IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

PHARMACEUTICAL RESEARCH AND MANUFACTURERS OF AMERICA, Plaintiffs, v. **UNITED STATES DEPARTMENT OF HEALTH AND HUMAN SERVICES**, *et al.* Defendants.	Civil Action No. 1:14-CV-01685-RC

BRIEF OF THE AMERICAN HOSPITAL ASSOCIATION AS *AMICUS CURIAE* IN SUPPORT OF DEFENDANTS' MOTION FOR SUMMARY JUDGMENT

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STATEMENT OF INTEREST

The American Hospital Association ("AHA") represents more than 5,000 hospitals, health care systems, and other health care organizations, plus 43,000 individual members. AHA members are committed to improving the health of the communities they serve and to expanding access to affordable health care for all Americans. The AHA advocates to ensure that the perspectives of their members are considered in formulating health policy.

AHA's members are deeply affected by the nation's health care laws, particularly the Patient Protection and Affordable Care Act ("ACA"), 42 U.S.C. § 18001, *et seq.*, enacted on March 23, 2010, as supplemented by the Health Care and Education Reconciliation Act of 2010 ("HCERA"), enacted on March 30, 2010 (H.R. 4872, 111th Cong.) (codified as amended in scattered sections of the U.S.C.). That is why AHA filed *amicus* briefs in support of the law in the United States Supreme Court and in courts across the nation. AHA is participating in this case for the same reason: the ACA's expansion of Section 340B of the Public Health Services Act ("PHSA") provides rural and cancer hospitals access to vitally-needed drugs, including drugs with orphan designation that may otherwise be unaffordable. The ACA's expansion of Section 340B thereby allows those hospitals to provide the needed drugs to their patients and provides patients access to drugs that might not otherwise be available in their communities.

AHA submits this brief to offer guidance, from the perspective of affected hospitals, on the importance of sustaining the validity of the "Interpretive Rule: Implementation of the Exclusion of Orphan Drugs for Certain Covered Entities Under the 340B Program," which was issued by Defendant United States Department of Health and Human Services' ("HHS") Health Resources and Services Administration ("HRSA"), under the direction of Defendant Sylvia Matthews Burwell, the Secretary of HHS (the "Secretary"). The Interpretive Rule properly

construes ACA's and HCERA's provisions and ensures that rural and cancer hospitals and their communities continue to have access to otherwise unaffordable drugs.

Seventy-two million Americans live in rural areas and depend upon the hospital serving their community as an important, and often only, source of health care. *See* AHA, *Trendwatch: The Opportunities and Challenges for Rural Hospitals in an Era of Health Reform* (April 2011)[1] Although rural hospitals make up half of all hospitals in the United States, they only represent about twelve percent (12%) of spending on hospital care. *Id.* Despite a smaller size and smaller base of patients from which to draw, rural hospitals provide their patients with high quality of care while simultaneously tackling challenges due to their often remote geographic location, small size, limited workforce, and constrained financial resources. *Id.* Rural hospitals' low-patient volumes make it difficult for these organizations to manage the high fixed costs associated with operating a hospital. *Id.*

The recent economic downturn put additional pressure on rural hospitals as they already operate with modest balance sheets and thin operating margins. *Id.* Compounding these challenges, rural Americans are more likely to be uninsured and to have lower incomes, and they are, on average, older and less healthy than Americans living in metropolitan areas. *Id.* The ACA's expansion of the 340B drug discount program enables rural hospitals to provide more patients much needed access to lower-cost medications. Interpreting the ACA to exclude all uses of drugs with an orphan designation, including indications for non-orphan diseases and conditions, would nullify the benefits of the expansion of the 340B Program.

SUMMARY OF ARGUMENT

Section 340B of the PHSA imposes ceilings on prices drug manufacturers may charge for medications sold to specified health care facilities, or "340B covered entities," predominantly,

[1] http://www.aha.org/research/reports/tw/11apr-tw-rural.pdf

local providers of medical care for the poor. *Astra USA, Inc. v. Santa Clara Cnty, California*, 131 S.Ct. 1342 (2011). Drug discounts to hospitals that serve indigent and uninsured populations may reach 50% under the 340B Program. 78 Fed. Reg. 44026 (July 23, 2013). The 340B Program is administered by the Health Resources and Services Administration ("HRSA"), part of the Department of Health and Human Services ("HHS"). *Astra*, 131 S.Ct. at 1343. The ACA expanded the definition of "340B covered entities" to include children's hospitals, cancer hospitals, critical access hospitals, rural referral centers and sole community hospitals. 42 U.S.C. § 256b(a)(4). Based on the regulatory requirements to be designated as a critical access hospital, rural referral center or sole community hospital, most if not all such hospitals are located in rural areas. For cancer hospitals and rural hospitals, Section 2302 of the HCERA supplement to the ACA excluded from the definition of 340B "covered outpatient drugs" drugs designated by the Secretary for a rare disease or condition, otherwise known as "orphan drugs." H.R. 4872, 111th Cong. § 2302. This means that cancer and rural hospitals could not acquire orphan-designated drugs for their orphan-designated purposes at 340B discounted prices.

Plaintiff Pharmaceutical Research and Manufacturers of America ("Plaintiff") is a trade association representing drug manufacturers. Plaintiff's complaint in this action argues that the Secretary in the Interpretative Rule improperly construes the ACA as limiting the applicability of the orphan drug exclusion to sales of the drug to only those occasions when the drug is used to treat the rare disease for which the drug received its orphan designation. Indeed, under the Interpretive Rule, the Secretary has concluded that the law allows for 340B discounted pricing on orphan drugs only when those drugs were *not* used for the rare disease for which the drug received its orphan designation. The Plaintiff's argument misconstrues the plain language of Section 340B(e) of the PHSA and Section 360bb of the Federal Food, Drug, and Cosmetic Act

("FFDCA"), which defines orphan drug status based upon the drug's "use" for "such" disease or condition. 21 U.S.C. § 360bb(a)(1).

The Plaintiff's argument also ignores the purposes of the Orphan Drug Act. Orphan drug status is designated by the Secretary for a particular drug when used for the rare disease or condition it was intended to treat. The rationale of the orphan drug program is to incentivize manufacturers to develop drugs for rare diseases and conditions. Drugs designated as orphan drugs may have multiple indications, only one or some of which qualify for orphan drug designation. In fact, a 2010 study found that orphan drugs may be used as much as 90% of the time for conditions or illnesses other than the designated orphan indication. B.A. Liang & T. Mackey, *Reforming Off-Label Promotion to Enhance Orphan Disease Treatment*, SCIENCE MAGAZINE, Jan. 14, 2010 at 273-274. All of the protections and incentives for pharmaceutical manufacturers under the orphan drug program apply only when the orphan drug is used for the orphan-designated rare disease or condition, the only purpose for which manufacturers were provided preferential treatment

The Interpretive Rule clarifies that the intent of Congress was to improve access to 340B discounted drugs for rural hospitals and cancer hospitals, while protecting and preserving the financial incentives to pharmaceutical manufacturers to develop orphan drugs in the first place. The Plaintiff's argument should be rejected, because it would deprive America's rural and cancer hospitals of the medically necessary drugs that in many cases are unaffordable without 340B pricing; it would jeopardize the financial sustainability of those hospitals, while at the same time providing a financial windfall to drug manufacturers for uses of the drug unrelated to the rare disease or condition for which it was designated; and it is inconsistent with the text and purpose of the legislation that it purports to construe. The Court should not adopt a reading so contrary to

the language and intent of both the Orphan Drug Act and the ACA. The Interpretive Rule should be sustained.

ARGUMENT

I. THE INTERPRETIVE RULE APPROPRIATELY BALANCES THE INTERESTS IN INCENTIVIZING ORPHAN DRUG DEVELOPMENT WITH THE INTERESTS IN PROVIDING 340B DISCOUNTS TO SAFETY NET HOSPITALS AND THEIR PATIENTS.

The Orphan Drug Act was enacted by Congress in 1983 to provide financial incentives to encourage pharmaceutical drug manufacturers to research and develop drugs for rare diseases that affect only small patient populations. *See Genentech, Inc. v. Bowen*, 676 F. Supp. 301, 302-303 (D.D.C. 1987).

The Act seeks to encourage the development of "orphan drugs" by reducing the overall financial cost of development, while enhancing the developer's ability to recover that cost through sale of the drug. Specifically, the Act attempts to reduce development costs by streamlining the FDA's approval process for orphan drugs, by providing tax breaks for expenses related to orphan drug development, by authorizing the FDA to assist in funding the clinical testing necessary for approval of an orphan drug, and by creating an Orphan Products Board to coordinate public and private development efforts. The Act seeks to enhance the orphan drug manufacturer's ability to recover its investment by granting the manufacturer seven years of exclusive marketing rights "for such drug for such [rare] disease or condition." *Genentech,* 676 F. Supp.303 (footnotes omitted).

The incentives offered by Congress have succeeded in bringing more orphan drugs to market. This court observed in *Baker Norton Pharm.*, 132 F.Supp. 2d at 31:

> According to the FDA, in the ten years prior to the passage of the Orphan Drug Act, only ten products for rare diseases were developed and approved for marketing without federal funding. Since the passage of the Orphan Drug Act, the FDA has approved at least 172 orphan drugs and biological products;

> furthermore, more than 700 orphan-designated products currently are being developed.

Currently, nearly 200 orphan drugs enter development each year, and about a third of the drugs are approved by the FDA for rare diseases. Jonathan D. Rockoff, "Drug Makers See Profit Potential in Rare Diseases," WALL ST. J., Jan. 30, 2013.[2] Thus, the incentives and the desired outcomes are aligned; however, the incentives are not needed and do not apply to the use of orphan drugs for non-orphan purposes—*i.e.*, treating diseases or conditions that are different from those rare conditions for which the orphan drug was developed and received its orphan drug designation.

Drugs with orphan designations often have more common applications, and the orphan indication may be just one of many approved uses of the drug — one study finding this occurs as much as 90% of the time.[3] As a result, the total use of an orphan product can be considerably more widespread than the "rare" designation would imply. For example, Botox is a drug approved with orphan status in 1984 to treat uncontrolled blinking, neck pain, and muscle spasms. Since then, the FDA has approved numerous additional indications, including the treatment of migraines (2008). Today, there are 5 million doses of Botox administered annually in North America, which translates into approximately $1.5 billion in sales. Rita E. Numerof & Michael N. Abrams "The Growing Orphan Drug Paradigm," BioPharm Int'l (April 1, 2012).[4]

Currently, the top revenue-producing orphan drug is Rituxan, licensed by the FDA for non-Hodgkin's lymphomas and rheumatoid arthritis, among others. Used widely off-label to treat other diseases such as multiple sclerosis and autoimmune anemia, the drug generates

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[2] http://online.wsj.com/news/articles/SB10001424127887323926104578273900197322758

[3] B.A. Liang & T. Mackey, *Reforming Off-Label Promotion to Enhance Orphan Disease Treatment*, SCIENCE MAGAZINE, Jan. 14, 2010 at 273-274.

[4] http://www.biopharminternational.com/biopharm/Quality/The-Growing-Orphan-Drug-Paradigm/ArticleStandard/Article/detail/767895

revenue of more than $7 billion a year. Michael J. Berens & Ken Armonstrong, *PHARMA's Windfall*, THE SEATTLE TIMES (Nov. 9, 2013).[5] Twenty-five of the top 100 pharmaceutical products in the U.S. market by sales in 2009 were drugs with an orphan designation. M. Bartholow, *Top 200 Prescription Drugs of 2009*, PHARMACY TIMES (May 11, 2009).

The use of drugs with orphan designations for indications other than the rare disease or condition for which it received the designation is especially common in the treatment of cancer. For example, if Taxol were still a single-source product today, its orphan designation for AIDS-related Kaposi's sarcoma would, under the Plaintiff's interpretation, deny newly covered 340B hospitals discounts when using Taxol to treat the far more common diseases of lung, breast, ovarian and other types of cancer. 340B discounts on cancer drugs are critical to "safety net" hospitals – *i.e.*, hospitals that provide a significant level of care to low-income, uninsured and vulnerable populations. Section 303 of the Medicare Modernization Act, Pub. L. No. 108-173 (codified as amended in scattered sections of the U.S.C.) changed reimbursement paid to physicians for cancer drugs under Medicare Part B, by reducing payments for chemotherapy drugs from 95% of average wholesale prices in 2003 to 85% in 2004. In 2005, payments were further reduced to 106% of manufacturer-reported average sales prices, which reflect the actual transaction prices of drug acquisition and are typically lower than the corresponding wholesale values. 42 U.S.C. § 1395w-3a. As a result of the reduction in Medicare reimbursement, more cancer patients were referred to hospital outpatient infusion centers for treatment, causing Medicare payments for chemotherapy administration in hospitals to increase from $98.3 million in 2005 to $300.9 million in 2011. Katie Peralta, *Trends in Patient Chemo Care Add Strain to Medicare*, MEDILL REPORTS (June 4, 2013).[6] Given this shift in chemotherapy site of service to

[5] http://apps.seattletimes.com/reports/pharma-windfall/2013/nov/9/mining-rare-diseases/
[6] http://news.medill.northwestern.edu/Chicago/news.aspx?id=222599

hospitals, the ACA's expansion of 340B to rural and cancer hospitals is vital to the economic sustainability of those institutions.

It is also important to recognize that the price of orphan drugs is substantially higher than non-orphan drugs, thereby allowing manufacturers more quickly to recover the cost of development, as reported by the Wall Street Journal—

> Big drug makers had "thought that orphan drugs were small, tiny things that didn't warrant their attention," says Angus Russell, chief executive of Shire [PLC], some of whose top-selling products treat rare enzyme disorders. The big companies watched Shire and other firms "develop drugs that have gone on to "reach sales of hundreds of millions, if not billions, of dollars, and have followed suit." . . . That said, the often-six-figure yearly price tag for each patient raises the question of whether drug makers' costs will be sustainable as efforts intensify to control health-care spending.

Jonathan D. Rockoff, *Drug Makers See Profit Potential in Rare Diseases*, WALL ST. J., Jan. 30, 2013.

Finally, it is important to recognize that the ACA's expansion of the 340B program benefits not just rural hospitals, but also the Medicare trust fund. Critical access hospitals comprise the vast majority of the new 340B covered entities. Medicare reimburses critical access hospitals on the basis of the hospitals' allowable costs. Thus, the reduced costs of orphan drugs realized by these hospitals from 340B discounts generate savings for the Medicare program.

The bottom line: The Secretary's limitation of the orphan drug exclusion from 340B pricing for rural and cancer hospitals is entirely consistent with the protections and incentives afforded orphan drugs by Congress and should not deter drug manufacturers from seeking orphan drug designation. The Plaintiff's interpretation of the orphan drug exclusion would result in windfall profits to drug manufacturers to the economic detriment of safety net hospitals and the Medicare trust fund.

II. EXPANDING THE SECTION 340B PROGRAM ORPHAN DRUG EXCLUSION TO DRUG USES UNRELATED TO THE DESIGNATED RARE DISEASE OR CONDITION WILL HARM RURAL AND CANCER HOSPITALS AND DENY PATIENT ACCESS TO MEDICALLY NECESSARY DRUGS.

Denying rural and cancer hospitals access to 340B discounts on drugs that will not be used for a rare disease will lead to an inevitable result: the limited resources of those safety net hospitals will be stretched even further and far more patients in the communities served by those hospitals will be adversely affected by reduced patient services and limited access to affordable drugs.

Congress created the 340B Program in 1992 to enable certain health care organizations to "stretch scarce Federal resources as far as possible, reaching more eligible patients and providing more comprehensive services." H.R. Rep. 102-384, pt. 2 at 12 (1992). Originally, eleven types of organizations, including federally qualified health centers and disproportionate share hospitals, were defined as "covered entities" under 340B. Section 340B discounts, estimated to be 20%-50%, result in significant savings for covered entities. The ACA added to the definition of "covered entities" children's hospitals, cancer hospitals exempt from the Medicare prospective payment system, sole community hospitals, rural referral centers, and critical access hospitals. With the exception of cancer hospitals, the added entities are small-scale hospitals serving rural communities. Congress expanded the 340B Program to include these hospitals in recognition that a hospital's safety net status is based on factors other than just its uncompensated care or disproportionate share levels. Safety net factors encompass circumstances that include the provision of unique services in the community, geographic remoteness, and the ability to serve hard-to-reach populations.

A June, 2011 study by two former HHS researchers found that 340B hospitals pass their program savings onto their indigent patients by eliminating or reducing barriers to care.

Madeline C. Wallack & Suzanne B. Herzog, *Demonstrating the Value of the 340B Program to Safety Net Hospitals and the Vulnerable Patients They Service*, SNHP (June 29, 2011).[7] Specifically, the 340B hospitals reported that they use 340B savings to reduce the price of drugs to low-income patients (including providing drugs at no cost to some indigent patients), increase patient access to pharmacy services, increase the choice of drugs available to patients, and enhance pharmacy and other health care services. *Id.* The June, 2011 report also found that hospital patients would be adversely impacted if 340B savings were eliminated. Seventy-seven percent of the hospitals reported that the uninsured and underinsured that they serve would see higher drug costs if the hospital did not have access to 340B discounts. *Id.* The 340B hospitals newly added by the ACA will use their 340B savings, including 340B savings on orphan drugs used to treat non-orphan conditions, to improve care and access for patients.

Each of the hospital types granted 340B covered entity status by the ACA has been recognized by Congress as requiring special reimbursement treatment under the Medicare Program to sustain the facility's financial viability and protect patient access. Critical access hospitals are by far the most numerous of the new 340B covered entities, representing over 1,300 hospitals in the United States.[8] Congress created the Critical Access Hospital Program in 1997 to preserve access to health care for rural beneficiaries. Under this program, critical access hospitals receive Medicare reimbursement at 101% of their allowable costs, rather than under the prospective payment system ("PPS"). 42 U.S.C. § 1395f(l), m(g). Cancer hospitals and sole community hospitals also receive an adjusted Medicare payment based upon costs rather than PPS rates. A recent study examined the financial performance of the special classes of rural

[7] http://www.snhpa.org/images/uploads/340B_Value_Report_06-29-11.pdf. The report was commissioned by the Safety Net Hospitals for Pharmaceutical Access.
[8] AHA, *Trendwatch: The Opportunities and Challenges for Rural Hospitals in an Era of Health Reform*, 6 (April 2011), http://www.aha.org/research/reports/tw/11apr-tw-rural.pdf

hospitals compared to those receiving PPS payments and found that critical access hospitals are under the most financial pressure.[9] The findings of this study suggest that while cost-based reimbursement does help rural hospitals increase revenue, it does not fully address all of the financial challenges rural hospitals face.

As observed above, the price of orphan drugs is significant. One of the commenters to the since vacated final rule noted that although orphan drugs made up only 1.5 percent of its pharmacy inventory in the prior year, orphan drug costs accounted for 52 percent of total inventory costs. 78 Fed. Reg 44024 (July 23, 2013).

The economic challenges facing rural hospitals may best be described by two real life examples from AHA members, one located in the Pacific Northwest and another located in the rural northeastern United States, both of which provided the following information to the undersigned for purposes of this brief. Providence Hood River Memorial Hospital, ("Hood River"), a 25-bed critical access hospital, is the only hospital in Hood River County, Oregon. The hospital and associated clinics provided more than 100,000 patient-centered visits in 2013. More than 20 percent of the patients are Medicaid or self-pay and another 42 percent are Medicare. In 2013, the hospital provided $6.9 million in uncompensated care. The savings from the 340B program helped the hospital establish and support programs that increase access to care for patients and allow the hospital to provide the right care at the right time for its poor and vulnerable patients.

For example, the savings helped the hospital establish a medication assistance program (MAP), and in 2013 it had 2,185 patient visits. Through MAP patients can receive co-pay assistance which lowers an individual's out of pocket expense and can make the difference

[9] Holmes, G.M., et al, *A Comparison of Rural Hospitals with Special Medicare Payment Provisions to Urban and Rural Hospitals Paid Under Prospective Payment*, OFFICE OF RURAL HEALTH POLICY, HEALTH RES. AND SERV. ADMIN. (2010).

between an individual completing the full course of a cancer drug treatment or skipping some purchases during difficult financial months. The proper application of the orphan drug exclusion, as set forth in the Interpretive Rule, will result in savings that contribute importantly to the hospital's ability to continue its MAP and other programs. For example, Hood River estimates that the savings it would receive on purchases of Remicade and Orencia, two drugs with orphan designations that the hospital uses for a non-orphan purpose (*e.g.*, infusions for arthritis) would be $485,000.

Claxton-Hepburn Medical Center ("Claxton") is a sole community hospital located in a rural part of upstate New York that prides itself on achieving "Center of Excellence" status for its cancer care and the role it provides to its community. Claxton tailors its services to the needs of its community, but its offerings depend on subsidies and savings from the 340B program. Claxton is the main provider of mental health services in its community, including a 28-bed inpatient unit specifically designated to care for this underserved population. The hospital also operates six community clinics, all located in manpower shortage areas, to provide access to physicians. If the Plaintiff's position in this case were to prevail, Claxton calculates that approximately $500,000 of annual financial support for these programs and services would be immediately lost.

There are at least two ways that the Plaintiff's challenge to the Interpretive Rule, if successful, would adversely affect Claxton. First, Claxton purchased approximately 30 units of Trastuzumab (Herceptin) at 340B prices that are used to treat patients with breast cancer and colo-rectal cancer although the orphan indication for this drug is for treatment of HER2 positive ***stomach*** cancer. This is a very rare cancer; hence, the orphan designation. Second, Claxton purchased Tocilizumab (Actemra) at 340B prices for treatment of patients with adult rheumatoid

arthritis but this medication has an orphan indication for ***pediatric*** rheumatoid arthritis. Claxton treats very few pediatric patients and therefore would rarely if ever use the drug for its pediatric indication.

The discounts afforded to Claxton and hospitals like it under the 340B Program are key to sustaining their operations and health care access for their communities. At the same time, the impact of the Interpretive Rule on drug manufacturers should be minimal. As noted in the since vacated final rule:

> Covered entity drug purchases under the entire 340B Program are estimated at $6 billion, making up an estimated 2 percent of the total prescription drug market. In fiscal year 2012, the covered entities to which this rule applies comprised an estimated 3.13 percent of total 340B sales for all covered entities. The purchase of orphan drugs would be a subset of these purchases.

78 Fed. Reg. 44024 (July 23, 2013).

Congress struck the appropriate balance between providing new 340B covered entities legislatively-required discounts, while preserving the incentives of manufacturers to continue to produce orphan drugs for rare diseases and conditions. This Court should not withdraw the needed 340B savings provided to these hospitals by the ACA and the Interpretive Rule in order to provide pharmaceutical manufacturers windfall profits on uses of orphan drugs for other than the rare conditions for which they were designated. Loss of 340B coverage for these drugs will make the drugs in many cases unaffordable to the new 340B hospitals and deny access to those drugs to patients.

III. THE INTERPRETIVE RULE IS THE CORRECT INTERPRETATION OF THE STATUTORY LANGUAGE AND GIVES EFFECT TO CONGRESSIONAL INTENT

This Court was right when it observed that the Secretary's originally promulgated final rule was "the most reasonable way of administering the statute...." *Pharmaceutical Research and Mfrs. of Am. v. United States Dept. of HHS*, 1:13-cv-1501 (Doc. #43), p. 27, 2014 U.S. Dist.

LEXIS 70894, *48 (D.D.C. May 23, 2014). While the Court ultimately concluded that the Secretary did not have the delegated authority to issue a legislative rule on the matter giving its position the force of law, the Court's observation nonetheless was a recognition not merely that the Secretary had the better argument as a matter of policy (as demonstrated above), but that she had, indeed, arrived at the best approach for "*administering the statute*" that Congress had written. *Id.* Unless the Court is now prepared to conclude that the "most reasonable way of administering the statute" is also one that is flatly inconsistent with that very statute's plain terms, it should uphold the Interpretive Rule as the "most reasonable" interpretation "of congressional intent as expressed in the [law]." *United Tech. Corp. v. EPA*, 821 F.2d 714, 720 (D.C. Cir. 1987).

Indeed, the validity of an interpretive rule "stands or falls on the correctness of the agency's interpretation of [the specific statutory provisions]," upon which it rests. *Id.* at 719. And while the principle is well-established that "the starting point in every case involving construction of a statute is the language itself," the plain language is only a starting point and "does not preclude consideration of persuasive evidence if it exists." *Watt v. Alaska*, 451 U.S. 259, 266 (1981) (citation omitted). Thus, the question is "whether this interpretative regulation constitutes a permissible gloss on the Act by the Secretary, in light of the Act's language, structure, and legislative history." *Whirlpool Corp. v. Marshall*, 445 U.S. 1, 11 (1980).

The language of the orphan drug exclusion itself supports the Secretary's position that the use of an orphan drug is essential to whether Congress intended to exclude the drug from 340B pricing. Specifically, the statute exempts from the 340B pricing requirements "a drug designated by the Secretary under section 526...*for a rare disease or condition.*" 42 U.S.C. § 256b(e) (emphasis added). If the formal designation of a drug, regardless of indication or use, under

section 526 were all that mattered, then the purposive language "*for* a rare disease or condition" (emphasis added) would be superfluous. *Davis Cty. Solid Waste Mgmt. v. EPA*, 101 F.3d 1395, 1404 (D.C. Cir. 1996) ("it is of course a well-established maxim of statutory construction that courts should avoid interpretations that render a statutory provision superfluous"). Instead, the text suggests that both the designation and the drug itself must be "for a rare disease or condition," or in other words, transferred, sold, or otherwise used to treat the rare disease or condition for which it was designated in the first place.

This reading is consistent with the statutory and regulatory meanings of "drug," which is frequently, at least in part, defined according to its intended or actual use, both by Congress and by the Secretary. *See, e.g.*, 21 U.S.C. § 321(g)(1)(B) (a drug is an article "intended for *use* in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals" (emphasis added)); 42 U.S.C. § 1396r-8(k)(2) (excluding from the definition of "covered outpatient drug" "a drug or biological product *used* for a medical indication which is not a medically accepted indication" (emphasis added)). *See also*, 21 C.F.R. § 316.3(10) and (14) (defining "orphan drug" as one "intended for *use* in a rare disease or condition" and defining "same drug" as one containing the same "active moiety as a previously approved drug and is intended for the same *use*") (emphases added). Plaintiff's attempt to establish an absolute distinction between a drug and its use is simply misplaced.

Further, the act of "designating" an orphan drug has always been highly dependent on the use of the drug. Specifically, Congress obligated the Secretary to designate a drug under 21 U.S.C. § 360bb only where the drug "is being or will be investigated for a rare disease or condition," and where "the approval, certification, or license would be for use for such disease or condition...." 21 U.S.C. § 360bb(a)(1). In addition, the regulations governing orphan drug

designation are replete with references to a drug's actual or intended use. *See, e.g.*, 21 C.F.R. § 316.20 ("[a] sponsor may request orphan-drug designation...of a new *use* for an already marketed drug"); § 316.26 (allowing for "amendment to the designated *use*"); § 316.28 (calling for FDA publication of the "designated *use*"); and § 316.30 (requiring progress reports to include discussion of "any disparity between the probable marketing indication and the *designated indication*...") (emphases added).

Importantly, Congress delegated to the Secretary the power to promulgate rules "governing the section 360bb designation process," (*Depomed, Inc. v. United States HHS*, 2014 U.S. Dist. LEXIS 126235, *10 (D.D.C. Sept. 5, 2014)), and so her interpretation of the meaning and significance of an orphan drug designation is itself entitled to great respect. *See*, *Platt College of Commerce, Inc. v. Cavazos*, 796 F.Supp. 22, 26 (D.D.C. 1992). Moreover, at least one federal court has implicitly recognized the importance of a drug's use to its orphan designation: "Orphan drugs are products *used* to treat diseases or afflictions that are rare...." *Cumberland Pharma., Inc. v. Mylan Inst. LLC*, No. 12 C 3846, 2012 U.S. Dist. LEXIS 177941, *4, n. 3 (N.D. Ill Dec. 14, 2012) (emphasis added).

The correctness of the Secretary's reading of the statute is only reinforced by the general rule that "'statutory exceptions are to be narrowly construed,' to those 'plainly and unmistakably within its terms and spirit.'" *Federal Trade Comm'n v. Alliant Techsystems, Inc.*, 808 F.Supp. 9, 22 (D.D.C. 1992). In other words, where, as here, the statute "[sets] forth a baseline rule and an exception," narrow construction of the exception is necessary "to preserve the primary operation of the [general provision]." *In re Woods*, 743 F.3d 689, 698-699 (10th Cir. 2014). The purpose of the 340B program is, as its title suggests, the "limitation on prices for drugs purchased by covered entities." The more broadly the orphan drug exclusion is drawn, the more it will

contravene the objectives and primary operation of the program itself—*i.e.*, making it affordable for safety net hospitals to purchase drugs that are essential to their treatment of patients in underserved populations.

Finally, relevant legislative history reveals that the Interpretive Rule reflects precisely how Congress intended the orphan drug exclusion to operate. The legislative history for the Orphan Drug Act, which enacted Section 526 of the FFDCA, makes clear that the incentives for developing orphan drugs were intended only when the drug is transferred, prescribed, sold or otherwise used to treat the designated rare diseases or condition.

> A drug can be tested and approved for more than one use. Many of the currently marketed drugs for rare diseases are also used in common diseases. The designation process established by the bill avoids this confusion *by designating the use of the drug which is for a rare disease or condition.*

H.R. Rep. No. 97-840 at 9 (1982) (emphasis added). This understanding is only confirmed by the fact that every statutory benefit tied to orphan drug status is specifically tied to an orphan drug's orphan use/indication. *See*, Memorandum in Support of Defendants' Motion for Summary Judgment, Doc. 14-1, pp. 20-21.

Even more, Congressmen Henry Waxman and Tom Harkin wrote the Administrator of the HRSA on July 7, 2011 in support of HRSA's interpretation of Section 2302 of HCERA, observing as follows--

> As Chairmen of the Committees with jurisdiction over the 340B program at the time the provision became law, we support section 10.21(a) of the proposed rule, which contains HRSA's interpretation of Section 2302(4) of the Health Care and Education Reconciliation Act of 2010. HRSA's interpretation of this provision is consistent with legislative intent, which was that the exclusion of orphan drugs from the 340B program for affected entities be construed as a narrow exclusion, applying only when drugs are legitimately used for rare diseases or conditions designated under Section 526.
>
> Section 2302(4) of the Health Care and Education. Reconciliation Act exempts "a drug designated by the Secretary under section 526 of the Federal Food, Drug, and Cosmetic Act for a rare disease or condition" from 340B pricing for entities

> that were added as covered 340B entities by the Patient Protection and Affordable Care Act.
>
> A designation under Section 526 consists of two components: the drug itself and the indication for which it is designated under Section 526. The same drug can be either a Section 526 designated drug or not a Section 526 designated drug depending on whether it is used for the indication described in Section 526 for that drug.
>
> For example, Albuterol is designated under Section 526 for "Prevention of paralysis due to spinal cord injury." Separately, the same drug is approved and widely used for a non-orphan designation, "treatment or prevention of bronchospasm with reversible obstructive airway disease." This use of the drug is not designated under Section 526.
>
> The reference in Section 2302(4) of the Health Care and Education Reconciliation Act of 2010 to a "drug designated by the Secretary under Section 526" is intended to mean that a drug is exempt from 340B pricing for relevant entities only when the drug is used in a way that satisfies both components of the Section 526 designation: the drug itself, and the indication for which it used. In the example above, when Albuterol is used for "prevention of paralysis due to spinal cord injury," it would meet the definition of a drug designated by the Secretary under Section 526. However, when Albuterol is used for "treatment or prevention of bronchospasm with reversible obstructive airway disease," or for any other use not designed under Section 526, it would not meet both components of the Section 526 designation, and hence would not be considered to be a "a drug designated by the Secretary under Section 526." For this use of the drug, the 340B exemption would not apply. Administrative Record (Doc. 20-2) at AR335.

Thus, the legislative history both confirms that the act of orphan drug "designation" was congressionally understood to be, in part, a use-based designation, *and* that the orphan drug exclusion from 340B pricing limitations was intended to apply only to orphan drugs ultimately used for the rare disease or condition for which they were designated.

Plaintiff's attempt to draw the court into a myopic parsing of a singular statutory phrase to the exclusion of any consideration of context or purpose is misguided. Even if Plaintiff's "reliance on the literal language of [the statute] and on the so-called 'plain meaning' rule of statutory construction is not entirely unpersuasive," its "assertion...is refuted when [the provision] is read together with the rest of the [law], as, of course, it must be." *Chemehuevi*

Tribe of Indians v. Federal Power Commn., 420 U.S. 395, 403 (1975) (considering text, context, legislative purpose, legislative history, and agency practice in ascertaining the meaning of a statutory provision). The Interpretive Rule correctly construes the orphan drug exclusion and properly gives effect to Congressional intent. It should be upheld.

CONCLUSION

For the foregoing reasons, the AHA urges the Court to find the Defendants' motion for summary judgment should be granted.

Dated: February 6, 2015

Respectfully submitted,

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CERTIFICATE OF SERVICE

The undersigned hereby certifies that a true copy of the foregoing will be served upon all registered parties by operation of the Court's CM/ECF filing system, on this 6th day of February, 2015.

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