No. 18-546

IN THE

Supreme Court of the United States

BRIAN E. FROSH, Attorney General of Maryland, and ROBERT R. NEALL, Maryland Secretary of Health,

Petitioners,

v.

ASSOCIATION FOR ACCESSIBLE MEDICINES,

Respondent.

On Petition for a Writ of Certiorari to the United States Court of Appeals for the Fourth Circuit

BRIEF OF *AMICI CURIAE* GERARD F. ANDERSON, PhD AND JOSHUA M. SHARFSTEIN, M.D. IN SUPPORT OF PETITIONERS

JAMES DABNEY MILLER
Counsel of Record
4110 Greenway
Baltimore, Maryland 21218
(410) 458-5445
jmill165@jhu.edu

Counsel for Amici Curiae

November 21, 2018

WILSON-EPES PRINTING CO., INC. – (202) 789-0096 – WASHINGTON, D. C. 20002

TABLE OF CONTENTS

TABLE OF AUTHORITIES

TABLE OF AUTHORITIES—Continued

TABLE OF AUTHORITIES—Continued

TABLE OF AUTHORITIES—Continued

TABLE OF AUTHORITIES—Continued

TABLE OF AUTHORITIES—Continued

INTEREST OF *AMICI CURIAE*[1]

Amicus curiae Gerard F. Anderson, PhD, is a professor of Health Policy and Management and International Health at the Johns Hopkins Bloomberg School of Public Health, in Baltimore City, Maryland. In addition, he holds a joint appointment at the Johns Hopkins School of Medicine and is the Director of the Johns Hopkins Center for Hospital Finance & Management. He has published more than 300 health care finance papers in peer-reviewed journals, many of which addressed drug-pricing issues.[2] He has been called to testify before congressional committees on issues of health care finance more than 50 times. Professor Anderson testified before the Maryland General Assembly in 2017 in support of the legislation that became the Maryland statute at issue here.

Professor Anderson is an internationally recognized expert in health care finance, including the pricing of prescription drugs.

---

[1] Pursuant to Rule 37.6, Counsel of Record for amici curiae states that no counsel for a party authored any part of this brief, and that neither counsel for any party nor any party made any monetary contribution intended to fund the preparation or submission of this brief. No person other than amici curiae and their Counsel of Record made such a monetary contribution. Both Petitioners and Respondent have filed blanket consents for amicus briefs with the Clerk.

[2] *E.g,* Greene JA, Anderson GF, Sharfstein JM. Role of the FDA in affordability of off-patent pharmaceuticals. *JAMA* 2016: 315(5); 461-462. Lilenquist D, Bai G, Anderson GF. Addressing Generic-Drug Market Failures: The Case for Establishing a Nonprofit Manufacturer. *N Engl J Med* 2018: 378(20); 1857-1859. Karas L, Shermock KM, Proctor C, Socal M, Anderson GF. Limited distribution networks stifle competition in the generic and biosimilar drug industries. *Am J Manag Care* 2018: 24(4); e122-e127.

Amicus curiae Joshua M. Sharfstein, M.D., is Professor of the Practice in the Department of Health Policy and Management of the Johns Hopkins Bloomberg School of Public Health in Baltimore City, Maryland. He also holds a joint appointment at the Johns Hopkins School of Medicine. Previously, he served as Secretary of the Maryland Department of Health and Mental Hygiene (and thus is a predecessor in that position of Petitioner Robert R. Neall).[3] He has also served as the Principal Deputy Commissioner of the U.S. Food and Drug Administration and as Commissioner of Health for Baltimore City.

Professor Anderson and Dr. Sharfstein acknowledge the research assistance of Mariana P. Socal M.D., PhD, and So Yeon Kang, M.P.H., in preparing this amicus brief. Dr. Socal is an Assistant Scientist and Ms. Kang is a Research Associate at the Johns Hopkins Bloomberg School of Public Health.

The views expressed in this brief are those of Professor Anderson and Dr. Sharfstein individually and do not reflect the views of the Johns Hopkins University or any of its divisions.

SUMMARY OF ARGUMENT

The Hatch-Waxman Act of 1984,[4] which authorized the U.S. Food & Drug Administration (the FDA) to approve generic drugs, has been a huge success in lowering drug prices in the United States. In 2017, according to data from Respondent Association for

---

[3] The Maryland Department of Health was formerly known as the Maryland Department of Health and Mental Hygiene.

[4] Drug Price Competition and Patent Term Restoration Act (popular name 'Hatch-Waxman Act'), P.L. 98-417, 98 Stat. 1585 (Sept. 24, 1984).

Accessible Medicines (AAM), 90% of doctors' prescriptions were filled with generic drugs, but these generic prescriptions represent only 23% of the total cost of all prescriptions in the United States that year.[5] Most generic drugs are inexpensive, and the quality of all generic drugs is carefully regulated by the FDA.

It is equally true, however, that a small handful of players in the off-patent and generic drug market have 'gamed the system' to impose astronomical increases in the price of some essential off-patent or generic drugs.[6]

The Maryland statute at issue here addresses only these few bad actors. It is not aimed at the responsible manufacturers represented by Respondent. To the contrary, *amici curiae* Professor Anderson and Dr. Sharfstein fully support the actions of responsible generic drug manufacturers.

Professor Anderson and Dr. Sharfstein, with all due respect, submit that the distribution and pricing of off patent and generic drugs offered for sale in Maryland

---

[5] Ass'n for Accessible Medicines. 2018 Generic Drug Access & Savings in the U.S.: Access in Jeopardy, at 33-34. (Attached as Ex. D to Respondent's complaint in the District Court). https://accessiblemeds.org/sites/default/files/2018_aam_generic_drug_access_and_savings_report.pdf. Accessed Nov. 16, 2018.

[6] *E.g.*, Patrick Thomas, Former Valeant Executive and Co-Defendant Sentenced to Prison. WALL STREET JOURNAL Oct. 30, 2018. https://www.wsj.com/articles/former-valeant-executive-and-co-defendant-sentenced-to-prison-1540928669?mod=searchresults&page=1&pos=1. Eric Knowles, The Making of Martin Shkreli as "Pharma Bro.' NEW YORK TIMES June 22, 2017. https://www.nytimes.com/2017/06/22/business/dealbook/martin-shkreli-pharma-bro-drug-prices.html.

is substantially more related to activities in Maryland than the Court below may have appreciated.

The decision below was made on the basis of Respondent's complaint without any factual record. As Judge Thacker, writing for the majority, stated: "We review the dismissal [of AAM's complaint] de novo, 'accepting [AAM's] well-pleaded allegations as true and drawing all reasonable inferences in [AAM's] favor.'"[7]

Nonetheless, the Court below remanded with instructions to enter judgment for Respondent, without allowing for any trial on the merits, or cross-motions for summary judgment under FED. R. CIV. P. 56.

A major generic drug manufacturer is based in Baltimore City, and a substantial part of the generic drug industry is registered as doing business in Maryland. The generic drug companies—all members of AAM—that are registered as doing business in Maryland together control 2,200 separate generic drug products and 807 different active ingredients.

All three of the dominant drug wholesale distributors hold permits from the Maryland Board of Pharmacy, and one of them has a large distribution warehouse in Maryland.

These all matters of public record.

One major health care system in Maryland—the Johns Hopkins Health System—contracts directly with generic drug manufacturers.[8]

---

[7] App. A at 6a (citation omitted).

[8] Bruhn WE, Frarica EA, Makary MA. Group Purchasing Organizations, Health Care Costs, and Drug Shortages. *JAMA* 2018: 320(18); 1859-1860, at 1860 (noting that the Johns Hopkins Health System recently started its own group purchasing

This case presents a question of great importance to patients' access to essential generic drugs in Maryland—which is a crucial issue for the public health.

Professor Anderson and Dr. Sharfstein ask that the petition for certiorari be granted.

ARGUMENT

I. Public Records Show That One Major Generic Manufacturer is Headquartered In Baltimore, and That Three Other Major Generic Manufacturers Do Business in Maryland

AAM, in its complaint, alleges that "***next to none*** of the largest generic drug manufacturers reside in Maryland."[9] The majority below took AAM's 'next to none' allegation to be true.

Maryland requires foreign corporations that do business within Maryland to register with the State.[10] Those registrations are available online to the public.

It is a matter of public record that Lupin Pharmaceuticals, Inc. (Lupin)—a member of AAM—has its sales and marketing offices in downtown Baltimore City.[11] When the FDA communicated with Lupin in early 2018 with respect to tentative approval of a generic drug, it addressed its letter to Lupin's

---

organization to obtain more competitive prices directly from manufacturers).

[9] Complaint ¶ 2, page 2 (emphasis added).

[10] Maryland Code Ann. Corporations and Associations §4A-1002; §7-202.

[11] https://egov.maryland.gov/BusinessExpress/EntitySearch/BusinessInformation/F17106915. Accessed Nov. 16, 2018.

Director of Regulatory Affairs at Lupin's office in Baltimore City.[12]

The FDA maintains an online, searchable database, available to the public, of approved drug products. This database is usually known as the 'Orange Book.'[13] As of November 16, 2018, the FDA's Orange Book shows that Lupin has currently effective approvals from FDA for 327 separate generic drug products and 114 different active ingredients.[14]

Lupin is a major generic drug manufacturer, and it has its United State headquarters in Baltimore City, Maryland. Any visitor to Baltimore's Inner Harbor will see a huge sign on the high-rise office building known as 'Harborplace Tower' that reads 'LUPIN.'[15] (Harborplace Tower, 111 South Calvert Street in Baltimore City, is Lupin's registered place of business in Maryland.)

Three other major generic drug manufacturers are also registered as doing business in Maryland:

---

[12] FDA. Letter to Lupin Pharmaceuticals, Inc. Harborplace Tower, Baltimore, MD 21202, dated February 2, 2018., regarding tentative approval of generic hydrocortisone butyrate lotion. https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2018/210209Orig1s000TAltr.pdf.

[13] FDA. Approved Drug Products With Therapeutic Equivalence Evaluations (the 'Orange Book'). https://www.accessdata.fda.gov/scripts/cder/ob/. Accessed Nov. 16, 2018.

[14] The same active ingredient can be approved by the FDA in different strengths, dosage forms, or packaging, which represent different generic drug products.

[15] Photo of LUPIN sign. https://www.loopnet.com/Listing/111-S-Calvert-St-Baltimore-MD/3965596/. Accessed Nov. 16, 2018.

- **Mylan**—a member of AAM— is registered as doing business within Maryland.[16] Mylan is notorious for the 10-fold increases in the price of its EpiPen (epinephrine injection, USP) product.[17] The active ingredient in EpiPen saves the lives of children and adults who suffer anaphylactic reactions to foods, bee stings, and other allergens. As of November 16, 2018, the FDA's Orange Book shows that Mylan has currently effective approvals from the FDA for 1,179 generic drugs and 419 different active ingredients. Records of the U.S. Securities & Exchange Commission (SEC), which are available online to the public, show that Mylan reported a gross profit for the three months ending June 30, 2018 of $962.5 million.[18] Mylan stated in its most recent quarterly (10-Q) report to the SEC that: "Generic products, particularly in the U.S., generally contribute most significantly to revenues . . . *in periods of limited generic competition*."[19] Mylan is a major generic drug manufacturer that does business within Maryland.

---

[16] Mylan. https://egov.maryland.gov/BusinessExpress/EntitySearch/BusinessInformation/F02278240. Accessed Nov. 16, 2018.

[17] Lyon J. Significant Increases in EpiPen Prices. *JAMA* 2016: 316(14):1439. Robert Cyran. Debate Over Mylan's EpiPen Exposes Health Care Flaws. NEW YORK TIMES (Aug 25, 2016). https://www.nytimes.com/2016/08/26/business/dealbook/debate-over-mylans-epipen-exposes-health-care-flaws.html.

[18] SEC. Mylan 10-Q for the period ending June 30, 2018, at 69. https://www.sec.gov/Archives/edgar/data/1623613/000162361318000027/myl10q_20180630xdoc.htm. Accessed Nov. 16, 2018.

[19] Id. at 70 (emphasis added).

- **Apotex Corp**.—a member of AAM—is registered as doing business within Maryland.[20] As of November 16, 2018, the FDA's Orange Book shows that Apotex has currently effective approvals from FDA for 447 separate generic drugs and 155 different active ingredients. Apotex is a major generic drug manufacturer that does business in Maryland.
- **Fresenius Kabi**—a member of AAM—is registered as doing business within Maryland.[21] As of November 16, 2018,the FDA's Orange Book shows that Fresenius Kabi has currently effective approvals from FDA for 247 separate generic drugs and 119 different active ingredients. Fresenius Kabi is a major generic drug manufacturer that does business in Maryland.

AAM did not advise the Court below that the FDA's Orange Book—a public record—shows that, taken together, these four AAM members doing business in Maryland control 2,200 separate generic drug products and 807 different active ingredients.

II. Public Records Show That The Dominant Wholesale Drug Distributors Have A Presence In Maryland

AAM alleges in its complaint that "***none*** of the 'Big Three' [drug] wholesalers—which collectively account for nearly 90% of the wholesale [drug] market [citation

---

[20] Apotex Corp. https://egov.maryland.gov/BusinessExpress/EntitySearch/BusinessInformation/F18054684. Accessed Nov. 16, 2018.

[21] Fresenius Kabi LLC. https://egov.maryland.gov/BusinessExpress/EntitySearch/BusinessInformation/Z18431452. Accessed Nov. 16, 2018.

omitted]—resides in Maryland. . . .”[22] AAM goes on to allege that the Maryland statute at issue here, “expressly targets pricing and conduct at the manufacturer-wholesaler level, which occurs largely, if not exclusively, outside the State [of Maryland].”[23]

The Maryland Board of Pharmacy is part of the State’s Department of Health, which is headed by Petitioner Robert R. Neall and was previously headed by *amicus curiae* Dr. Sharfstein. Maryland by statute requires pharmaceutical distributors to obtain permits from the Board of Pharmacy,[24] and these permits are available to the public online.

These public records show that one of the dominant wholesale distributors, Cardinal Health,[25] has a large distribution warehouse located at 7611 Brandon Woods Boulevard, Baltimore, Maryland 21226. Cardinal Health first obtained a distributor permit from the Maryland Board of Pharmacy in 2003. Its current permit, as shown on the Board’s public website, runs until May 2019. [26]

Records of the SEC, which are available online to the public, show that for the three months ending

---

[22] Complaint ¶25, at page 14 (emphasis added).

[23] Complaint ¶49, at page 23.

[24] Md. Code Ann. Health Occ. §12-6C-03 (“A wholesale distributor shall hold a wholesale distributor permit issued by the Board [of Pharmacy] before the wholesale distributor engages in wholesale distribution in the State”).

[25] Complaint ¶25, at page 13.

[26] Maryland Board of Pharmacy. https://egovpharmacy.dhmh.maryland.gov/verification/Search.aspx?facility=Y. (Enter search terms ‘Pharmacy,’ ‘Distributor,’ ‘Active,’ ‘Cardinal Health,’ ‘Baltimore,’ and ‘Maryland.’) Accessed Nov. 21, 2018.

March 31, 2108, Cardinal Health reported profit from its pharmaceutical operations of $596 million.[27]

The other two dominant wholesale distributors—AmerisourceBergen and McKesson—also hold distributor permits from the Maryland Board of Pharmacy,[28] which means these companies engage in wholesale drug distribution in Maryland. Both of these drug distributors are large, publicly-traded corporations.

Amici curiae Professor Anderson and Dr. Sharfstein believe AAM's allegation that the three dominant drug distributors control "nearly 90% of the wholesale [drug] distribution market" is correct, and that the market dominance of three wholesale drug distributors is a significant part of the problem of prescription drug pricing.

Nonetheless, AAM's allegation that: "***none*** of the 'Big Three' [drug] wholesalers—which collectively account for nearly 90% of the wholesale [drug] market [citation omitted]—resides in Maryland"[29] is shown by public records to be—at best—misleading. All three dominant wholesale distributors are registered with the Maryland Board of Pharmacy, which means they

---

[27] SEC. Cardinal Health, Inc. Form 10-Q for the Quarter Ending March 31, 2018, at 8. https://www.sec.gov/Archives/edgar/data/721371/000072137118000038/a18q3_10qx033118xform10-q.htm. Accessed Nov. 16, 2018.

[28] Maryland Board of Pharmacy. AmerisourceBergen. https://egovpharmacy.dhmh.maryland.gov/verification/Search.aspx?facility=Y. (Enter search terms 'Pharmacy,' 'Distributor,' 'Active,' and 'AmerisourceBergen'). Accessed Nov. 21, 2018. McKesson. https://egovpharmacy.dhmh.maryland.gov/verification/Search.aspx?facility=Y. (Enter search terms 'Pharmacy,' 'Distributor,' 'Active,' and 'McKesson'). Accessed Nov. 16, 2018.

[29] Complaint ¶ 25, at page 14 (emphasis added).

engage in drug distribution within Maryland, and Cardinal Health owns a large warehouse in Maryland.

III. Maryland Healthcare Organizations Directly Contract with Generic Drug Manufacturers

Professor Anderson and Dr. Sharfstein believe that Maryland health care providers can contract for generic drugs directly with generic drug manufacturers. One example is the Johns Hopkins Health System Corporation, which is a non-profit organization—based in Baltimore City, Maryland—that is part of Johns Hopkins University.[30] The Johns Hopkins Health System includes the Johns Hopkins Hospital, as well as other hospitals in Maryland. While the Johns Hopkins Health System currently participates in a hospital group purchasing organization based outside Maryland, in some instances the Johns Hopkins Health System negotiates the purchase of off patent or generic drugs directly with the manufacturers of those drugs.

IV. Each State Determines a Different Price For Generic Drugs Under the Federal Medicaid Program

Each State determines its own pricing benchmarks for paying for outpatient drugs (which include off patent and generic drugs) under the Medicaid program. The Centers for Medicare & Medicaid Services (CMS) makes public on its website the details of each

[30] The Johns Hopkins Health System Corporation. https://www.hopkinsmedicine.org/about/governance/jhhsc_trustees.html. Accessed Nov. 16, 2018.

State's benchmarks.[31] Maryland, for example, pays for outpatient generic drugs based on the lowest of several different pricing benchmarks, including the National Averaged Drug Acquisition Cost (NADAC) benchmark, plus a $10.49 'dispensing fee,' which Maryland pays to the dispensing pharmacy.

Each State has a different set of pricing benchmarks, and each State is required to submit its particular formula and benchmarks to CMS for approval.

Medicaid, however, is far too large a market for any generic drug manufacturer to ignore, and as a consequence those manufacturers adjust their pricing to the benchmarks adopted by the different States.

V. The Maryland Statute Is A Reasonable Response To Lack of Competition In The Market For Off Patent & Generic Drugs

The market for off patent and generic drugs differs from the market for drugs that are protected by patents. Generic drugs generally lack brand or trade names and instead are sold under the official or proper name of their active ingredient. Patent protected drugs usually are sold under a trademark or brand name. Also, generic drug manufacturers generally conduct only the limited clinical research required to obtain approval from the FDA for a generic drug.[32]

---

[31] Centers for Medicare and Medicaid Services. Medicaid Covered Outpatient Prescription Drug Reimbursement Information by State (Sept. 2018). https://www.medicaid.gov/medicaid/prescription-drugs/state-prescription-drug-resources/drug-reimbursement-information/index.html. Accessed Nov. 18, 2018.

[32] A generic drug manufacturer must demonstrate that a proposed generic drug is 'bioequivalent' to another drug that has previously been approved by the FDA on the basis of full clinical

In the off patent and generic drug market, competition is based primarily on price since the active ingredient must be the same for the multiple generic products of the same drug on the market.

Petitioners here, in their petition for certiorari, list five off patent or generic drugs identified in a report by a committee of the U.S. Senate as having experienced dramatic price increases.[33] Congress held hearings on these findings and Dr. Anderson testified in three of these hearings. These five drugs are not the only examples of rapid price increases; there are many other examples as well, all which all create a serious public health problem of access to essential drugs.

In a market with robust competition, large, rapid price increases generally do not occur. Economic studies of the off patent or generic drug market have produced evidence that markets with four or more manufacturers of generic drugs with the same active ingredient will exhibit robust competition (assuming the absence of illegal price fixing conspiracies).[34]

This is the reason the Maryland statute at issue here is strictly limited to cases where only three or fewer manufacturers are selling generic drugs with the same active ingredient. The Maryland General Assembly, in the statute, defined an 'off patent or

---

studies of safety and effectiveness. Food Drug & Cosmetic Act §505(j), 21 U.S.C. §355(j).

[33] Petition for Certiorari 5-6.

[34] FDA. Generic competition and drug prices. https://www.fda.gov/aboutfda/centersoffices/officeofmedicalproductsandtobacco/cder/ucm129385.htm. Accessed Nov. 16, 2018. Alpern JD, Zhang L, Stauffer WM, Kesselheim AS. Trends in pricing and generic competition within the oral antibiotic drug market in the United States. *Clin Infect Dis* 2017; 65(11): 1848-1852.

generic drug' in part as one "that is actively manufactured and marketed for sale in the United States *by three or fewer manufacturers.*"[35] (*Amicus curiae* Professor Anderson testified before the Maryland General Assembly in support of the legislation and explained the rationale for the three or fewer manufacturers that became part of this statue.)

It is also the reason that Mylan—a major generic drug manufacturer—candidly noted in its recent quarterly report to the SEC that generic drugs "generally contribute most significantly to revenue . . . in periods of limited generic competition."[36]

A small number of competitors in the market for off patent and generic drugs can occur for many different reasons. One reason may be that the patient population for particular generic drug is relatively small.[37]

---

[35] Maryland Code Ann., Health-Gen §2-801(b)(iii). App. D 116a (emphasis added).

[36] SEC. Mylan 10-Q for the period ending June 30, 2018, at 70. https://www.sec.gov/Archives/edgar/data/1623613/000162361318000027/myl10q_20180630xdoc.htm

[37] An example is pyrimethamine (Daraprim®, Vyera), which is intended to treat toxoplasmosis, a rare fungal infection that afflicts patients suffering from AIDS. The sponsor of pyrimethamine is Vyera, which was formerly named 'Turing' when it was headed by Martin Shkreli. Although Mr. Shkreli is now in federal prison, the price of pyrimethamine has not decreased. Shefali Luthra. KAISER HEALTH NEWS. 'Pharma Bro' Shkreli is in Prison, but Daraprim's Price Is Still High. May 4, 2018. https://khn.org/news/for-shame-pharma-bro-shkreli-is-in-prison-but-daraprims-price-is-still-high/?utm_campaign=KHN%3A%20First%20Edition&utm_source=hs_email&utm_medium=email&utm_content=62676655&_hsenc=p2ANqtz-8TucJjSXdwTgT-XqicfJFW4ZrWymex4bFxLYOMxmysNmCYeXX6gVknUgxmGY_yM4aJk7-Mzirtl4fV3TLFujcfwTiFSg&_hsmi=62676655.

Entering a competitive market when the potential for sales is only perhaps a few thousand patients may not make economic sense for most generic drug companies. As a result, the companies already in the market can take advantage of this market failure.

Large, rapid price increases for particular off patent or generic drugs are usually not the result of increases in the price of raw materials or other economic inputs to the manufacturing process. Also, as noted earlier, generic drug manufacturers generally conduct only limited clinical research, and so the cost of such research is usually not a major cost input for generic manufacturers.

In any event, the Maryland statute at issue here is carefully crafted to protect generic manufacturers in situations where their cost inputs do force them to raise prices. An 'unconscionable increase' in the price of an off patent or generic drug is defined in the statute one that "is not justified by the cost of producing the drug or the cost of appropriate expansion of access to the drug to promote public health."[38] With this statute, Maryland can take action to address the increases and preserve access to essential medications for state residents.

Maryland's significant involvement in the generic drug industry should be sufficient to justify the State's interest and engagement in solving this public health issue.

---

[38] Md. Code Ann., Health-Gen §2-801((f)(1). App. D 117a.

CONCLUSION

The petition for certiorari should be granted.

Respectfully submitted,

JAMES DABNEY MILLER
Counsel of Record
4110 Greenway
Baltimore, Maryland 21218
(410) 458-5445
jmill165@jhu.edu

Counsel for Amici Curiae

November 21, 2018