(e) (emphasis added).

<sup>8</sup> See *Moskal v. United States*, 498 U.S. 103, 109 (1990); See *McDonald v. Thompson*, 305 U.S. 263, 266 (1938). See also [Davis v. Michigan Dept. of Treasury, 489 U.S. 803, 809 \(1989\)](#) (noting the canon of statutory construction that "[S]tatutory language cannot be construed in a vacuum . . . [T]he words of a statute must be read in their context and with a view to their place in the overall statutory scheme."); *Astoria Federal Savings & Loan Ass'n v. Solimino*, 501 U.S. 104, 112 (1991); see also *Connecticut Nat'l Bank v. Germain*, 503 U.S. 249, 253-54 (1992) ("[C]ourts must presume that a legislature says in a statute what it means and means in statute what it says there.").

<sup>9</sup> Federal Food, Drug, and Cosmetic Act § 526; 21 U.S.C. 360bb (emphasis added).

<sup>10</sup> See *Moskal v. United States*, 498 U.S. 103, 109 (1990); See *McDonald v. Thompson*, 305 U.S. 263, 266 (1938). See also [Davis v. Michigan Dept. of Treasury, 489 U.S. 803, 809 \(1989\)](#) (noting the canon of statutory construction that "[S]tatutory language cannot be construed in a vacuum . . . [T]he words of a statute must be read in their context and with a view to their place in the overall statutory scheme.").

<sup>11</sup> *Chevron, U.S.A. v. Natural Resources Defense Council*, 467 U.S. 837, 842-43 (1984).

<sup>12</sup> *Id.*

address the precise question at issue in statutory language because the statute is silent on the issue or is unclear, an agency may implement the law using a reasonable and permissible interpretation of the statute.<sup>13</sup> An agency's interpretation is reasonable if it is consistent with Congressional intent and not "arbitrary, capricious, or manifestly contrary to the statute."<sup>14</sup>

In this case, HRSA's interpretation carries out Congressional intent with regard to the treatment of orphan drugs. As HRSA stated in the proposed rule, one purpose of the orphan drug exclusion is to protect "the financial incentives for manufacturing orphan drugs designated for a rare disease or condition . . . ."<sup>15</sup> The Secretary awards these incentives to manufacturers that want to bring to market a drug to treat the rare disease or condition for which it receives an orphan designation.<sup>16</sup> There is no orphan drug designation without a rare disease or condition to which the designation is attached. Accordingly, SNHPA concurs with HRSA's interpretation that the exclusion applies only when an orphan drug is being used for the condition for which it was designated, as that interpretation is consistent with the plain meaning of the statute, Congressional intent, and is neither arbitrary nor capricious.

### **III. SNHPA Hospitals Can Comply with the Proposed Rule**

We agree with HRSA's decision to allow hospitals flexibility in how they comply with the proposed regulation. Our members understand that the proposed regulation requires hospitals to ensure that orphan drugs are not purchased under 340B when the drugs are used for the rare condition or disease for which the drugs were designated. They also understand that hospitals would be required to maintain separate purchasing accounts and auditable records to demonstrate compliance with the orphan drug exclusion. We have asked our members to evaluate these requirements, and they report to us that they would be able to ensure, on a drug-by-drug basis, that 340B pricing is not used to purchase orphan drugs that are used to treat an orphan indication. Their methods of compliance are discussed below, along with the request that HRSA permit alternative tracking systems and clarify several compliance issues.

Compliance proposals generally fall into two categories. Some hospitals report that they would manually compare the patient's diagnosis (by referring to the single or multiple ICD-9 codes assigned to each patient) for each prescribed orphan drug against the indications listed in the FDA's orphan drug database. (Pharmacists in the hospital already have access to ICD-9 diagnosis codes assigned to the patient.). In most cases, referring to the ICD-9 code will be sufficient to determine whether the drug is being used for an orphan indication. There will be some cases, however, where the ICD-9 code(s)

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<sup>13</sup> *Id.*

<sup>14</sup> *Id.* (upholding an agency's interpretation of a statutory definition by looking to the policy concerns that motivated the statute's enactment); *see* 5 U.S.C. § 706(2)(A).

<sup>15</sup> Exclusion of Orphan Drugs for Certain Covered Entities Under 340B Program, 76 FED. REG. 29183, 29184 (May 20, 2011).

<sup>16</sup> *Id.*

may not offer enough specificity to make that determination. In those cases, hospitals report that they will either contact the patient's physician or simply not use 340B pricing for that drug.

Other hospitals would use existing or updated computer software to identify orphan drugs, the indications listed on the FDA website for those drugs, and the diagnosis assigned to the patients. Our members already contract with vendors that supply them with computer software to manage their 340B inventory. We have been told by both vendors and hospitals that some of these systems are already able to provide the necessary information to allow hospitals to determine when 340B could or could not be used to fill an orphan drug prescription under the terms of the proposed rule. We expect other vendors to follow suit and provide this capability in the future.

Hospitals that use contract pharmacies have informed us that the contract pharmacy would not generally have access to diagnosis codes. They have also explained that most orphan drugs are physician-administered drugs that are dispensed only by the hospital, and not by contract pharmacies. For those relatively few orphan drugs that are dispensed by contract pharmacies, hospitals report to us that they intend to block those drugs from being filled using 340B pricing. In fact, many hospitals report they are doing that now since they are not sure whether they are permitted to purchase any orphan drugs using 340B pricing. Most hospitals inform us that because the number of orphan drugs filled by contract pharmacies is so small, they intend to forego 340B pricing for those drugs. Some hospitals report that they may review such claims manually and make a determination as to whether the drug qualifies for 340B pricing.

#### **IV. HRSA Should Allow Hospitals to Use Alternative Tracking Systems**

Though most hospitals report that it is physically and economically feasible to comply with the proposed regulation, other hospitals, particularly those that do not spend a significant amount on orphan drugs, report that the cost of compliance may outweigh the savings they would receive from the 340B program. We urge HRSA to permit hospitals to use alternative compliance systems that do not require separate purchasing accounts for 340B and non-340B orphan drugs.

HRSA has granted such flexibility to covered entities in the past, such as in the area of complying with the prohibition against diversion. Federal guidelines published in 1994 require hospitals to maintain a system to track 340B drugs on a drug-by-drug basis.<sup>17</sup> Nevertheless, HRSA allows hospitals to submit for approval alternative tracking systems that are not conducted on a drug-by-drug basis.<sup>18</sup> We understand that, during the early years of the program, some hospitals implemented a stock replacement system that relied

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<sup>17</sup> 59 FED. REG. 25110, 25113 (May 13, 1994) (stating that a covered entity may develop an alternative tracking system "short of tracking each discounted drug through the purchasing and dispensing process" but that such a system must be approved by HRSA).

<sup>18</sup> *Id.*

on historical utilization data rather than NDC-by-NDC tracking to determine replacement orders.

HRSA should allow similar flexibility for orphan drug compliance. Not only would this flexibility increase the number of hospitals and patients that benefit from the 340B program, but alternative tracking systems may prove to be more efficient and equally effective.

#### **V. HRSA Should Clarify That the Exclusion Does Not Apply for Orphan Drugs That Have Exceeded Their Seven-Year Market Exclusivity Period**

Under the FDCA, sponsors of an orphan drug receive a seven-year period of market exclusivity upon receiving approval to market an orphan drug for its orphan designation.<sup>19</sup> During such time, the Food and Drug Administration (FDA) cannot approve an application from another manufacturer to market the same drug for the same purpose.<sup>20</sup> We presume that under the proposed rule, an orphan drug would qualify for 340B pricing when used for its orphan designation after the seven-year market exclusivity period expires, since the drug no longer receives nor requires financial incentives to develop the drug for a rare disease or condition.

The drug Topamax provides an example of this situation. The FDA granted Johnson & Johnson an orphan designation to, and approved marketing of, Topamax to treat Lennox-Gastaut Syndrome. The seven-year market exclusivity period has now expired. We presume that under HRSA's proposed rule, a 340B hospital could purchase Topamax from Johnson & Johnson, and obtain the 340B price, even if the hospital used the drug to treat Lennox-Gastaut Syndrome.

This position is consistent with Congressional intent. As HRSA notes in the proposed rule, one purpose of the orphan drug exclusion is to protect "the financial incentives for manufacturing orphan drugs designated for a rare disease or condition."<sup>21</sup> These financial incentives include the "7-year market exclusivity to sponsors of approved orphan products."<sup>22</sup> With regard to the financial incentive of market exclusivity, Congress mandated that manufacturers only receive this incentive for seven years from the date of market approval.<sup>23</sup> The FDA does not intend for the sponsor of an orphan drug to receive these financial benefits beyond the seven-year market exclusivity period.<sup>24</sup> In the final rule implementing the Orphan Drug Act, the FDA noted that manufacturers submitting applications for orphan drug designations should provide data

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<sup>19</sup> FDCA § 527(a)(2); 21 U.S.C. § 360cc.

<sup>20</sup> FDCA § 527(a)(2); 21 U.S.C. § 360cc.

<sup>21</sup> Exclusion of Orphan Drugs for Certain Covered Entities Under 340B Program, 76 FED. REG. 29183, 29184 (May 20, 2011).

<sup>22</sup> *Id.*

<sup>23</sup> FDCA § 527(a)(2); 21 U.S.C. § 360cc.

<sup>24</sup> See Final Rule, Orphan Drug Regulations, 57 FED. REG. 62076 (Dec. 29, 1992).

justifying the need for the financial incentives.<sup>25</sup> This data includes marketing costs the manufacturer has incurred and expects to incur in the first seven years of the drug's marketing as well as expected revenues from sales during the first seven years of marketing.<sup>26</sup>

The FDA's interest in costs incurred and revenue expected during the first seven years of marketing demonstrates that the financial incentives provided under the FDCA are necessary only for the first seven years after market approval. Upon expiration of the market exclusivity period, orphan drug sponsors no longer need the benefit of orphan drug incentives, including the 340B orphan drug exclusion. If Congress intended for the orphan drug exclusion to protect the incentives given to a manufacturer under the FDCA, the 340B orphan drug exclusion should not extend these benefits beyond the time period envisioned under the FDCA. We urge HRSA to clarify the definition of orphan drug to include in the definition of "covered outpatient drug" those drugs that have been designated and approved as orphan drugs by the FDA, but that have exceeded the seven-year market exclusivity period.

## **VI. HRSA Should Clarify That the Exclusion Applies Only for a Drug Manufactured by the Sponsor of the Orphan Drug**

The FDA designates orphan drug status upon approval of an application submitted by the manufacturer of the drug. Thus, the orphan designation is linked to the manufacturer that produces the drug and sought the designation. There are situations, such as with generic drugs, when multiple manufacturers produce the same drug for which one manufacturer has received orphan designation.<sup>27</sup> For example, the drug Topamax that was mentioned above, has been approved to be marketed for the orphan indication of Lennox-Gastaut Syndrome, but its seven-year market exclusivity has expired. That drug is now produced by other manufacturers (under the name Topiramate) and is even marketed by at least one manufacturer for Lennox-Gastaut Syndrome.<sup>28</sup> This manufacturer is not listed in the FDA's orphan drug database.<sup>29</sup> We presume that under the proposed rule, drugs that

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

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

<sup>27</sup> FDA, A New Resource for Drug Developers: The Rare Disease Repurposing Database (RDRD) Table 3, Orphan-designated products with marketing approvals for both common and rare disease indications, <http://www.fda.gov/downloads/AboutFDA/CentersOffices/OC/OfficeofScienceandHealthCoordination/OfficeofOrphanProductDevelopment/UCM215813.xls>. Table 3 of the RDRD shows, for example, that Protherics, Inc. has received an orphan drug designation for Paclitaxel aqueous gel when used to treat brain cancer and that multiple manufacturers market the brand version of this drug for common indications. Similarly, Thomas P. Kanyok, Pharm.D. has received an orphan designation for Aminosidine when used to treat Mycobacterium avium complex and multiple manufacturers market the brand version of this drug for common indications.

<sup>28</sup> Watson Pharmaceuticals, Topiramate U.S. Prescribing Information, [http://pi.watson.com/data\\_stream.asp?product\\_group=1681&p=pi&language=E](http://pi.watson.com/data_stream.asp?product_group=1681&p=pi&language=E). At least 20 other manufacturers also produce this drug, but we have not confirmed how the drugs are marketed.

<sup>29</sup> Orphan Drug Designations and Approvals, Topamax, [http://www.accessdata.fda.gov/scripts/opdlisting/oopd/OOPD\\_Results\\_2.cfm?Index\\_Number=070792](http://www.accessdata.fda.gov/scripts/opdlisting/oopd/OOPD_Results_2.cfm?Index_Number=070792); FDA Approved Drug Products, Topiramate,

have received orphan designation, but are not produced by the manufacturer that sought and obtained orphan designation, are not included in the exclusion under section 340B(e) of PHSA.

This interpretation is consistent with Congressional intent. As explained in the preamble to the proposed rule, Congress intended for the orphan drug exclusion to protect the incentives given to a manufacturer that is developing a particular orphan drug for a rare disease or condition. A regulatory agency is legally authorized to implement statutes in a manner that is reasonable and not arbitrary and capricious.<sup>30</sup> Therefore, the orphan drug exclusion should not extend these benefits to another manufacturer that also happens to sell that drug, but is not involved in developing the drug for a rare disease or condition. We urge HRSA to clarify this issue in the final rule.

#### **VII. HRSA Should Issue Informal Guidance to Ensure Immediate Access to Orphan Drugs at 340B Pricing and Make Clear in the Final Rule That Hospitals Are Entitled to Retroactive Relief**

We strongly concur with HRSA's position that a manufacturer has a legal obligation to offer 340B pricing for orphan drugs to covered entities. Unfortunately, many manufacturers continue to withhold 340B pricing on orphan drugs.<sup>31</sup> We urge HRSA to issue informal guidance making clear that this statutory obligation means manufacturers must *immediately* provide 340B pricing on orphan drugs during the period before this rule is finalized. The guidance should state that manufacturers that fail to do so will be required to issue retroactive refunds and will be subject to civil monetary penalties, as provided under 42 USC §256b(d)(vi), for knowingly and intentionally withholding 340B pricing. Further, HRSA should make clear in the final rule that hospitals are entitled to retroactive relief from those drug manufacturers that have withheld 340B pricing on orphan drugs as a result of the orphan drug exclusion.

As noted in the preamble to the proposed rule, the statute states that agreements between manufacturers and the Secretary "require that the manufacturer offer each covered entity covered outpatient drugs for purchase at or below the applicable ceiling price if such drug is made available to any other purchaser at any price."<sup>32</sup> This language, which has been referred to as the "must-sell" provision, was added to the 340B statute by the Patient Protection and Affordable Care Act (PPACA).<sup>33</sup> There is no exception to this rule. Therefore, manufacturers are prohibited from refusing to offer 340B pricing or from

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<http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?fuseaction=Search.Overview&DrugName=TOPIRAMATE>.

<sup>30</sup> See *Chevron, U.S.A. v. Natural Resources Defense Council*, 467 U.S. 837, 842-43 (1984).

<sup>31</sup> See e.g., Letter from Serafina Oxner, Executive Director, Healthcare Contract Administration, Novartis Pharmaceuticals Corporation, to SNHPA Member Hospital (June 9, 2011) (attached).

<sup>32</sup> Exclusion of Orphan Drugs for Certain Covered Entities Under 340B Program, 76 FED. REG. 29183, 29185 (May 20, 2011).

<sup>33</sup> Patient Protection and Affordable Care Act § 7102(b)(1).

imposing any limits on the sale of 340B drugs, such as by conditioning sales on promises that the orphan drugs will be used only for non-orphan indications.<sup>34</sup>

We understand that some manufacturers disagree with this position, arguing that the “must-sell” provision is not in effect until HRSA amends the pharmaceutical pricing agreement (PPA) referenced in section 340B(a)(1) of the Public Health Service Act. This position has no legal basis. As recently held by the U.S. Supreme Court, the statute, not the PPA, is the source of a manufacturer’s obligations under the 340B program.<sup>35</sup> The PPA is merely a way to record that entities have agreed to opt-in to the program.<sup>36</sup> It is not intended to independently determine a manufacturer’s obligations, as it is merely a form agreement with no negotiable terms.<sup>37</sup> Thus, when Congress amended the 340B statute to include the “must-sell” provision, the law immediately required manufacturers participating in the 340B program to offer to a 340B covered entity a covered outpatient drug at 340B pricing if it offers the same drug to another purchaser.

HRSA has already established a precedent of implementing statutory changes absent amendment of the PPA. In 2009, HRSA issued a final rule to enroll children’s hospitals in the program, per a provision of the Deficit Reduction Act (DRA) that added children’s hospitals as covered entities eligible for 340B discounts.<sup>38</sup> The DRA did not amend the PPA. However, the DRA amended section 1927(a) of the Social Security Act, which is the statute that requires manufacturers to provide the 340B discount.<sup>39</sup> Even though no amendment was made to the PPA, HRSA stated that the amendment to the SSA was sufficient to alter a manufacturer’s obligations under the program.<sup>40</sup> An agency’s statutory interpretation is reasonable and deserves deference if the agency has already established a precedent of that interpretation.<sup>41</sup>

We understand that some commentators assert that if drug manufacturers give 340B pricing on orphan drugs, that pricing is not exempt from Medicaid best price provisions. We applaud HRSA for addressing this issue in the preamble to the proposed rule by making clear that manufacturers are permitted to make reasonable assumptions regarding Medicaid best price calculations.<sup>42</sup> Government action in the area of best price generally involves violations of federal or state fraud statutes, which requires evidence that a drug company knowingly violated the law, and, in the case of the federal False Claims Act,

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<sup>34</sup> Exclusion of Orphan Drugs for Certain Covered Entities Under 340B Program, 76 FED. REG. 29183, 29185 (May 20, 2011).

<sup>35</sup> *Astra USA, Inc. v. Santa Clara County, California*, 131 S. Ct. 1342, 1348 (2011).

<sup>36</sup> *Id.* at 1346.

<sup>37</sup> *Id.* at 1348.

<sup>38</sup> Notice Regarding 340B Drug Pricing Program—Children’s Hospitals, 74 FED. REG. 45206 (Sept. 1, 2009); Deficit Reduction Act § 6004, Pub. L. 109-171.

<sup>39</sup> Social Security Act § 1927(k); 42 U.S.C. 1396r-8.

<sup>40</sup> Notice Regarding 340B Drug Pricing Program—Children’s Hospitals, 74 FED. REG. 45206, 45207 (Sept. 1, 2009).

<sup>41</sup> *Barnhart v. Walton*, 535 U.S. 212, 220 (2002) (upholding an agency’s statutory construction because it was consistent with the agency’s longstanding interpretation).

<sup>42</sup> 76 FED. REG. 29183, 29185.

acted with deliberate ignorance or reckless disregard for the law.<sup>43</sup> Government action is not taken in situations where the drug company is following a rational interpretation of existing law or a published government interpretation, as would be the case here.

Many manufacturers have inappropriately denied 340B pricing for all orphan drugs regardless of use, resulting in significant lost savings for affected entities. As explained earlier, many hospitals are losing \$30,000 to \$40,000 a month as a result of the inability to use 340B for orphan drugs. Specific guidance is required as some manufacturers have indicated a willingness to issue refunds only if the government's implementation of the orphan drug exclusion requires them to do so. As explained by one manufacturer:

In the event the law or regulation requires a change in [the manufacturer's] obligations under the 340B program or if changes in the law or regulation require a different treatment for new covered entity types, [the manufacturer] will work in good faith to meet those new requirements in an expedient manner.<sup>44</sup>

Retroactive relief is not new to the 340B program. HRSA has allowed retroactive relief in the past, including when initially implementing the program in 1993 and again when implementing the addition of children's hospitals to the program in 2009.<sup>45</sup>

HRSA should also make clear that failure to offer immediate access to 340B pricing as well as retroactive refunds for orphan drugs used for non-orphan indications shall be subject to civil monetary penalties pursuant to PHSA § 340B(d)(1)(B)(vi). That section states that drug manufacturers will be subject to civil monetary penalties for "knowingly and intentionally" charging covered entities prices higher than the price permitted under the 340B statute.<sup>46</sup> Failure to offer 340B pricing on orphan drugs that are used for non-orphan indications is contrary to the plain meaning of the 340B statute, and represents knowing and intentional action that should be subject to civil monetary penalties under the 340B statute.

### **VIII. SNHPA Hospitals Are Prepared to Submit to Manufacturer Audits**

SNHPA supports the proposed rule's requirement that covered entities submit to government audits or government-approved manufacturer audits that "directly pertain to the covered entity's compliance with this [orphan drug] requirement."<sup>47</sup> We are aware that some commentators argue there is no legal authority to allow manufacturers to

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<sup>43</sup> 31 U.S.C. § 3729.

<sup>44</sup> Letter from Kent Lieginger, Senior Vice President, Managed Care and Customer Operations, Genentech, to SNHPA Member Hospital (Oct. 4, 2010) (attached).

<sup>45</sup> Final Notice Regarding Section 602 of the Veterans Health Care Act of 1992 Entity Guidelines, 50 FED. REG. 25110 (May 13, 1994) (making PPAs effective as of December 1992); Final Notice Regarding 340B Drug Pricing Program—Children's Hospitals, 74 FED. REG. 45206, 45211 (Sept. 1, 2009) (permitting enrollment dating back to December 2006).

<sup>46</sup> 42 U.S.C. § 256b(d)(1)(B)(vi).

<sup>47</sup> Proposed 42 § 10.21(c); 76 FED. REG. 29183, 29184 (May 20, 2011).

conduct audits to ensure compliance with the orphan drug exclusion because such authority is not explicitly spelled out in the 340B statute.<sup>48</sup> This is incorrect. As explained by HRSA in guidance from 1994, use of the 340B program to purchase drugs that are excluded from the definition of covered outpatient drugs constitutes diversion.<sup>49</sup> In that guidance, HRSA was referring to the use of 340B pricing to purchase drugs used in the inpatient setting. An agency's statutory interpretation is reasonable and deserves deference if the agency has a longstanding history of that interpretation.<sup>50</sup> Under the orphan drug exclusion, orphan drugs that are used for an orphan indication are excluded services under the 340B statute because, like inpatient drugs, they are excluded from the definition of "covered outpatient services." Therefore, any hospital that obtained 340B pricing on such drugs would be guilty of diversion in the same way that a hospital commits diversion by using 340B pricing for inpatient drugs.

## **IX. SNHPA Supports the GPO Prohibition Exception for Cancer Hospitals**

On behalf of the free-standing cancer hospitals enrolled and eligible for the 340B program, we applaud HRSA's decision to permit free-standing cancer hospitals to opt-out of using 340B for all orphan drugs and to permit use of a group purchasing organization (GPO) instead. This option provides cancer hospitals with some flexibility as they evaluate their compliance options. We encourage HRSA to keep this provision in the final rule.

Although the 340B statute prohibits certain covered entities from using a GPO and purchasing 340B drugs simultaneously,<sup>51</sup> HRSA has the legal authority to interpret this provision flexibly as it relates to cancer hospitals. An agency's statutory interpretation is reasonable and deserves deference if the agency has a longstanding history of that interpretation.<sup>52</sup>

Free-standing cancer hospitals have informed us that they have a much higher volume of orphan drugs than other affected covered entities. Given the specialized nature of their work, cancer hospitals provide significant amounts of infusion services in their chemotherapy clinics, which heavily rely on orphan drugs. If a cancer hospital was not able to comply with the orphan drug exclusion compliance requirements and did not have the option to opt out and purchase orphan drugs through its GPO, the cancer hospital

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<sup>48</sup> Kirschenbaum, Alan M., *To Implement Health Reform Orphan Drug Exclusion, HRSA Issues First-Ever Proposed Regulation on 340B Drug Discount Program*, FDA Law Blog (May 20, 2011).

([http://www.fdalawblog.net/fda\\_law\\_blog\\_hyman\\_phelps/2011/05/to-implement-health-reform-orphan-drug-exclusion-hrsa-issues-first-ever-proposed-regulation-on-340b-.html](http://www.fdalawblog.net/fda_law_blog_hyman_phelps/2011/05/to-implement-health-reform-orphan-drug-exclusion-hrsa-issues-first-ever-proposed-regulation-on-340b-.html)).

<sup>49</sup> Final Notice Regarding Section 602 of the Veterans Health Care Act of 1992 Entity Guidelines, 59 FED. REG. 25110, 25112-13 (May 13, 1994) (describing the use of the 340B program to purchase drugs used in the inpatient setting as diversion).

<sup>50</sup> *Barnhart v. Walton*, 535 U.S. 212, 220 (2002) (upholding an agency's statutory construction because it was consistent with the agency's longstanding interpretation).

<sup>51</sup> 42 U.S.C. § 256b(a)(4)(L)(iii).

<sup>52</sup> *Barnhart v. Walton*, 535 U.S. 212, 220 (2002) (upholding an agency's statutory construction because it was consistent with the agency's longstanding interpretation).

would be forced to buy orphan drugs at the Wholesale Acquisition Cost (WAC). WAC prices are significantly higher than GPO prices. Allowing the hospital to buy at GPO prices removes what otherwise appears like a penalty and encourages hospitals to be conservative when deciding which orphan drugs to buy through 340B.

Furthermore, because cancer hospitals rely heavily on these expensive drugs, they have existing purchasing relationships with GPOs. If they are not able to opt out of 340B for their orphan drugs and continue purchasing through their GPOs, they may lose tremendous purchasing power through the loss of purchasing volume. This could jeopardize manufacturer relationships and the current drug pricing levels offered by manufacturers.

Applying the GPO prohibition flexibly for cancer hospitals is necessary in order to carry out Congressional intent. Congress intended for cancer hospitals to benefit from the 340B program, and without this flexible application, cancer hospitals would simply not be able to benefit from the program.

HRSA has applied the GPO prohibition flexibly in the past. In the early stages of the 340B drug discount program, HRSA permitted DSH hospitals to use GPOs *and* to receive 340B discounts, provided a 340B discount was not received for a covered outpatient drug obtained through a group purchasing arrangement.<sup>53</sup> HRSA amended that policy to disallow 340B participation for DSH hospitals participating in GPOs for any covered outpatient drugs as of May 1994, but still permitted DSH hospitals that had used GPOs to receive retroactive 340B discounts, so long as they did not receive such discounts on drugs purchased through a GPO.<sup>54</sup>

Therefore, HRSA's position on this issue is supported by Congressional intent and its history of applying the prohibition flexibly.

## **X. SNHPA Urges a Full Repeal of the Orphan Drug Exclusion**

Although SNHPA applauds HRSA for its balanced interpretation of the orphan drug exclusion, we nevertheless ask HRSA to support repealing the orphan drug exclusion in its entirety. Estimates of the benefit to CAHs of obtaining orphan drugs at 340B prices are in the range of \$227 million.<sup>55</sup> This is very significant to these individual hospitals, representing approximately 16% of their total potential 340B savings.<sup>56</sup> To drug manufacturers on the other hand, this \$227 million represents only 0.6 percent of their total orphan drug sales.<sup>57</sup> It is unlikely that a manufacturer would choose not to invest in orphan drug research and development based on discounts affecting such a small share of

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<sup>53</sup> See 58 FED. REG. 27289, 27290 (May 7, 1993).

<sup>54</sup> See 59 FED. REG. 25110, 25112 (May 14, 1994).

<sup>55</sup> Presentation at 15<sup>th</sup> Annual 340B Coalition Conference in Washington, D.C. by Madeline Carpinelli Wallack, PRIME Institute, University of Minnesota (July 13, 2011).

<sup>56</sup> *Id.*

<sup>57</sup> *Id.*

the market. The harm to the nation's rural communities clearly outweigh any benefit to drug manufacturers of an exclusion of orphan drugs from the 340B program.

Further, we expect costs to the affected covered entities to grow. We understand that the FDA has stepped up its efforts to approve orphan drugs. Many drugs that are currently in the experimental phase will soon be available on the market, with some estimates indicating more than 400 orphan drugs are currently in the clinical trial phase or under review by the FDA. As the FDA continues to approve more drugs with an orphan designation, the orphan drug exclusion will have an increasingly devastating effect on our member hospitals.

As the number of orphan drugs approved to be marketed grows, so too will the cost of complying with the proposed rule. As we have explained, some of our hospitals do not stand to gain enough savings from accessing 340B discounts on orphan drugs to make the participation in the 340B program worthwhile.<sup>58</sup> As the number of approved orphan drugs grows, the number of hospitals that won't be able to afford compliance will also grow. These hospitals will no longer be able to access the full benefit of the 340B program.

Finally, the 340B program reduces costs for both the Medicare and Medicaid programs, as Medicare and many states pay these hospitals on the basis of cost. When these hospitals' costs increase, so do costs for Medicare and Medicaid. Therefore, the exclusion of any drugs from 340B pricing immediately increases costs for both programs. Program costs will also increase as the number of drugs with an orphan designation increase.

For these reasons, we strongly urge HRSA to work with Congress to repeal this unfair and detrimental orphan drug exclusion.

#### **XI. The Definition of "Covered Outpatient Drug" Should Incorporate Existing Descriptions in Existing Guidance**

The proposed rule contains a definition of the term "covered outpatient drug." The definition proposed cites to section 1927(k) of the Social Security Act. HRSA provided additional guidance on the meaning of this term in a final notice published in May 1994.<sup>59</sup> SNHPA recommends that HRSA include that additional guidance in its definition of covered outpatient drug.

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<sup>58</sup> JOHN J. CASTELLANI, PRESIDENT AND CEO PHRMA, 2011 REPORT: ORPHAN DRUGS IN DEVELOPMENT FOR RARE DISEASES, PhRMA (2011), *available at* <http://www.phrma.org/sites/default/files/878/rarediseases2011.pdf>.

<sup>59</sup> 59 FED. REG. 25110, 25113 (May 14, 1994).

CDR Krista Pedley

July 19, 2011

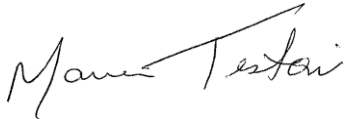
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Thank you for the opportunity to submit these comments. Please feel free to contact SNHPA President and General Counsel William von Oehsen at 202-872-6765, [william.vonoehsen@snhpa.org](mailto:william.vonoehsen@snhpa.org), or SNHPA Assistant General Counsel Maureen Testoni at 202-552-5851, [maureen.testoni@snhpa.org](mailto:maureen.testoni@snhpa.org), or SNHPA Associate Counsel Jeff Davis at 202-552-5867, [jeff.davis@snhpa.org](mailto:jeff.davis@snhpa.org), if you have any questions about these comments.

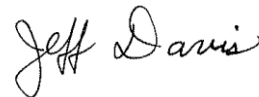
Sincerely,



William von Oehsen  
President and General Counsel



Maureen Testoni  
Assistant General Counsel



Jeff Davis  
Associate Counsel

Attachment

# Genentech

A Member of the Roche Group

1 DNA Way  
South San Francisco, CA 94080

October 4, 2010

**SUBJECT: 340B Ceiling Pricing for Orphan Drugs**

Dear [REDACTED]:

The Patient Protection and Affordable Care Act and the Health Care and Education Affordability Reconciliation Act of 2010 (collectively, the "Affordable Care Act") expanded the types of entities that are eligible to receive 340B pricing for outpatient drugs to include children's hospitals, free-standing cancer hospitals, critical access hospitals, and rural referral centers/sole community hospitals pursuant to the new subparts M, N and O added to the statutory definition of covered entity ("new covered entity types"). Under the Affordable Care Act, a covered outpatient drug is defined to exclude any drug with an orphan designation when it is sold to any one of the new covered entity types. Thus, these orphan drug products do not qualify to receive the 340B ceiling prices when provided to the new covered entity types. Additionally, to date the government has not specified that such prices, if offered voluntarily, are excluded from the government price reporting calculations.

There is no current regulation that clarifies the definition of a drug with an orphan designation for 340B program purposes. Until such time as new laws are passed, regulations are promulgated, or guidance is issued, Genentech will treat any drug that has been designated "orphan" by the Federal Food and Drug Administration (as evidenced by <http://www.accessdata.fda.gov/scripts/opdlisting/oodp>), as an orphan drug for 340B purposes.

The current list of Genentech drugs meeting the above description are as follow:

RBC Number	Genentech Product Description
50242-0085-27	Acthase® (allopurinol) 100 mg vial
50242-0044-19	Acthase® (allopurinol) 50 mg vial
50242-0060-01	Avastin™ (bevacizumab) 100mg (25mg/mL) 4mL vial
50242-0061-01	Avastin™ (bevacizumab) 400mg (25mg/mL) 16mL vial
50242-0041-64	Cathin® Acthase® (allopurinol) 2 mg vial
00004-0259-01	CELLCEPT® (mycophenolate mofetil) Capsules, 250 mg
00004-0259-43	CELLCEPT® (mycophenolate mofetil) Capsules, 250 mg
00004-0260-01	CELLCEPT® (mycophenolate mofetil) Tablets, 500 mg
00004-0260-43	CELLCEPT® (mycophenolate mofetil) Tablets, 500 mg
00004-0259-06	CELLCEPT® CAPSULES (mycophenolate mofetil) Capsules, 250 mg
00004-0259-09	CELLCEPT® IV (mycophenolate mofetil hydrochloride) Vial, 500 mg (20mL glass vial)
00004-0261-20	CELLCEPT® ORAL SUSPENSION (mycophenolate mofetil) Bottle, 200mg/mL
50242-0134-68	Herceptin® (trastuzumab) 440 mg mpvli-68se vial
50242-0043-14	Nutropin AQ Pen® (somatropin (rDNA origin) injection) Cartridge -2 mL (5 mg/mL)
50242-0073-01	Nutropin AQ Pen® (somatropin (rDNA origin) injection) Cartridge -20 mg/2 mL (10 mg/mL)
50242-0074-01	Nutropin AQ Pen® (somatropin (rDNA origin) injection) NuSpin 10mg/2 mL (5 mg/mL)
50242-0076-01	Nutropin AQ Pen® (somatropin (rDNA origin) injection) NuSpin 20mg/2 mL (10 mg/mL)
50242-0078-01	Nutropin AQ Pen® (somatropin (rDNA origin) injection) NuSpin 5mg/2 mL (2.5 mg/mL)
50242-0122-20	Nutropin AQ® (somatropin (rDNA origin) injection) 2 mL (5 mg/mL) sngl vial crtn
50242-0049-21	Nutropin® (somatropin (rDNA origin) injection) 10 mg (1 x 10 mg w/diluent)
50242-0072-63	Nutropin® (somatropin (rDNA origin) injection) 5 mg (1 x 5 mg w/diluent)
00004-0352-09	PEGASYS® (peginterferon alfa-2a) 4 Single Use Pre-filled Syringe, 180mcg/0.5mL, 4 Needles, 4 Alcohol Swabs
00004-0352-09	PEGASYS® (peginterferon alfa-2a) VIAL, 1mL Vial, 180mcg/mL
50242-0100-40	Pulmozyme® (dornase alfa) 30 ampule (2.5 ml per amp) carton
50242-0051-21	Rituxan® (rituximab) 100mg/10ml Vial
50242-0053-06	Rituxan® (rituximab) 500mg/50ml Vial
50242-0063-01	Tarceva® (erlotinib) 100mg Tablets
50242-0064-01	Tarceva® (erlotinib) 150mg Tablets
50242-0062-01	Tarceva® (erlotinib) 25mg Tablets

Attachment

[REDACTED]

[REDACTED]

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Genentech will not be offering 340B ceiling prices for the above list of orphan drugs to the new covered entity types. In the event the law or regulation requires a change in Genentech's obligations under the 340B program, or if changes in the law or regulation require a different treatment for new covered entity types, Genentech will work in good faith to meet those new requirements in an expedient manner.

If you have any questions, please contact Phil Matheny, Senior Federal Account Manager, at 402-431-0281 or matheny.phillip@gene.com.

Sincerely,



Kent Lieginger

Senior Vice President, Managed Care and Customer Operations