



July 16, 2018

The Honorable Alex M. Azar II
Secretary
U.S. Department of Health and Human Services
200 Independence Ave. SW, Room 600E
Washington, DC 20201

RE: HHS Blueprint to Lower Drug Prices and Reduce Out-of-Pocket Costs [RIN 0991-ZA49]

Dear Secretary Azar:

The Association for Accessible Medicines (AAM) and its Biosimilars Council appreciate the opportunity to provide comments in response to the agency’s request for information on the *HHS Blueprint to Lower Drug Prices and Reduce Out-of-Pocket Costs [RIN 0991-ZA49]* (“Drug Pricing Blueprint”). AAM and the Council work to expand patient access to safe, quality and effective generic and biosimilar medicines, including through promoting a positive regulatory, reimbursement, political and policy environment, and supporting education about the safety and effectiveness of generics and biosimilars. As manufacturers of nine out of every 10 prescriptions dispensed in the U.S., our members form an integral and powerful part of the health care system for America’s patients. Enhancing patient access to generic and biosimilar medicines is key to lowering drug prices, as demonstrated in AAM’s report 2018 *Generic Drug Access & Savings in the U.S.*

AAM and the Council appreciate the Administration’s leadership and approach in issuing the Drug Pricing Blueprint. The Blueprint identifies four overarching goals for lowering drug prices:

1. Increasing Competition
2. Better Negotiation
3. Creating Incentives for Lower List Prices
4. Reducing Patient Out-of-Pocket Spending.

Enhancing patient access to generic and biosimilar medicines is foundational to each of these – providing competition and reducing patient out-of-pocket, as well as overall system, costs through significantly lower list prices that decline further over time. Simply put, generic and biosimilar medicines make health care more accessible and affordable for all patients.

Therefore, we applaud and share the Department’s interest in supporting a health care system that provides high-quality care at affordable prices for the American people. This is the core mission of the generics and biosimilar medicines industry. It is also the congressional goal in

enacting the 1984 Hatch-Waxman Act¹ and the 2009 Biologics Price Competition and Innovation Act (BPCIA)².

These bipartisan laws have produced a thriving and constantly changing pharmaceutical marketplace by balancing innovation in drug development with competition from lower-cost generic and biosimilar alternatives. As a result, the U.S. health care system has saved \$1.79 trillion in the last decade due to the availability of low-cost generics.³ And additional savings to come from new biosimilar medicines means greater access for patients. This has important, positive effects on public health, including reducing medicine abandonment, increasing medication adherence and generally allowing patients to live longer, healthier lives.⁴

Yet it is clear that too many financial incentives around prescription medicines are aligned to benefit various supply chain actors, rather than supporting competition to benefit patients through lower costs.

Market-based competition from generic and biosimilar medicines consistently delivers lower prices for patients, making our sector unique in the health care ecosystem. Although generics make up 90 percent of all prescriptions filled in the U.S., they are only 23 percent of the cost. In fact, generic and biosimilar medicines are the most effective solution for combating high list prices and growing prescription drug spending.

However, significant pressures threaten the future of a sustainable and competitive generic and biosimilar market. Manufacturers of these more affordable medicines increasingly face obstacles to entering the marketplace, and staying in the marketplace, threatening reduced savings and increasing risks of drug shortages. Indeed, you noted one such challenge of market consolidation causing underpricing of generic drugs in your June 2018 testimony before the Senate Finance Committee: “We may be driving those prices so low that we’re creating manufacturing anomalies that lead to sole-source products there with others exiting.”⁵ Accordingly, HHS should work not only to help generics and biosimilars come to market, but also should take steps to ensure they are able to stay on the market.

As such, successfully lowering drug prices and reducing out-of-pocket costs for patients calls for significant disruption, and realignment, of economic incentives to prioritize the delivery of medicines with the lowest list price. AAM and the Council recommend the following five priorities for HHS:

¹ Drug Price Competition and Patent Term Restoration Act, Pub. L. No. 98-417 (1984).

² Biologics Price Competition and Innovation Act (Public Law 111-148).

³ Association for Accessible Medicines, *2018 Generic Drug Access & Savings in the U.S.* <http://RxAccessReport.us>

⁴ AAM Savings Report Choudhry NK, Denberg TD, Qaseem A, for the Clinical Guidelines Committee of the American College of Physicians. Improving Adherence to Therapy and Clinical Outcomes While Containing Costs: Opportunities from the Greater Use of Generic Medications: Best Practice Advice From the Clinical Guidelines Committee of the American College of Physicians. *Ann Intern Med.* 2016;164:41-49. doi: 10.7326/M14-2427 <http://annals.org/aim/fullarticle/24271597/improving-adherence-therapy-clinical-outcomes-while-containing-costs-opportunities-from>

⁵ Senate Finance Committee Full Committee Hearing on Prescription Drug Affordability and Innovation: Addressing Challenges in Today’s Market. June 26, 2018.

1. **Re-examine the role of rebates.** While rebates have not historically affected the availability of generic drugs, it has become clear that recent changes in formulary design, as well as exclusionary brand drug rebate and bundling contracts, may undermine patient access to new generic and biosimilar medicines offering lower list prices.
2. **Prevent the misuse of restricted access programs to block generic and biosimilar competition.** We commend the FDA’s efforts to address brand manufacturer shenanigans that abuse patient safety programs, and ensure access to reference product samples needed for development of generic and biosimilar competitors. However, FDA unfortunately lacks the ability to compel brand companies to sell samples to generic manufacturers.⁶ We encourage the Administration to endorse the bipartisan CREATES Act, recently passed by the Senate Judiciary Committee on a 15-6 vote.⁷
3. **Protect incentives for generic competition.** Proposals to alter the 180-day term of exclusivity for first-to-file generics are a solution in search of a problem – and would undermine one of the most critical incentives for generic medicines to come to market. The proposed changes risk fundamentally destabilizing and undermining the successful generic drug system for patients, which has encouraged earlier entry of safe and effective generic alternatives for more than three decades. AAM encourages HHS to withdraw its proposed amendments to 180-day exclusivity.
4. **Foster the development of a robust competitive U.S. biosimilars market.** Biologics make up 16 of the top 20 drugs by spend in Medicare Part B. Biosimilars promise significant newfound savings for patients and payers alike. To realize the full potential of biosimilar competition, the Administration should prioritize the timely review of applications; accelerate the education of physicians, patients and other key stakeholders regarding the safety and effectiveness of FDA-approved biosimilars; and advance incentives to ensure further market penetration and timely adoption of these lower-priced, life-saving biologic medicines.
5. **Combat patent abuse.** Abusive patent gamesmanship continues to prevent lower-priced generic and biosimilar medicines from entering the market at the earliest possible date. While AAM supports innovation, the creation of “patent thickets” serves only to delay competition beyond the timeframe envisioned by Congress. AAM encourages the Administration to ensure lower-priced generic and biosimilar medicines are able to launch at the earliest possible date and are not blocked by abusive patent gamesmanship.

⁶ Association for Accessible Medicines. “Transparency an Important Step in Ending the Shenanigans.” Available at: <https://bit.ly/2IWD532>. Accessed: July 5, 2018

⁷ <https://www.congress.gov/bill/115th-congress/senate-bill/974/actions>

Attached are more detailed comments in response to the Department's Request for Information. Because we support the Administration's interest in moving quickly to address this issue, we have organized our comments and recommendations according to the relevant agency. We have also included a summary of AAM's recommendations in Appendix 1.

Again, we appreciate the opportunity to provide comments in response to the Request for Information. If you have questions, please do not hesitate to contact us.

Sincerely,

A handwritten signature in black ink that reads "Chester Davis Jr." in a cursive script.

Chester "Chip" Davis, Jr.

President and CEO

Attachment:

- Detailed AAM comments

Comments from the Association for Accessible Medicine regarding: HHS Blueprint to Lower Drug Prices and Reduce Out-of-Pocket Costs [RIN 0991-ZA49]

Generic and Biosimilar Medications Play a Critical Role in Lowering Drug Costs

In the last decade, the U.S. health care system has saved \$1.79 trillion due to the availability of low-cost generics.¹ In 2017 alone, generic medicines generated \$265 billion in savings for patients and taxpayers. Savings that year to the two largest government health care programs, Medicare and Medicaid, totaled \$82.9 billion and \$40.7 billion, respectively. This translates to an average annual savings of \$1,952 per Medicare enrollee and an average savings of \$568 per Medicaid enrollee.²

Today's generics industry includes a range of diverse companies that have become global leaders both in providing safe and effective FDA-approved medicines and in pioneering new treatment options for patients. Generic competition continues to play a vital role in improving access to pharmaceuticals and driving cost savings for American patients and the health care system. This growth in the generics industry has led to the creation of thousands of new jobs across the country and to the improvement of the quality of life for millions of people.

Nowhere is the need for lower-priced alternatives, and the challenges facing them, more real than among high-priced specialty medicines, including biologic and complex non-biologic medicines. Specialty medicines as a group now are responsible for more than 40 percent of all spending on medicines.³ For instance, originator biologics, many of which are specialty medicines, are the most rapidly growing segment of increasing prescription drug costs in the United States, with more than \$120 billion in annual spending.⁴ And while only 2 percent of America's patients use biologics, they account for about 26 percent of prescription drug spending in the United States.⁵

To help bring down prices of biologic medicines for patients, Congress drafted and enacted the Biologics Price Competition and Innovation Act (BPCIA) – creating an abbreviated pathway for biologics that FDA determines are “highly similar” (biosimilar) to, or “interchangeable” with an FDA-approved/licensed biological product. Before this legislation, biosimilars had no abbreviated pathway for FDA licensure. To balance patient access while still supporting innovation, the BPCIA also gave brand biologic drug manufacturers a 12-year market exclusivity period for their products to ensure a return on investment for new medicines. This period is longer than anywhere else in the world that has a similar abbreviated pathway for biosimilars, including Canada and the European Union.⁶

¹ Association for Accessible Medicines, *2018 Generic Drug Access & Savings in the U.S.* Available at: <http://bit.ly/rxaccessreport>.

² *Id.*

³ IQVIA Institute for Human Data Science: “Medicine Use and Spending in the U.S.: A Review of 2017 and Outlook to 2022.” (April 2018)

⁴ IQVIA Institute for Human Data Science: “Medicine Use and Spending in the U.S.: A Review of 2017 and Outlook to 2022.” (April 2018)

⁵ *Id. Id.*

⁶ OnPoint Analytics. “Biologics Exclusivity and the TPP: An International Balancing Act.” Available at: <https://bit.ly/2NnJ0SI>. Accessed: July 5, 2018.

Biosimilar medicines represent a key step forward in reducing high drug prices. They are safe, effective and affordable versions of costly brand biologics. By the year 2025, more than 70 percent of drug approvals are expected to be biological products.⁷ Experts estimate that FDA-approved biosimilars could save between \$44 billion and \$250 billion over the next 10 years, if the commercial market is allowed to mature and proper incentives are in place to drive biosimilar utilization.⁸ That means that 1.2 million U.S. patients could have greater access to lifesaving cures.⁹ Women, lower income and elderly patients would particularly benefit from access to biosimilar medicines.¹⁰

Today's Market Presents Challenges to a Thriving Generic and Biosimilar Industry

It is sobering to consider what America's patients would face if there were no FDA-approved generic or biosimilar medicines to provide reliable access to affordable treatments. Generics do not merely deliver the most medicine at the lowest cost and greatest savings. Every day, generics cushion the significant financial impact of high brand name drug prices for patients and the health care system.

Put another way, the availability of low-cost generics helps to offset the financial impact of high brand drug prices. While prices for FDA-approved generic medicines are currently declining by more than 7 percent year over year¹¹, prices for brand drugs, especially biologics and specialty medicines, are increasing at an unsustainable rate – 62 percent from 2011 to 2015.¹²

However, the sustainability, competitiveness and reliability of both the generic and biosimilar markets are in jeopardy. These markets are confronted by the same destructive forces, yet face distinct challenges. Threats facing both markets include:

- (i) changing and increasingly challenging market and reimbursement frameworks, including significant and monopolistic purchaser consolidations;
- (ii) the abuse of laws and regulations by bad actors; and
- (iii) policy miscues that ignore the unique challenges facing generic and biosimilar medicines and unfairly penalize generic drugs.

As part of this, older generic medicines face aggressive price deflation and other hurdles to remaining in the market. For instance, market consolidation has winnowed the buyer side to three main purchasing consortia that buy 90 percent¹³ of the prescription drugs for wholesale distribution. With more than 200 multi-source manufacturers recognized by the FDA, competition is fierce and prices decline rapidly.

⁷ U.S. Pharmacist, "Biosimilars: Current Approvals and Pipeline Agents," October 2016. Available at: <https://bit.ly/2dV5oiS>. Accessed: July 5, 2018. .

⁸ AAM, "Generic Drug Access & Savings in the U.S.," June 2017 Available at: <https://bit.ly/2r6d4Z9> . Accessed: July 5, 2018..

⁹ The Biosimilars Council. "Biosimilars in the United States: Providing More Patients Greater Access to Lifesaving Medicines" - Available at: <https://bit.ly/2fAWtXB>. Accessed: July 5, 2018.

¹⁰ Id.

¹¹ Morgan Stanley. June 29, 2018. "*Spec/Gx Trends in Pictures*"

¹² U.S. Department of Health and Human Services Office of Inspector General. June 2018. Data Brief: Increases in Reimbursement for Brand-Name Drugs in Part D

¹³ Fein, A. The 2016-2017 Economic Report on Pharmaceutical Supply Chain.

In addition, newer, highly desirable generics and biosimilars face barriers to entering the market.

Following are a series of specific steps that the Administration can take to address these challenges and reduce drug costs for patients and the federal government alike.

Because we support the Administration's interest in moving quickly to address this issue, we have organized our comments and recommendations according to the relevant agency. We have also included a summary of AAM's recommendations in Appendix 1.

HHS and CMS Can Take Important Steps to Lower Drug Costs, but Must Ensure that Public Policy is Tailored to the Unique Differences between the Sole-Source and Multiple-Source Markets

Multiple-Source (Generic) Markets

Overall, the market for most generic drugs differs from that for brand drugs, and it is critical that any effort to address drug pricing consider and account for those differences. Most of what is understood as the "generic market" is actually a "multiple source" or "multi-source" market in which multiple manufacturers compete against one another to sell the same drug. Its accompanying incentives have generally worked well to encourage generic utilization, resulting in great savings for patients, employers, insurers, the federal government and the states. However, the generic marketplace is experiencing rapid changes with significant and unique pressures that distinguish it from the originator drug market and that call into question its long-term sustainability.

Manufacturers of multi-source products make decisions influenced by a range of factors and challenges, including ambiguous or burdensome regulatory requirements, rapidly evolving competition and difficult market conditions. These hurdles include delays in approval; the inability to acquire the active pharmaceutical ingredient (API); other ingredient cost and supply fluctuations; a low potential for return on investment driven by extensive consolidation in the wholesale and retail markets for generics; and wide-scale annual price deflation. Even when multi-source companies bring generic drugs to market, they often must intermittently market their drugs and may lose money, particularly in low-volume markets that may not support ongoing manufacturing.

Prices for multi-source products fall precipitously as competitors enter the market, typically settling at 80 percent less than the original branded product's price. This creates a volatile marketplace in which pricing pressure often drives multi-source manufacturers' decisions on market entry and, in some cases, exit.¹⁴

Secretary Azar described the issue and its public health impact before the Senate Finance Committee in June. "We need to examine whether we are underpaying for and under-reimbursing for generics. We need a strong, robust generic market. We may be driving those prices so low that we're creating manufacturing anomalies that lead to sole-source products with others exiting. We need to look at that and be open minded about whether we've actually made it too low."¹⁵

¹⁴ Koons, C. (April 11, 2018). *Why We May Lose Generic Drugs*. Bloomberg Businessweek.

¹⁵ Senate Finance Committee Full Committee Hearing on Prescription Drug Affordability and Innovation: Addressing Challenges in Today's Market. June 26, 2018

Sole-Source (Brand) Markets

In contrast, manufacturers of sole-source products, which are generally “brand-name” drugs, but which can also include off-patent sole-source products, maintain more control over their prices and rarely take price decreases as long as they remain the sole manufacturer. Brand drugs are often referred to as “sole source” drugs.

Rebates Play Different Roles in Sole-Source and Multi-Source Markets

The balance created by Hatch-Waxman established a new and different market for multi-source drugs – separate from sole-source drugs – that has supported increased generic utilization and savings for patients. The supply chain and pricing models that include rebates and ever-rising list prices do not apply to the vast majority of prescription drugs distributed in this country – the result of multiple manufacturers marketing identical products and competing exclusively on price, in a commodity-style market.

When sole-source manufacturers leverage pricing power granted by patents and regulatory exclusivities, pharmacy benefit managers (PBM), distributors and payors use formulary management and rebate agreements to control costs. In the multi-source market, payors generally set a maximum price and rely on pharmacies to negotiate low acquisition prices with wholesalers. The wholesalers, often in collaborative purchasing agreements with pharmacies across the country, distribute multiple-source medicines to various retail pharmacies. Multi-source manufacturers also may have to negotiate separate payments to pharmacies to stock their product.

Payors rely on manufacturer rebates to reduce costs for sole-source products, and rely on a competitive, commodity-like market to reduce costs for multi-source products. These differences in the generic and brand marketplaces create vastly different incentives for the manufacturers, wholesalers, distributors, PBMs, insurers and retail pharmacies that make up the supply chain.

Rebate Traps and Exclusionary Contracting Can Distort the Market for Generic and Biosimilar Medicines

The RFI asks if the Centers for Medicare and Medicaid Services (CMS) should consider restricting or reducing the use of rebates in Medicare Part D. Rebate agreements are proprietary and confidential, making it difficult to determine whether the rebated product is really a net cost saver to the plan or whether any savings accrues to the patient. Historically, originator manufacturers negotiated rebates with PBMs in order to secure favorable formulary placement. Favorable formulary placement, which can result in lower copayments for patients, was seen as a way to increase market share, justifying the rebates. As noted above, rebates in exchange for formulary placement have not been relevant to generics due to their lower list prices.

Theoretically, these rebates should result in lower net costs to payors, and eventually patients, but only if PBMs pass through a large enough portion of the rebates to plans. Because rebates do not impact pharmacy acquisition costs, PBMs and health plans rarely consider rebates when setting pharmacy reimbursement rates. At the same time, health plans are incorporating deductibles and coinsurance

payments into pharmacy benefit design, and moving away from first-dollar coverage and flat copayments. The price used to calculate patient financial liability for deductibles and coinsurance is frequently based on the pharmacy reimbursement price, which as noted previously, generally does not include rebates. While patients may benefit from rebates in the form of lower premiums, patients taking certain expensive medications are likely to have higher out-of-pocket costs.

Therefore, the role of rebates has been the subject of increasing controversy and debate.

In the current landscape, more modern, complex generics and biosimilars that have lower list prices than their reference product may face new, significant challenges to market competition. This manifestation of system misalignment that disfavors lower-priced products has been referred to as the “rebate trap”.¹⁶ Upon entry of a competitive biosimilar or complex generic, some reference manufacturers (which naturally have significant market share due to more than a decade of exclusivity) have threatened to remove rebates they provide to payors unless the biosimilar is effectively excluded from formulary. Some brand manufacturers have even threatened to withdraw the rebates on a bundle or portfolio of unrelated products in the event that the contracted entity utilizes a biosimilar or generic in place of the reference product.

In such a situation, an insurer must decide to either keep the lower-priced competitor off its formulary or pay the full, non-rebated list price not only for the reference product, but also for the other products included in the bundle, knowing that prescribing patterns may be slow to change. These aggressive negotiation tactics, which block lower-priced biosimilar and complex generic medicines from being available to patients, also discourage future investment in developing new products.¹⁷ Given that biosimilars include costs of \$200-\$300 million to bring to market, such barriers to market access pose a significant deterrent to continued investment in lower-priced generic and biosimilar competitors for costly and complex medications.

These “rebate traps” (which FDA Commissioner Scott Gottlieb, M.D. has also called “stacked rebates”¹⁸) deter price competition by generic and biosimilar manufacturers, and undermine competition. This dynamic is a significant obstacle to a robust and stable complex generic and biosimilars market in the U.S. The following table shows a hypothetical example of the rebate trap in practice, in which a payor must assume that not all patients will switch to the biosimilar if the decision is made to add it to the formulary. In such a situation, the loss of a rebate will lead to increased net expenditures even though a lower-priced alternative is being used in 50 percent of patients:

¹⁶ Hakim, A, Ross JS. Obstacles to the Adoption of Biosimilars for Chronic Diseases. JAMA. June 6, 2017. 317:21:2163-4.

¹⁷ Biosimilar Development: “Why So Slow? Demystifying the Barriers to U.S. Biosimilar Adoption.” Available at: <https://bit.ly/2BxnHbj>. Accessed: May 15, 2018.

¹⁸ FDA Head: On Board with ‘Right To Try’. MEDPAGETODAY. Available at: <https://bit.ly/2J1bNjX>. Accessed: May 29, 2018.

Example of the “Rebate Trap”

	Pre-Biosimilar	Post-Biosimilar	
		50% of Patients Switch	100% of Patients Switch
Reference biologic list price, US \$	50,000	50,000	50,000
Reference biologic postrebate price, US \$	25,000	NA (no longer offering rebate)	NA (no longer offering rebate)
Biosimilar price, US \$	NA	10,000	10,000
Patients taking branded biologic, No.	1,000	500	0
Patients taking biosimilar, No.	NA	500	1,000
Payer cost, US \$	25,000,000	30,000,000	10,000,000

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A recent high-profile example of this anti-competitive tactic is the subject of a lawsuit Pfizer filed against Johnson & Johnson (J&J). Pfizer has accused J&J of "exclusionary contracts" and price manipulation "to maintain its monopoly" for its reference product Remicade®.²⁰ This lawsuit stems from Pfizer’s entrance to the market with its Remicade biosimilar, Inflectra, which Pfizer has reported is currently priced at a 17 percent discount to Remicade.²¹ While J&J claims that “Pfizer has failed to demonstrate sufficient value to patients, providers, payors and employers”²² with its biosimilar, it is important to note that in J&J’s motion to dismiss the lawsuit, the company did not dispute any of Pfizer’s claims. Remicade reportedly earned \$5.4 billion in revenue in 2017; Inflectra had 2017 revenue of \$420 million.²³

In June 2018, Walgreen Company and The Kroger Company filed an antitrust lawsuit against J&J, making similar allegations that J&J unlawfully excluded biosimilar competition.²⁴ To be clear, this challenge is not unique to Pfizer’s Inflectra – it affects the overall market viability for future biosimilar competitors.

¹⁹ Hakim, A, Ross JS. Obstacles to the Adoption of Biosimilars for Chronic Diseases. JAMA. June 6, 2017. 317:21:2163-4.

²⁰ USA Today: “Pfizer accuses Johnson & Johnson of 'anticompetitive practices' in lawsuit.” September 20, 2017. Available at: <https://usat.ly/2xgWxFW>. Accessed: May 15, 2018.

²¹The Center for Biosimilars: “Pfizer Execs Underscore the Need for a Level Playing Field for Biosimilars.” Available at: <https://bit.ly/2wLDMLQ>. Accessed: May 15, 2018.

²² Reuters: “Pfizer files suit against J&J over Remicade contracts.” Available at: <https://reut.rs/2Hurmgc>. Accessed: May 15, 2018.

²³ The Center for Biosimilars: “Pfizer Execs Underscore the Need for a Level Playing Field for Biosimilars.” Available at: <https://bit.ly/2wLDMLQ>. Accessed: May 15, 2018.

²⁴ The Center for Biosimilars: “Walgreen, Kroger File Antitrust Suit Against J&J, Janssen Over Remicade.” Available at: <https://bit.ly/2u76AKg>. Accessed: June 21, 2018.]

If brand-name manufacturers can eliminate the financial viability of manufacturing less-expensive competitors, there will be no potential for future investment, effectively ensuring long-term market protection far beyond congressional intent.

Dr. Gottlieb has recognized this threat, noting:

“Manufacturers are using several schemes to hamstring biosimilar competition... restrictive contracting, rebating, and distribution agreements deter coverage and reimbursement...the net result is a lopsided playing field that disincentives biosimilar developers from making the sizable investment in bringing such products to market. I am concerned this will lead to reduced competition in the long run and unsustainable costs.”²⁵

In order to return to a stable system that ensures the long-term, uninterrupted, availability of generics and biosimilars for patients, the role of rebating schemes in driving formulary design should be reduced after a generic or biosimilar medicine is launched, in particular when it involves rebate stacking and bundled contracts that obstruct price competition. Greater discounts will be reached only if biosimilars and generics are able to compete on volume in a robust and open marketplace. Therefore, AAM suggests that CMS consider a range of proposals to limit the role of brand drug stacked rebates in driving formulary design when a generic or biosimilar medicine has been approved.

Recent Actions Creating Patient Access to Generic and Biosimilar Medicines in Part D

Congress recently enacted legislation that amended the Part D Coverage Gap Discount Program to allow biosimilar manufacturers to pay the discount previously paid only by their brand competitors. Because biosimilar manufacturers were prevented from participating in the discount program, beneficiaries taking biosimilars were responsible for the full cost of their medication while in the coverage gap, while they were eligible for generous discounts if they took the reference product. This policy change now allows biosimilars to compete for placement on Part D plans’ formularies, and will reduce beneficiaries’ out-of-pocket costs and Part D program spending.²⁶

Additionally, CMS recently lowered the biosimilars and interchangeable biologics copay for the Low-Income Subsidy (LIS) and catastrophic-phase non-LIS population to be equal to the copay of generic products. Previously, these patients taking a biosimilar were forced to pay the higher brand product copay for biosimilar products. This change will increase patient access and lower beneficiaries’ out-of-pocket costs.²⁷

These new policies represent the types of incentives necessary to foster a competitive biosimilars market, but are not in themselves sufficient to create a sustainable market. Additional, systemic changes are needed to align incentives across the value chain. Given that biologics play a significant role in Medicare Part B spending, it is important that CMS consider incentive realignment within both Part B

²⁵ CNBC Interview of FDA Commissioner Gottlieb, March 28, 2018. Available at: <https://cnb.cx/2pNVVlh>. Accessed: April 30, 2018.

²⁶ AARP: “Medicare Part D Discounts Now Cover Biosimilar Drugs.” Available at: <https://bit.ly/2L0gcxQ>. Accessed: May 15, 2018

²⁷ Kaiser Family Foundation: “Summary of Recent and Proposed Changes to Medicare Prescription Drug Coverage and Reimbursement.” Available at: <https://kaiserf.am/2ETkF5s>. Accessed: May 15, 2018.

and Part D. There are several other steps that CMS can take to develop a sustainable market for generic and biosimilar medicines

Prioritize the Placement of Biosimilars and Generics on Medicare Advantage and Part D Formularies and Examine the Impact on Cost-Sharing

CMS should consider how to encourage utilization of lower-priced generic and biosimilars, including through Medicare Advantage and Part D formulary design.

Increasingly, Medicare Part D plans are putting generic drugs into higher formulary tiers to compensate for escalating brand-name drug prices. A recent report found that in 2011, 71 percent of generic drugs were placed on tier 1 (representing the lowest possible cost sharing for patients). By 2015, only 19 percent of generic drugs were on tier 1; almost half (46 percent) of all generic drugs were on tier 2 and the remaining 35 percent were on tier 3 or higher. This led to a \$6.2 billion increase in additional out of pocket spend by Medicare beneficiaries, *even though prices for those drugs declined*. One thing that didn't change was the market price for the generic drugs that were shifted to higher cost-sharing tiers.²⁸

In addition, for biosimilars, there have been examples of health plans requiring patients to “fail first” on a reference product before they can access the biosimilar.²⁹ This is despite the fact that FDA's licensure of a biosimilar means that the agency has deemed that there is no meaningful clinical difference between the biosimilar and the reference product. As a scientific matter, it would be clinically irresponsible for a provider to prescribe a patient a biosimilar once they have failed on the reference product, given that the biosimilar has the same active ingredient and mode of action as the reference product. Thus, access to a lower priced biosimilar is effectively blocked. This type of rebate-driven utilization management furthers no medical or policy goal and only serves to further deter market entry of lower priced competition. Ensuring lower cost-sharing for biosimilars and generics prioritizing biosimilar and generic formulary placement could help expand patient access to needed medicines.

CMS should review Medicare Advantage and Part D formulary placement and consider tools to ensure lower-priced products can more fairly compete on price and clinical quality.

CMS Should Review Part D Plan Rating Methodology Regarding Management of High-Cost Drugs

The pharmaceutical market that existed when the Medicare Modernization Act of 2003 (MMA) was drafted and passed is dramatically different from the pharmaceutical market that exists today. Studies have shown that spending on high-cost drugs tripled between 2003 and 2014, while the use of generic drugs has continued to increase and save trillions for taxpayers while ensuring patient access. It is critical that CMS continually evaluate the structure of Part D Prescription Drug Plans to make sure they fit the contours of the pharmaceutical market as it exists today. As previously noted, a recent Avalere analysis found that since 2011, generic drugs more often share the same tier as nonpreferred brands.

²⁸ Avalere Health: “Generic Drugs in Medicare Part D: Trends in Tier Structure and Placement.” May 22, 2018). Available at: <https://bit.ly/2kx8cIP>. Accessed: July 5, 2018.

AAM supports the use of incentives for Part D plan sponsors to manage the utilization of high-cost drugs in a clinically appropriate manner. The RFI poses a hypothetical update to the methodology for calculating Drug Plan Customer Service star ratings for Part D plans that are appropriately managing utilization of high-cost drugs. We note that MedPAC has previously raised concerns that the current structure of the Part D benefit may actually provide incentives for plans to move beneficiaries into the catastrophic coverage portion of the benefit quickly, which increases costs the Medicare program itself.³⁰ To that end, program changes that encourage the use of clinically appropriate options that have the lowest list price should be considered.

However, there are some conditions for which all therapeutic options are high cost. Any changes that CMS considers to Part D should be narrowly tailored not to block access to high-cost clinically appropriate products. Generic drugs and biosimilars reduce costs for both Medicare beneficiaries and taxpayers and Part D plan sponsors should be rewarded for designing benefits that encourage their use. This is particularly important as complex generic and biosimilar medicines face brand drug attempts to block market access through restrictive contracting arrangements.

One way to align Part D plan incentives with low- cost clinically appropriate options is to evaluate ease of patient access to biosimilar or generic medicines with lower list prices. Specifically, by understanding the difference in formulary treatment of biologic and biosimilar products, and brand and reference generics, CMS could undertake policies that better ensure beneficiaries are not being steered away from clinically appropriate options that will cost them less over the period of the plan year. This could encourage plans to provide preferential, or exclusive, formulary treatment for generic and biosimilar drugs with lower list prices – resulting in greater utilization of drugs with lower list prices and savings for the Medicare program and Medicare beneficiaries.

CMS Should Review the Medicare Part D Risk Adjustment Formula’s Impact on Use of Lower-Priced Medicines

Currently Part D does not have a mechanism for countering drug rebate agreements and related incentives that push plans to favor brand biologic drugs over biosimilars in their product formularies. CMS could consider options to provide a counterweight to current financial incentives that move beneficiaries more quickly to the catastrophic phase — shifting risk from plans onto the Medicare program for much of the plan year — and to rebates that skew the prescription drug market.

One option would be to examine the risk adjustment guidelines and the ways in which they affect utilization of generic or biosimilar medicines with reference products exceeding the CMS specialty drug threshold.

CMS Should Ensure Timely Formulary Review of New Biosimilar Products

Part D plan sponsors are required to review new FDA-approved drug products within 90 days of the product’s release onto the market, and to decide on coverage for each drug within 180 days of the drug’s release onto the market. CMS should ensure these rules are being applied to biosimilar therapies,

³⁰ Medicare Payment Advisory Commission. March 2018 Report to Congress, Chapter 14: The Medicare Part D Prescription Drug Program Status Report.

in addition to small-molecule products. CMS should ensure these guidelines and expectations are met when biosimilars also become available.

Considerations for Reforms to Medicare Part B

The RFI solicits feedback and input on several specific Part B reforms. As CMS considers proposals such as shifting products from Part B to D or the proposed reintroduction of the Competitive Acquisition Program (CAP), it is important to take into account the risk of inviting greater abuse of exclusionary contracts and rebate traps, as discussed above. Biologics constitute the majority of Part B drug costs, and significant savings can be achieved if appropriate systemic levers are in place to maximize the potential of biosimilar medicines. Therefore, it is important to ensure appropriate incentives for biosimilar utilization in Part B.

Coverage Transition of Some Part B Drugs to Part D Requires Further Study

The idea of transitioning coverage of some prescription drugs from Medicare Part B to Medicare Part D has been considered and studied for more than 10 years. A 2010 report commissioned by CMS found that transitioning coverage of some prescription drugs from Medicare Part B to Medicare Part D could have potentially complex results.³¹ On average, beneficiary out-of-pocket spending increased when a drug was transitioned from Medicare Part B to Medicare Part D. However, for beneficiaries that were in the catastrophic coverage portion of the Part D benefit, out-of-pocket costs decreased. Overall program costs for Medicare were projected to decrease less than 1 percent, resulting in minimal program savings while risking uncertain effects on beneficiary out-of-pocket costs.³²

According to data compiled by the Medicare Payment Advisory Commission (MedPAC), the majority of Medicare beneficiaries (~86 percent) have access to some sort of supplemental coverage that helps to defray cost-sharing for services covered under Parts A and B.³³ However, supplemental coverage cannot be applied toward Medicare Part D benefits. Additionally, as the RFI notes, about 27 percent of Medicare beneficiaries do not currently have Part D benefits. That means a sizeable portion of beneficiaries could be subject to changes in cost-sharing or coverage if changes to the existing benefit structure were changed or products would still have to be available under traditional Part B channels, thus adding to provider administrative burden. We encourage CMS to undertake a similar analysis prior to formalizing any policy to transition coverage of a prescription drug from one Medicare benefit to another.

Moreover, while the idea of extending the negotiating power of plans and PBMs in the Part D program to medications currently covered by the Part B program may seem straightforward on its face, some of the more complex products and biologic medications commonly administered through the Part B program may not be subject to the same types of market forces as traditional medications dispensed through Medicare Part D. Moving management and distribution of these products from Part B to Part D

³¹ CMS. "Estimating the Effects of Consolidating Drugs under Part D or Part B." Available at: <https://go.cms.gov/2zcfmME>. Accessed: July 5, 2018.

³² *Id. Id.*

³³ MedPAC: "June 2017 DataBook Healthcare Spending and the Medicare Program." Available at: <https://bit.ly/2tWEHoL>. Accessed: June 12, 2018.

may not result in the desired cost savings. The coverage of complex products and biologic medications in the Part B program rather than Part D reflects the fundamental differences in the market for these medications:

- Physician-administered products currently covered in the Medicare Part B program may have fewer competitors (both generic and brand) in each therapeutic area, making these medications less suited for the competitive negotiating structure that is one of the hallmarks of Part D plans.
- Any consideration of moving medications from Part B to D should include strong incentives and guidance to promote uptake of biosimilar products, including immediate coding of biosimilar products (discussed later in this response) and requiring biosimilars to have equal or more favorable cost sharing than the reference product.
- Even in the Part D program, where commoditized generics have shown high levels of uptake, savings to both patients and the federal government through use of generics may have been dampened due to the significant rebating offered by brand manufacturers to garner advantageous tier placement. Products with fewer therapeutic alternatives and multi-source competitors may be subject to even more competitive market distortions by branded biologic manufacturers that are incentivized to protect market share and discourage entry of cheaper biosimilar products.

As discussed above, originator biologics have aggressively pursued advantageous formulary placement in Part D through deep rebates. These tactics have dampened uptake and coverage of off-patent competition, threatening manufacturer investment in this fledgling industry. AAM and the Biosimilars Council are concerned that moving physician-administered medications from Part B to Part D may result in higher patient out-of-pocket costs, while limiting patient choice and access as brand manufacturers offer significant rebates in exchange for advantageous formulary placement without passing savings on to patients. Other considerations include operational and logistical challenges associated with procuring and billing physician-administered medications when they are covered under a patient's pharmacy benefit. Therapy could also be delayed if there are issues with the drug being out of stock at a retail pharmacy, or delayed in shipping from a specialty pharmacy. Any change in benefit structure should appropriately address these issues.

Before moving medications from Part B to Part D, reforms to the Part B program should be examined, including incentives to strengthen the biosimilar market by both increasing uptake of existing biosimilar products and supporting additional development of new biosimilar products.

Implementation of a Competitive Acquisition Program (CAP), or Other System, for Part B Drugs Must Take into Account Unique Attributes of Generic and Biosimilar Markets

While the lack of details makes it difficult to provide focused comments, AAM and the Biosimilars Council encourage CMS to consider the unique attributes of the generic and biosimilar markets to prevent any unintended consequences from any alternative acquisition program offered to physicians. In almost every competitive market, producers compete to sell products at the lowest price. However, with physician-administered drugs there is little incentive for manufacturers to compete on price. Payment to physicians for the drugs themselves are tied to the sales price of the drug, and the add-on

payment intended to compensate physicians for the costs of acquiring and storing the product are based on a percentage of the drug's price. This creates an environment where there is little competitive pressure for manufacturers to leverage lower prices to secure market share.

We encourage CMS to consider whether a CAP or CAP-like program would meaningfully address some of the underlying problems of the current payment system. Any system that encourages a race to the bottom among manufacturers of lower-priced products, but does nothing to incent physicians or patients to choose generics or biosimilars over reference products, will not lead to sustainable off-patent competition, particularly for high-investment products like biosimilars and complex generics. It is incumbent upon the Medicare program to assure a thriving generic and biosimilar market and not institute payment policies that could discourage market entry.

If designed well, it is possible that a CAP-like program could disrupt current incentives for the utilization of drugs with higher list prices and support an increase in competition.

We encourage HHS to consider the following as it considers updating the CAP program:

- Placing competitive price pressure on products costing Part B the most, without compromising patient access, is achieved only with a robust Part B biosimilar market.
- Allowing a CAP-like system to use a utilization management tool or access benchmark that favors biosimilar products. While we understand the Administration's interest in allowing utilization management within Part B, we encourage HHS to consider and ensure the appropriate alignment of roles and expertise. For instance, it is not clear that vendors capable of the purchasing role in a CAP-like system are the same entities qualified to develop and apply utilization management tools. Likewise, if CMS introduces both a CAP-like acquisition system and utilization management tools, it should ensure that evaluation of the two remain separate in order to assess the impact of acquisition and utilization management appropriately.
- CMS should contract with third-party vendors to operationalize the program. To ensure a more competitive market among vendors, vendors should not share common financial interests (outside of both benefiting from shared savings) with plans or providers. Incentives for participation from multiple vendors could also add a competitive element that could reduce costs and increase provider satisfaction.

CMS Should Award Biosimilars HCPCS Billing Codes at Launch

AAM commends CMS for its actions to support a competitive biosimilars market. This includes a policy change to create separate Healthcare Common Procedure Code Set (HCPCS) billing codes to biosimilars with the same reference product, beginning this year. We believe that separate codes and payment rates for biosimilars is the best way to ensure patient access and encourage manufacturers to invest in developing biosimilar products. Each biosimilar that has not also been determined to be interchangeable (i.e., non-interchangeable) will be paid at a uniquely-calculated payment rate based on that biosimilar's ASP.

A recent study also found that this policy is expected to save the Medicare program \$11.4 billion over 10 years by fostering biosimilar competition in the market.³⁴ Therefore, we support CMS maintaining current agency policy with respect to coding for biosimilars. We also look forward to working with the agency when the first “interchangeable” biosimilar is approved by the FDA to determine appropriate coding at that point.

One additional step that CMS could make would be to award a unique, permanent HCPCS code to biosimilars at launch. This change would reduce administrative burdens for providers that could discourage biosimilar adoption, and also reduce the likelihood that inappropriate payments will be made. Currently, when a new product is approved providers must use either a miscellaneous HCPCS code (J3490 for drugs or J3590 for biologics) or a temporary “Q-code.” Use of miscellaneous codes trigger manual review by claims processors and requires providers to provide additional documentation. Manual review also introduces the possibility of inaccurate payment rates. While Q-codes are unique to specific products, they are still temporary and not all payors recognize them in billing systems. With both miscellaneous codes and Q-codes, providers and payors have to update coding practices and billing systems in order to accommodate the permanent “J code” once assigned.

Due to the structure of the HCPCS coding cycle, a product could be on the market for up to 21 months before receiving a permanent code. This also requires providers continue to update internal billing practices to accommodate the changes in codes, which could prove to be a deterrent to providers to quickly switching to biosimilars. In contrast, established originator products are likely to already have a permanent HCPCS code. With a permanent HCPCS code, payors can set a reimbursement rate and process claims electronically and without manual review.

AAM and the Biosimilars Council are concerned that this delay in receiving a permanent code could deter providers from adopting of biosimilars. Slow adoption of products is not only difficult for the manufacturer of the product itself, but could also dissuade other manufacturers from investing in the development of biosimilars. This problem could be solved by issuing HCPCS codes (e.g., J-codes) for new biosimilar products on a quarterly basis, which is how frequently the master HCPCS file is updated to accommodate other changes. While the Medicare OPPS issues temporary “C” codes on a quarterly basis for pass-through products, and biosimilars are eligible for pass-through, C-codes are not typically used in physician offices or other settings of care. Issuing a permanent HCPCS code in the same quarter in which a new biosimilar launches will reduce provider burden, improve payment accuracy and help new biosimilars thrive in the market. In addition, to create a consistent coding structure, if there are any currently-marketed biosimilars that do not have unique HCPCS codes, they should have unique permanent HCPCS codes assigned.

CMS Should Continue Pass-Through Status for Biosimilars

Biologic medicines are often administered at various sites of care. As a result, there are multiple payment systems that biosimilar manufacturers will rely on to ensure patients have access to their medicines, including the distinct systems set up by multiple federal payors (i.e., Medicaid and Medicare

³⁴ The Moran Company: “Discrete Codes for Biosimilars: Fiscal Implications.” Available at: <https://bit.ly/2xf1M95>. Accessed: May 15, 2018.

programs). For the numerous products traditionally administered in physicians' offices or hospital settings, Medicare Part B plays an important role in driving provider adoption.

As federal agencies have been working to create new policies to incent biosimilar utilization, some policymakers have sought changes to outpatient reimbursement that would disadvantage biosimilar manufacturers when compared to their branded counterparts. To encourage the use of innovative products and help ensure they would be available to Medicare patients, Congress in 1997 established "transitional" pass-through reimbursement payments for new medical devices, drugs and biologics in the Medicare Part B program.³⁵ These payments are designed to support the introduction of new products, by providing reliable reimbursement and assist in provider education of new products, as well as provide time for Medicare claims records to incorporate utilization of these new products and for standard payment rates to be updated accordingly.

AAM and the Biosimilars Council agree with CMS's existing policy to deem each biosimilar product eligible for transitional pass-through payments. Biosimilars that meet the statutory criteria established under section 1833(t)(6)(A)(iv) of the Social Security Act, and for which CMS has approved an application for transitional pass-through status, should continue to be granted the additional payments. This will give CMS adequate time to collect cost information and appropriately adjust the payments for the related Ambulatory Payment Classifications (APC).

Considerations for Other Reforms in Medicare Part D

CMS Should Carefully Consider Policies Granting Part D Plan Sponsors Flexibility in Reacting to So-Called "Sole-Source Generics"

The RFI notes that HHS may allow Part D plans to adjust formulary or benefit design during the benefit year if necessary to address a price increase for a "sole source generic drug."

It is first important to note that "sole-source generic" is not a legal or regulatory definition. Any policy based on this premise should specifically reference the products to which it would apply. Over the past several years, there have been newsworthy examples of sole-source, off-patent products that were approved as branded drugs and lacked generic alternatives and that were subject to astronomical price increases. For instance, Turing Pharmaceuticals acquired exclusive rights to Daraprim (pyrimethamine) and increased the list price of a course of therapy from \$1,130 to \$63,000³⁶, threatening access for patients with HIV. This price increase was possible only because Turing Pharmaceuticals was the sole manufacturer of pyrimethamine, even though the molecule was approved by the FDA in 1953. This behavior has also been witnessed in off-patent, sole-source products such as Isuprel, Nitropress and HP Acthar.

Each of these products was approved as a brand drug. Each has seen its patent protection expire without entry of generic alternatives. Each of these sole-source branded drugs, no longer patent-protected but having no generic competition, has been able to utilize brand contracting tactics

³⁵ Public Law No: 106-113. Available at: <https://bit.ly/2jX2RtS>. Accessed: May 15, 2018.

³⁶ LA Times. "A huge spike in the cost of an old drug reignites the pharma pricing debate." September 21, 2015. Available at: <https://lat.ms/1FdqMwN>. Accessed: July 5, 2018.

(including use of specialty pharmacies to increase reimbursement and limited distribution to prevent development of generic alternatives) to increase the price while shielding itself from competition. Lacking the competition from a second or third manufacturer, manufacturers of these drugs felt free to take price increases.

CMS should carefully consider policies that would grant Part D plan sponsors additional flexibility in reacting to these types of market dynamics. The agency should ensure that the policy is narrowly tailored to apply only to instances in which a true sole-source product, whether patent-protected or not, is subject to a price increase. In a multiple-source market, which describes the majority of what many consider the “generic” market, the presence of multiple manufacturers ensures a competitive balance that discourages irresponsible price hikes that threaten patient access.

Moreover, it is not clear what “flexibility” is envisioned by CMS. AAM notes that some have suggested greater reliance of compounded drugs as an alternative to price increases, but commercial-scale drug compounding is outside of the safeguards established by Congress in 2013.³⁷ These protections, established in the wake of patient deaths across multiple states, are critically necessary to the public health.

CMS Should Ensure that Changes to Classes of Clinical Concern Do Not Encourage Rebate Gamesmanship that Undermines Patient Access to Lower-Cost Products

The RFI appears to suggest adjusting coverage requirements for the six classes of clinical concern (“protected classes”) – an area in which the impact of generic drugs is notable. According to a recent Pew Charitable Trusts analysis, generic substitution rates for the protected classes are higher than other, non-protected classes (92 percent and 84 percent, respectively).³⁸ According to MedPAC, prices for protected-class drugs have increased at the same rate as all Part D drugs, and cumulative prices actually decreased by 16 percent between 2006 and 2013 due to generic substitution.³⁹

For five of the six protected classes, generic drugs have helped plan sponsors hold down costs and minimize cost increases. CMS should be sure to study the impact of such a policy before moving forward with a proposal to change coverage requirements. In particular, CMS should ensure that removal of these requirements does not open the door to new brand drug rebate gamesmanship that undermines patient access to lower-priced alternatives.

CMS Should Structure Any Drug Price Transparency Efforts to Take Net Financial Impact into Account

The RFI asks for input on how price transparency in Medicare and Medicaid could be improved, including the potential to highlight products that have not taken price increases above a certain threshold over a specified period. It is critical for CMS to consider that in many cases, drug price

³⁷ Public Law No: 113-54.

³⁸ Pew Charitable Trusts. “Policy Proposal: Revising Medicare’s Protected Classes Policy.” March 2018. Available at: <https://bit.ly/2DImLWQ>. Accessed: July 5, 2018

³⁹ MedPAC. “The Medicare prescription drug program (Part D): Status report” March 2017. Available at: <https://bit.ly/2NsTxeX>. Accessed: July 5, 2018.

increases should be considered within the frame of their overall impact to program costs, not merely a percentage price increase.

Financial impact, not just percentage changes, should be prioritized when adopting new policies. Price increases for low-cost generic drugs do not have the same impact to costs in federal health programs as an increase on a higher-priced branded product. A smaller increase in the price of a branded product often has a greater impact on costs than a larger price increase for a generic.

For example, if the price of the branded product Humira is raised 22 percent, as it was between 2014 and 2015⁴⁰, the total cost for Medicare (excluding volume growth) would be \$270 million, or about \$124 million per 10 percent increase. However, raising the price of phenazopyridine HCl by 121 percent would cost Medicare \$4 million, or \$383,000 per 10 percent increase. In this example, a penalty that would be triggered by a hypothetical 25 percent increase in year-to-year list prices would penalize the manufacturers of phenazopyridine HCl, but would not penalize the manufacturer of Humira, even though the price increase to Humira much more dramatically affected program spending.

This is why, for example, when exploring a Medicare inflation rebate, MedPAC included an exemption for low-cost drugs (<\$100), noting that price increases for these low-cost products represent a small increase in actual dollar amounts.⁴¹

CMS Should Prohibit Part D Plans from Preventing Pharmacists from Disclosing Cost Information

The RFI notes that HHS may prohibit Part D plan contracts from preventing pharmacists from telling patients when they could pay less out of pocket by not using their insurance. AAM opposes contracts that prohibit a pharmacist from discussing lower out-of-pocket cost options with beneficiaries. Medicare beneficiaries should not be subject to higher out-of-pocket costs when products with lower list prices exist.

CMS Should Require Part D Plans to Provide Certain Cost Information in Explanation of Benefit (EOB) Statements

AAM supports policies that encourage beneficiaries and prescribers to discuss lower-cost therapeutic options, whether that is through educational material provided to prescribers and pharmacists or through information provided to beneficiaries via their EOB. Beneficiaries can only be empowered to reduce out-of-pocket expenses when they understand what options, if any, are available to them. The EOB, physician office and the pharmacy at point-of-sale all offer opportunities to provide this information so the patient can open a dialogue with their physician and pharmacist about making the most clinically and financially appropriate decision. Providing this information in three separate venues also reduces the burden from being placed on a single stakeholder and offers the opportunity to consider options in an environment that suits the beneficiary best (home, physician office or pharmacy).

⁴⁰ Democratic Staff Report: Committee on Oversight and Government Reform, U.S. House of Representatives. "Skyrocketing Drug Prices: Year One of the Trump Administration." March 2018. Available at: <https://bit.ly/2IWSpgi>. Accessed: July 5, 2018.

⁴¹ MedPAC June 2017 Report to the Congress Available at: <https://bit.ly/2JOOPI4>. Accessed: July 5 2018.

CMS Should Continue Efforts to Increase Generic Drug Adoption Among Low-Income Medicare Beneficiaries

MedPAC has estimated that “nearly 70 percent of Medicare’s total spending for Part D plans was on behalf of the 30 percent of Part D enrollees who receive the LIS.”⁴² Compared with other Part D beneficiaries, Low-Income Subsidy (LIS) enrollees not only fill more prescriptions but fill more expensive prescriptions.

While it is true that LIS beneficiaries tend to have greater health needs requiring more prescriptions, LIS beneficiaries typically utilize more expensive brand-name drugs even when lower-cost options such as biosimilars and generics are available. This phenomenon seems to occur, at least in part, because Medicare Part D plans have limited ability to modify cost sharing for LIS enrollees. In 2017, the prescribed cost sharing for full benefit dual eligible LIS enrollees is \$8.25 for a one-month supply of a branded drug and \$3.30 for a one-month supply of a generic drug. We surmise the \$4.95 differential is not economically significant enough to encourage LIS enrollees to elect to utilize a generic over a brand.

This is evidenced by the significant differences in generic dispensing rates between the LIS population versus all Medicare Part D beneficiaries. For instance, a MedPAC analysis of Medicare Part D Prescription Drug Event data revealed for the antipsychotic therapeutic drug class that only 58 percent of total LIS enrollees utilized generics versus 78 percent of all Medicare Part D enrollees using an antipsychotic.⁴³ This difference in generic utilization appears across multiple therapeutic classes when generic equivalents are available and represents a missed opportunity for patients and the federal government.

Estimates from the Office of Management and Budget (OMB) and the Congressional Budget Office (CBO) suggest that addressing this issue could reduce Medicare spending by anywhere from \$9 billion to \$18 billion over 10 years.⁴⁴

MedPAC has recommended changes to Medicare Part D cost-sharing policies for LIS enrollees to improve generic utilization. Specifically, MedPAC recommended that Congress:

- “modify copayments for Medicare beneficiaries with incomes at or below 135 percent of poverty to encourage the use of generic drugs, preferred multisource drugs, or biosimilars when available in selected therapeutic classes;
- direct the Secretary to reduce or eliminate cost-sharing for generic drugs, preferred multisource drugs, and biosimilars; and
- direct the Secretary to determine appropriate therapeutic classifications for the purposes of implementing this policy and review the therapeutic classes at least every two years.”⁴⁵

⁴² MedPAC. June 2016 Report to the Congress. Available at: <https://bit.ly/2tXyQzP>. Accessed: July 5 2018..

⁴³ *Id.*

⁴⁴ U.S. Department of Health and Human Services. Fiscal Year 2016 Budget in Brief. Available at: <https://bit.ly/2zdaoid>. Accessed: July 5, 2018

⁴⁵ MedPAC June 2016 Report to the Congress. Available at: <https://bit.ly/2tXyQzP>. Accessed: July 5 2018

AAM commends HHS for proposing to lower cost sharing for LIS enrollees using generics and biosimilars, and we encourage HHS to support legislation to modify the Medicare Part D LIS copayment structure to achieve this goal that has been endorsed by a range of nonpartisan experts, including MedPAC, the Bipartisan Policy Center and Simpson-Bowles Moment of Truth Project.

Government Policies Can Contribute to the Underpricing of Generic Drugs

The RFI solicits comments on whether government programs are causing underpricing of generic drugs, and thereby reducing long-term competition. Several such policy miscues have contributed to challenges that today threaten a stable supply of low-price, commoditized generic medicines.

HHS Should Support Congressional Withdrawal of Medicaid Generic Drug Rebates that Threaten the Viability of Low-Cost Generics

In 2015, Congress created a new inflation-based penalty in the Medicaid program for generics as part of the Bipartisan Budget Act⁴⁶. Generic manufacturers are now subject to additional rebates for products *even in the absence of changes in the actual price* of the product. This flawed application of a brand drug scheme that fails to recognize the significant volatility in generic prices is a direct result of policymakers conflating what transpires in the branded drug market with what occurs in a commoditized market with multiple competitors.

Consequently, manufacturers of affordable generic medicines are now paying millions of dollars in “penalties” on products that have not been subject to a price increase. In many instances, changes in customer mix from one quarter to another have triggered penalties solely due to purchasers getting lower discounts on smaller volume orders – a normal occurrence in a competitive market. These changes do not necessarily reflect any new price being set by the manufacturer, but may merely reflect new purchasing patterns.

These unpredictable, onerous penalties on often low-margin medicines create significant risk for manufacturers that would consider entering these markets, and make it more challenging for manufacturers to continue participating in those markets, negatively affecting patient access. A recent analysis concluded that the penalty would “increase uncertainty, reduce revenues, encourage manufacturers to exit the market, and discourage the entry of new manufacturers. The predictable effect of discouraging entry into competitive markets is that product availability will be hampered: shortages will be more likely, and the market forces that lead prices to fall will be dampened.”⁴⁷

Ironically, the analysis also concluded that the penalty “will not only have little effect on generic prices, but it will also have the unanticipated and unintended consequence of increasing the likelihood of shortages for generic medicines.”⁴⁸

⁴⁶ Public Law No: 114-74.

⁴⁷ Manning and Selck, “Penalizing Generic Drugs with the CPI Rebate will Reduce Competition and Increase the Likelihood of Drug Shortages,” September 2017. <https://www.accessiblemeds.org/sites/default/files/2017-09/Bates-White-White-Paper-Report-CPI-Penalty-09-12-2017.pdf>

⁴⁸ *Id.*

We urge HHS to work with Congress to mitigate the harmful effects of this policy and amend the policy to focus on metrics that are within the control of generic drug manufacturers.

Removal of the 100 Percent Maximum Rebate Amount for Generic Drugs Could Harm Patient Access

The RFI notes concern that limiting manufacturer rebates on brand and generic drugs in the Medicaid program to 100 percent of calculated average manufacturer price (AMP) may allow for price increases to be taken without manufacturers facing the full effect of the price inflationary penalty established by Congress. The RFI requests feedback on when this is a valid constraint and what impact removing the cap might have.

As previously noted, because of the new inflation-based penalty in the Medicaid program for generics created in 2015, generic manufacturers are now paying additional, inflation-penalty rebates for products *for which they did not take a price increase.*

Because generic manufacturers face an inflation-based penalty that can be triggered by factors entirely outside of their control, it is critical that policymakers maintain the limitation that such rebates may not exceed 100 percent of AMP. Failure to reform this proposal to reflect factors within a manufacturer's control already threatens continued sustainability of certain generic drug markets, but allowing such payments to exceed the manufacturer price could quickly drive generic manufacturers out of low-margin markets – harming patient access and potentially creating shortages.

HHS Should Ensure that Government Payment Policies Do Not Create or Exacerbate Drug Shortages

In addition, AAM is concerned that current payment policies for physician-administered drugs covered under Medicare Part B lead to underpricing that can cause manufacturers of generic injectables to leave the market, or can discourage market entry in the first place. This can have a direct impact on the issue of drug shortages. FDA Commissioner Gottlieb referenced this market dynamic in 2011 testimony before the Senate Finance Committee:

When demand for these drugs increases, or more importantly, when the cost of developing these medicines rises, manufacturers can't take and sustain price increases to make up for these market changes. This makes it hard for manufacturers to make the long-term (2-7 year) investments needed to stand up new facilities or upgrade existing facilities to produce more supply.⁴⁹

Dr. Gottlieb went on to cite current Medicare Part B payment policy as the source of these issues. Currently, CMS uses a volume-weighted average to determine pricing for generic injectables. This creates a race to the bottom where manufacturers are incentivized to continually undercut each other on price. The short-term gain realized from low prices can have long-term consequences as manufacturers can be pushed from the market or discouraged from entering markets in the first place.

⁴⁹ Scott Gottlieb, MD, Statement before the Senate Finance Committee (December 7, 2011). Available online: <https://www.finance.senate.gov/imo/media/doc/Gottlieb%20Testimony1.pdf>

Purchaser Consolidation Poses Significant Challenges to a Sustainable Market & Supply of Low-Cost Generic Medicines for Patients

Lastly, increasing consolidation among pharmaceutical purchasers represents an increasing threat to maintaining a stable supply of generic medicines. In fact, today roughly 200 generic companies compete to sell to three purchasing groups that collectively control 90 percent of the market.⁵⁰

This often leaves generic companies without contracts, and requires generic companies to suspend marketing their drugs until such contracts become available again. These challenges are particularly acute in low-margin or low-volume markets. They play an important role in companies' decisions to market FDA-approved generic drugs or even to submit an abbreviated new drug application (ANDA).

As these purchasing consortia move more and more toward single-source contracts for generic drugs, it creates a dynamic where it is possible that no more than three generic manufacturers may be able to market any given product successfully. Notwithstanding the economic principle that more suppliers of a good or service creates lower prices for consumers, it is unclear that the new imbalance between approximately 200 generic competitors and a handful of purchasers is sustainable. This undermines future competitive success in the generic market as generic drug manufacturers are forced to maximize economies of scale and consolidate. In fact, it poses a number of dangers — including of critical drug shortages.

Excessive consolidation of purchasing power among the consortia presents the risk of exerting undue market power over generic suppliers, driving wholesale prices below marginal costs and reducing output. In turn, this may lead to producers exiting the market, reduction of output, ceasing production of unprofitable drugs and shortages of critical medicines. Such consolidation also poses a danger of stabilizing and elevating downstream costs to end users and payors in the market.

Alternative, Value-Based Payment Mechanisms Should be Designed to Avoid Reducing Incentives for Manufacturers to Enter Aggressively-Priced Markets

The Hatch-Waxman Act, as well as the BPCIA, create a carefully balanced framework designed to incentivize pharmaceutical manufacturers for both innovation and price competition. Any value-based tools that CMS implements must not undermine this balance. Specifically, products that function in well-established multi-source environments must be allowed to continue to operate in an unencumbered market, while products in newly developing markets must be allowed the opportunity to compete with their reference products in competitive pricing markets without comparisons to other options they were never designed to compete against.

For more than 30 years, generic manufacturers have successfully fostered a competitive marketplace that has expanded patient access to life-saving medication while helping to reduce health care costs. Biosimilars, a market that is currently in its infancy, hold the promise of reducing spending and expanding beneficiary access to high-cost biologics. It is imperative that CMS maintains this market dynamic with any new payment policies, and not reduce incentives for manufacturers to develop lower-

⁵⁰ Fein, A. The 2016-2017 Economic Report on Pharmaceutical Wholesalers and Specialty Distributors, September 2016.

cost alternatives. Any short-term savings resulting from such comparison would over the long term reduce competitive options (and greater savings) and access to important, affordable medical alternatives.

Generics and biosimilars are developed under the presumption that once approved, they will compete with their reference brand products. By creating other points of reference in situations in which there are multiple therapeutic alternatives, this framework risks reducing the incentives for manufacturers to enter aggressively priced markets. This is particularly concerning for biosimilar manufacturers who face significant research and development costs associated with bringing new products to market.

CMS Should Ensure that Value-Based Payment Arrangements Do Not Harm Utilization of Lower-Priced Medicines

It is critical that CMS maintain the incentive for providers to choose the lower-cost therapeutic option that is clinically appropriate. Generic and biosimilar competition is inherently high-value based on a direct comparison of cost and outcomes as compared to the higher-priced originator medicine. CMS should ensure that any value-based strategies include a focus on quantifiably reducing out-of-pocket costs for patients as well as the overall costs to the program.

We ask CMS to keep in mind the following principles when considering the design of any value-based payment model:

- Consider the effects of sequestration on any proposed payment limit;
- Continue to base the add-on percentage for any biosimilar included in a model on the ASP of the reference product;
- Continue current policy to assign non-interchangeable biosimilars unique HCPCS codes and ASP calculations;
- Any evaluation of value-based purchasing tools must consider the total cost of patient care outside of pharmaceutical costs;
- Any value-based model must maintain direct, price-based competition between reference products and their lower-cost alternatives;
- Value-based purchasing tools should be applied to biosimilars only when an applicable reference product is also subject to the tool;
- Value-based purchasing tool implementation should occur in a deliberate fashion and allow for adequate stakeholder input; and
- The scope of any proposed demonstration should best create a model that will truly test innovative payment models.

AAM Supports Continued Improvement of the Generic and Biosimilar Drug Review Process at FDA

There are opportunities for HHS/FDA to use their existing statutory authority to generate greater generic and biosimilar competition through actions that deter anti-competitive brand drug tactics, streamline and expedite the approval/licensure process, and increase transparency into Agency actions and decisions. This includes steps that can be taken under existing authority, as well as support for bipartisan legislation that would support greater generic and biosimilar competition.

HHS/FDA Should Support Congressional Action to End Anticompetitive and Abusive Restricted Access Programs that Delay Generic and Biosimilar Development

As HHS and FDA officials have noted, a significant barrier to competition is restrictions by brand manufacturers who block the sale of reference product for generic and biosimilar development. This includes simple refusals to sell reference product as well the abuse of Risk Evaluation and Mitigation Strategies (REMS) to delay and prevent generic and biosimilar development.⁵¹

A fundamental premise since 1984 under Hatch-Waxman and since 2010 under the BPCIA is that generic and biosimilar manufacturers must test their product in comparison to the reference product to demonstrate “sameness” for generics and “biosimilarity” for biosimilars. If purchase of the reference product is blocked by a brand manufacturer, then there is no opportunity to develop affordable medicines when exclusivity expires. This practice emerged in the last 10 years and has been highly profitable for brand companies as their peak sales (and profits) occur at the end of the life cycle and this has the effect of extending exclusivity well beyond appropriate regulatory protection and patent life. This has a major impact on drug pricing and if not stopped, will interfere with continued generic and future biosimilar savings.

In addition, brand companies are using REMS to block sales and restrict access to samples necessary for testing and approval of generic and biosimilar products as well. Congress established the REMS authority in 2007 to further assure the safety of drugs.⁵² Pursuant to a REMS, the FDA can require a sponsor to implement a broad range of risk-mitigation tools to ensure that the benefits of a drug outweigh its risks to patients. Such tools include medication guides, communication plans and other distribution and use restrictions, called “elements to assure safe use,” or ETASU. A REMS with ETASU may impose strict requirements on who may prescribe or dispense the drug, where the drug may be dispensed and on patients to whom the drug may be prescribed or dispensed.⁵³ If a brand drug is subject to a REMS with ETASU, generic and biosimilar versions are subject to the same distribution and use restrictions and, unless waived by FDA, must utilize a shared system (SSRS) with the brand drug.⁵⁴

At the time of enactment, Congress acknowledged there was the potential for the REMS tools to be gamed, and outright abused, by branded manufacturers to extend patent protection and delay robust

⁵¹ Senate Finance Committee Full Committee Hearing on Prescription Drug Affordability and Innovation: Addressing Challenges in Today’s Market. June 26, 2018.

⁵² See 21 U.S.C. § 355-1.

⁵³ *Id.* § 355-1(f)(3).

⁵⁴ *Id.* § 355-1(i)(1)(B).

generic competition.⁵⁵ Congress specifically prohibited brand manufacturers from using any element of a REMS to “block or delay” generic competition or to interfere with adoption of an SSRS.⁵⁶ Contrary to the intent of Congress, however, brand companies routinely use REMS and other restricted access strategies to impede generic and now biosimilar competition. They do so with little fear of adverse regulatory action by FDA or other governmental authorities.

REMS and restricted access abuses generally fit into two categories, each presenting an opportunity for stronger, more effective administration and oversight by FDA. First, brand companies use their REMS with ETASU or self-imposed restricted access programs to deny generic companies access to the brand company reference listed drug (RLD) samples needed to support ANDAs. Second, brand companies use the requirement for an SSRS⁵⁷ to forestall approval of generic drugs by delaying or refusing to agree to an SSRS. Both strategies are discussed in more detail below.

These abuses are significant. According to a recent study,⁵⁸ as of May 2017, 74 drugs are subject to restricted access programs (that is, drugs that are either subject to REMS or self-imposed restricted distribution programs) with total sales of \$22.7 billion in 2016. Of these, 41 drugs are restricted by REMS programs, with \$11.5 billion in sales in 2016. The remaining 33 drugs are restricted by the brands in a voluntarily imposed non-REMS program, with \$11.2 billion in sales in 2016.

Brand abuse of restricted access and the REMS process imposes substantial costs on consumers and other participants in the health care system. A 2014 study concluded that REMS abuse costs the U.S. health care system \$5.4 billion annually.⁵⁹ Consumers bear \$960 million of that cost while Medicare and Medicaid incur \$1.8 billion; private insurers bear the remaining \$2.4 billion.⁶⁰ This estimate is conservative “and should not be construed as the entirety of the lost savings from REMS misuse, either currently or going forward.”⁶¹

Moreover, the opportunities for abuse are growing. This is due, in part, to the fact that (a) FDA increasingly is requiring REMS as a condition for new drug approvals, and (b) these REMS programs increasingly include ETASU. In 2014, it was estimated that nearly 40 percent of new FDA approvals are subject to REMS.⁶² While only approximately 25 percent of REMS programs included ETASU in 2009,⁶³

⁵⁵ An early version of the Food and Drug Administration Amendments Act of 2007 (“FDAAA”) would have required brand companies to sell their drugs subject to distribution restrictions to generic companies at fair market value for bioequivalence testing. Food and Drug Administration Amendments Act of 2007, H.R. 2900 § 901(f)(6), 110th Cong. (1st Sess. 2007).

⁵⁶ 21 U.S.C. § 355-1(f)(8).

⁵⁷ *Id.* § 355-1(i)(1)(B).

⁵⁸ Alex Brill “REMS and Restricted Distribution Programs: An Estimate of the Market (June 2017),” Available at http://www.gphaonline.org/media/cms/Alex_Brill_REMS_Study_June_2017.pdf. Accessed: July 5, 2018.

⁵⁹ Alex Brill, “Lost Prescription Drug Savings from Use of REMS Programs to Delay Generic Market Entry, at 5 (2014), . Available at: http://www.gphaonline.org/media/cms/REMS_Studyfinal_July2014.pdf. Accessed: July 5, 2018.

⁶⁰ *Id.*

⁶¹ *Id.* at 5.

⁶² *Id.* at 6

⁶³ *Id.* at 3.

now nearly 60 percent of REMS programs (42 of 71) include the types of distribution and use restrictions that can be used by brand companies to delay generic and biosimilar competition.⁶⁴

The FTC and senior FDA officials have identified restricted access and REMS abuse as a significant problem that impairs generic competition and increases drug costs. Specifically, the FTC has warned that REMS abuse “threatens to undermine the careful balance created by the Hatch-Waxman Act and potentially preserve a brand company’s monopoly indefinitely.”⁶⁵ In his recent testimony to Congress, FDA Commissioner Gottlieb stated that statutory and regulatory requirements established to ensure the safety and quality of drugs approved by FDA, such as the REMS requirements, can be “gamed ... in an effort to delay generic drug approvals beyond the timeframe the law has intended. *This can serve to thwart expected competition.*”⁶⁶ Likewise, in earlier testimony to Congress, FDA Center for Drug Evaluation and Research (CDER) Director Janet Woodcock, M.D., stated that REMS abuse “can delay timely consumer access to less expensive generic medicines.”⁶⁷

While AAM commends the FDA and FTC for seeking to address REMS and restricted access abuses, as well as to publicize these abuses and seek additional support from stakeholders, they are limited in their capacity as federal agencies. The Federal Food Drug & Cosmetic Act’s penalties are insufficient to effectively deter bad behavior by the brands. Ultimately, the FDA lacks the ability to compel brand companies to sell samples to generic manufacturers.

AAM encourages HHS to support enactment of the CREATES Act.⁶⁸ This bipartisan bill would prevent the misuse of REMS and voluntarily imposed restricted access programs to delay generic drug competition.

HHS Should Withdraw the Proposed Amendments to 180-Day Generic Exclusivity that Threaten Future Generic Competition

AAM has significant concerns with the proposal in the President’s FY 2019 Budget for the Department of Health and Human Services to alter the 180-day term of exclusivity to which first generic drug applicants are entitled. Instead of fulfilling its stated goal of “spurring access and competition,” AAM believes this proposal could have precisely the opposite effect. It would undermine one of the most critical incentives for generic medicines to come to market, hindering price competition and patient access to the critical savings generics provide. Addressing other types of gamesmanship by some branded drug companies would save the federal government far more in taxpayer dollars — and provide greater competition and patient access to affordable medicines.

For its entire history, the 1984 Drug Price and Competition Act, also known as the Hatch-Waxman Amendments, has granted a 180-day period of market exclusivity to the first generic company that

⁶⁴ Alex Brill, *REMS and Restricted Distribution Programs: An Estimate of the Market*, p. 2.

⁶⁵ FTC Amicus Brief, *Actelion Pharmaceuticals LTD. v. Apotex Inc.*, Case No. 1:12-cv-05743 (D.N.J.).

⁶⁶ FDA Commissioner Scott Gottlieb, M.D., Congressional Testimony before House Committee on the Judiciary, Subcommittee on Regulatory Reform, Commercial and Antitrust Law, at 2 (July 27, 2017). (emphasis added).

⁶⁷ Janet Woodcock, M.D., Congressional Testimony before House Committee on Oversight & Investigations (Mar. 22, 2017). In addition, in 2015, Dr. John Jenkins, then-Director of FDA’s Office of New Drugs stated that brand companies are aggressively using REMS to block generic competition. Gingery, Derrick. REMS That Block Generics Are “Major” Problem for FDA, Jenkins Says. *The Pink Sheet Daily*. January 8, 2015. [random capitalization]

⁶⁸ Creating and Restoring Equal Access to Equivalent Samples Act of 2017, S. 974, 115th Cong. (2017).

challenges a patent protecting an expensive branded drug. This provides a strong incentive for generic companies to shoulder the financial and legal burden of contesting weaker patents that nevertheless block generic competition. By promoting patent challenges, the exclusivity period encourages earlier entry of safe and effective generic alternatives that are less expensive than the brand. The 180-day exclusivity provision thus has been critical to the success of the Hatch-Waxman Amendments over its 30-year track record in promoting generic competition, saving patients and the health care system trillions of dollars.

According to the FY 2019 Budget proposal, this legislative proposal would make the tentative approval of a subsequent generic drug applicant that is blocked solely by a first applicant's 180-day exclusivity, where the first applicant has not yet received final approval, a trigger of the first applicant's 180-day exclusivity. This is unnecessary because the statute already contains provisions that address situations where 180-day exclusivity may block approval of additional generic products for extended periods of time. In particular, the 180-day exclusivity term can be forfeited in several ways that prevent it from being "gamed" by brand or generic companies. These forfeiture provisions were added by Congress in 2003 and carefully balance the need for reasonable certainty of 180-day exclusivity with the need to prevent unduly delaying the approval of subsequent generic products. The HHS proposal could undermine this carefully crafted congressional solution.

The proposal thus far fails to describe the scope and nature of the problem at issue. While more detail is necessary, AAM believes that the HHS proposal could significantly weaken the primary incentive for generic companies to challenge branded drug patents. In many cases, generic drug approval or tentative approval occurs before the completion of patent litigation. In such situations, Congress and FDA have agreed it is reasonable for generic companies to wait until they prevail in patent litigation before going to market in order to avoid potential treble damages.

If the 180-day exclusivity were triggered by the tentative approval of a subsequent applicant rather than commercial marketing by the first applicant, the incentive would become virtually worthless. Without reasonable certainty that the 180-day exclusivity could be retained with a sufficient degree of predictability, generic drug manufacturers will be much less likely to take on the enormous expense of challenging brand name drug patents in the first place.

With fewer patent challenges, more weak and questionable patents will stay in place, often for up to 20 years, blocking the entry of generic drugs into the marketplace. With less generic competition, drug prices are likely to increase for patients, payors and the health care system.

AAM is concerned this policy proposal could harm generic competition and exacerbate the struggles of America's patients to afford their medications. Reducing or otherwise undermining the incentive for first-to-file generics threatens the foundation of the system that has generated trillions of dollars in savings for patients and payors.

FDA's Leadership is Critical to Foster Confidence in Biosimilars and Correct Misinformation

The RFI highlights the importance of physician and patient confidence in biosimilar medicines and the role of education in building this foundation. With the cost of prescription drugs an ongoing concern, the growing market for lower-cost biosimilars can offer more price competition and options for patients,

and it is critical that consumers and prescribers alike understand what these drugs are, and how they can help patients. We applaud FDA’s introduction of biosimilar educational materials last fall that are focused on educating providers about the FDA approval pathway for these products, the data and information that FDA reviews to determine biosimilarity and basic definitions of key terms. These resources serve as an important first step to ensuring that stakeholders—including patients and their health care providers—are well informed about biosimilars and the tremendous potential they offer patients in expanding cost-saving options.

However, as the biosimilars market in the United States continues to grow and more products are approved and available to patients, it is paramount that biosimilar education continue in tandem and at pace with the emerging marketplace. As the FDA works to develop additional resources for stakeholders, we urge that any such new resources focus on: promoting and instilling confidence in biosimilar safety, efficacy and quality; defining and utilizing terminology and key concepts in a manner that is easily comprehended by a variety of stakeholders; and prioritizing and targeting stakeholder audiences who stand to benefit most from a comprehensive understanding of biosimilar and interchangeable products, and tailoring resources for their unique information needs. More specifically, we offer the following recommendations:

FDA Should Continue to Emphasize the Safety and Effectiveness of FDA-Approved Biosimilars

FDA approval requires a rigorous standard of quality, safety and efficacy of medicines. Understanding the rigorous process the FDA uses to evaluate and approve biosimilars will not only enhance prescriber and patient confidence in these safe, effective and innovative products, but also ensure that patients are able to maximize their benefits. Therefore, it will be critical to emphasize throughout all materials the concepts of safety and efficacy, quality and potential for increased access by conveying the following principles:

- Biosimilars are designed to match the structure and function of the reference biologic and patients can be assured that FDA-approved biosimilars have the same safety and efficacy profile as their reference biologics;
- The FDA approves biosimilars based on the same high standards for manufacturing and quality used for all biologics; and
- The introduction of biosimilars is anticipated to help drive lower cost burdens for the U.S. health care system and help expand earlier and more consistent access to biological medicines.
- Biosimilar and interchangeable biologic products can be prescribed for treatment-naive and treatment-experienced patients.

Furthermore, all educational resources should stress the rigor of the FDA approval process to create understanding and confidence in the products being deemed “highly similar” but not identical. These resources should clearly explain aspects of the structure, the function, the pharmacology and clinical value of biosimilars, as well as the fact that these products are clinically the same as the reference product. Generic drugs can be identical to their reference products as they are chemical compounds;

however, given that biologics are developed in a living system, they cannot be identical and thus they are instead highly similar. In addition, interchangeable biologics will be shown to provide the same clinical effect in any given patient; authorizing their substitution at the pharmacy, like generic drugs without the intervention of a physician. All biologics, whether a reference product or a biosimilar, are subject to variability from batch to batch. Indeed, reference biologic manufacturers must demonstrate their products are within acceptable levels of variation from lot to lot. Reference products evolve over time, and those changes are made regularly based on analytical testings that demonstrate comparability. Biosimilars and interchangeable biologics are thoroughly tested to achieve the same level of quality. This provides health care professionals confidence through the development of the biosimilar and the FDA approval process that when a biosimilar is proven to be "highly similar" in all respects, it will have no clinically meaningful differences from the reference product.; and that an interchangeable biologic may be substituted at the pharmacy in the same fashion as a generic drug.

And finally, and perhaps most important for patient acceptance of these products, all resources should emphasize that the biosimilar regulatory framework does not interfere with the patient-physician relationship. The physician's obligation and responsibility is to the patient to ensure the best outcome possible when prescribing medicines.

FDA Should Define Biosimilar Terminology and Concepts for Key Stakeholders

Non-biased educational resources from FDA are essential to foster patient, provider and payer acceptance and utilization of these therapies, and the work FDA has already initiated will help correct misinformation and further understanding of the value biosimilars bring to patients. To that end, as additional resources are developed for a varied audience of biosimilar stakeholders, it is critical that key terms and concepts be defined and explained in a way that is consistent, clear and easily understood by all audiences. Such terminology should serve to further engender confidence in these new products.

Specifically, we encourage the FDA to define and utilize the term "Clinically Equivalent" to mean "no clinically meaningful differences" in all education efforts. The current terminology of "no clinically meaningful differences" is a double negative, which can be more difficult to grasp rather than a simple positive concept.

Additionally, we urge the FDA to clarify that patients are routinely transitioned by providers from one biologic to another clinically equivalent biologic. This type of transitioning in the biologic and biosimilar space is well-established, as biosimilars are clinically equivalent to their reference products and physician intervention authorizes the change. Characterizing these transitions as well as automatic pharmacy substitution of an FDA approved interchangeable biologic as so-called "non-medical switching" is inaccurate.

Finally, as FDA works to finalize its guidance on interchangeable products and manufacturers await clarity on what is required to receive such a designation, it remains critical for stakeholder confidence that the FDA define the concept of interchangeability in easily understandable terms. To do so, the FDA must underscore that the product quality requirements for biosimilars and interchangeable biologics are identical. Moreover, a biosimilar need not be designated as interchangeable for a physician to transition

a patient from a reference biologic to a biosimilar, and the FDA should emphasize that a switch, or transition, from a reference biologic to an FDA-approved biosimilar does not affect safety and effectiveness. The FDA can also educate physicians why pharmacy substitution is an acceptable practice for interchangeable biologics as it is for generic drugs.

FDA Should Target Gaps in Stakeholder Education

To effectively promote acceptance of biosimilar and interchangeable products, the Agency must identify and prioritize those stakeholders whose increased understanding of these products can serve to augment patient confidence and market acceptance. While biosimilar education is underway in some segments of the health care delivery spectrum, there are many still who lack a comprehensive understanding of these products—or worse yet, have been exposed to inaccurate or misleading information. We urge FDA to prioritize education efforts and the unique information needs of the following categories of health care professionals: physicians; nurses; and pharmacists, particularly community pharmacists and pharmacists who practice in ambulatory care settings that host treatment sites for administration of biologics.

Furthermore, we believe that key industry stakeholders have an important role to play in amplifying public education around biosimilars, and the FDA should work collaboratively with both industry and other key stakeholders (e.g., payors, patients, clinicians, pharmacists) to promote much-needed educational campaigns. Indeed, many stakeholder organizations have developed their own educational resources targeted to the respective patient, provider or pharmacist constituencies they represent. We urge the FDA to engage those organizations to ensure that all future FDA educational materials include a variety of perspectives for a balanced product that can be tailored to the unique needs of different stakeholder audiences. Such a collaborative educational effort will yield a key and independent source of accurate and trusted information regarding biosimilar products, their safety and scientific development.

As more biosimilars are approved by the FDA, the promise of a robust biosimilars market in the United States represents not only a significant savings opportunity for patients and the health care system, but also an opportunity to increase patient access to life-changing biologic therapies. We look forward to continuing our work with FDA to educate all stakeholders about the benefits of biosimilars.

FDA Should Improve the Purple Book to Advance Biosimilar Development and Market Entry

The current version of the Purple Book contains very little information about exclusivity for most currently marketed biological products. FDA has explained that “[a]lthough FDA has not made a determination of the date of first licensure for all 351(a) biological products included on the lists, it does not mean that the biological products on the list are not, or were not, eligible for exclusivity. A determination of the date of first licensure and of when any remaining reference product exclusivity will expire for a biological product submitted under section 351(a) of the PHS Act will generally be made for reasons of regulatory necessity and/or at the request of the 351(a) application license holder.”⁶⁹

⁶⁹ FDA. “Background Information: Lists of Licensed Biological Products with Reference Product Exclusivity and Biosimilarity or Interchangeability Evaluations (Purple Book).” Available at: <https://bit.ly/2tWK07F>. Accessed: July 5, 2018.

AAM requests that FDA update the Purple Book to clarify which products have been determined not to have exclusivity (e.g., those where any period would have expired, if it applied in the first place) and those that are still subject to pending decisions. This will provide greater clarity to sponsors who may be considering developing biosimilar and interchangeable biologics and allow them to request exclusivity determinations for specific reference products, if necessary. e We suggest that a mechanism be created whereby FDA makes an exclusivity determination upon the request of a biosimilar applicant, not just the BLA holder or on the Agency's own initiative.

FDA can also improve the Purple Book by adding the same guidance about interchangeability as it does in the Orange Book. The Purple Book should clarify, like the Orange Book, that a interchangeability determination under the BPCIA, by definition, means therapeutic equivalence and authorizes substitution at the pharmacy. Moreover, FDA should ensure ongoing refinements so that the Purple Book is an effective resource for both the agency and industry.

Additionally, at present, the Purple Book is comprised of static tables. We suggest that the Purple Book be converted into a single searchable electronic database combining the current separate CDER and CBER list of approved products with a preamble/introduction that defines basic terms. It would also be helpful if the Purple Book identified the reference product for the approved biosimilars product. Especially if the FDA implements the new biologics naming convention and assigns suffixes to the reference product instead of only biosimilars and interchangeable biologics, as is the current practice, it will not be possible to identify the reference product. The addition of this information would be vital for pharmacists to determine which reference product could be substituted by an interchangeable biologic.

FDA Can Advance Biosimilar Interchangeability Through Final Guidance

We are concerned that several recommendations in the Draft Guidance on “Considerations in Demonstrating Interchangeability with a Reference Product” impose unnecessary scientific standards on interchangeability determinations and/or are inconsistent with the relevant statutory requirements.⁷⁰ For example, we strongly oppose FDA’s “expect[ation] that sponsors will submit data and information to support a showing that the proposed interchangeable product can be expected to produce the same clinical result as the reference product in all of the reference product’s licensed conditions of use.” The agency lacks the authority to require sponsors to conduct studies and submit data for conditions of use for which they do not intend to seek licensure. Accordingly, we ask FDA to clarify that a sponsor of an interchangeable biologic need not demonstrate interchangeability in those indications for which it is not seeking licensure.

Likewise, with regard to the endpoints for switching studies, we are concerned FDA’s focus on pharmacokinetic and pharmacodynamics endpoints are too narrow and, accordingly, we ask that FDA acknowledge that alternative endpoints may be used when pharmacokinetic or pharmacodynamics endpoints are not appropriate. In our view, these and other requirements set forth in the Draft Guidance are not scientifically justifiable and are? inconsistent with the streamlined licensure pathway

⁷⁰ FDA. “Considerations in Demonstrating Interchangeability wWith a Reference Product: Draft Guidance for Industry; Availability;” Draft Guidance.

envisioned by Congress. If finalized, these requirements not only will create significant disincentives for sponsors to develop interchangeable biologics but, more importantly, will also significantly affect patient access to affordable alternatives to brand-name biologics, contrary to congressional intent.⁷¹

FDA Should Allow Use of Non-U.S. Licensed Reference Product for Biosimilars

AAM and the Council appreciate FDA's continued prioritization of efforts to improve the efficiency of the biosimilar and interchangeable product development and approval process. The ability of U.S. biosimilar manufacturers to use development data for biosimilars generated with reference products licensed outside of the U.S., provided the reference product is authorized in an economic area with high scientific and regulatory standards such as the European Union, has been particularly helpful in realizing improvements to efficiency of the development and approval process.

Currently, biosimilar sponsors must submit analytical and clinical bridging studies between the proposed biosimilar, the non-U.S. -licensed reference product used during the biosimilar development, and the U.S.-licensed reference product, per FDA guidance on the issue.⁷² These additional studies add significant expense to a development process that is estimated to cost between \$100 and \$300 million.⁷³ Further, these bridging studies do not bring any added scientific value, nor increase the safety profile of the biosimilar product or the safety of the patient.⁷⁴ Bridging between reference products sourced outside of the US reference products potentially also exposes subjects to unnecessary, and therefore unethical, clinical trials.

FDA Commissioner Gottlieb has recently indicated that the Agency is actively exploring eliminating the requirement for sponsors to conduct these expensive and unnecessary studies.⁷⁵ AAM and the Council support such efforts. The BPCIA does not require these studies to be conducted, rather they are recommended as FDA's policy in the Agency's own discretion. Therefore, AAM and the Council recommend the Agency expeditiously review its current regulatory requirements for these bridging studies. Removing this requirement would reduce the development cost for sponsors of biosimilars and interchangeable products, in turn leading to increased patient access to more- affordable alternatives to costly reference biologics.

⁷¹ See Docket No. FDA-2017-D-0154 for "Considerations in Demonstrating Interchangeability with a Reference Product: Draft Guidance for Industry; Availability;" Comments of the Association for Accessible Medicines and the Biosimilars Council, May 19, 2017

⁷² FDA Guidance for Industry "Biosimilars: Questions and Answers Regarding Implementation of the Biologics Price Competition and Innovation Act of 2009". Accessed: June 25, 2018. Available at: <https://bit.ly/2y1l60y>.

⁷³ CNBC Interview of FDA Commissioner Gottlieb, March 28, 2018. Accessed: April 30, 2018. Available at: <https://cnb.cx/2pNVVlh>.

⁷⁴ "A 'Global Reference' Comparator for Biosimilar Development." Christopher J. Webster and Gillian R. Woollett. Accessed: June 25, 2018. Available at: <https://doi.org/10.1007%2Fs40259-017-0227-4>.

⁷⁵ Kaiser Health News, "FDA Head Vows to Tackle High Drug Prices And Drugmakers 'Gaming The System'". Accessed: June 25, 2018. Available at: <https://bit.ly/2C052rX>

Steps FDA Can Take to Improve the Generic Drug Review Process

FDA Should Continue Efforts to Improve Reviewer Quality

Agency feedback on generic drug applications varies by individual reviewer, across divisions and offices, and over time. Needless to say, this makes it very difficult for industry to learn from reviewer feedback. A few ways to address this concern include:

- Improve training for reviewers. AAM believes that improving training to achieve greater consistent processes/procedures across all reviewers so that they all have the same understanding of Agency expectations is critical in making feedback to sponsors consistent. AAM member companies have noted, in addition, that some reviewers are reporting deficiencies in areas that do not necessarily have anything to do with the approval requirements– the reviewers may have a personal interest in a topic or feel that something is relevant when it is not – in the Commissioner’s words, the “nice to know verses the need to know” (e.g., including the address of the manufacturing site at the top of each page of a batch record). The effect, from the sponsor’s perspective, is that the reviewer is conducting a “nice to know verses need to know” exploration for something that is not tied to the statutory approval standard. These requests from the reviewer may translate to expensive or time-consuming rework on the sponsor’s part, redesign of quality and manufacturing procedures that affect and add cost to every product produced at the manufacturing facility and in the end may have nothing substantive to do with the application. In other cases, companies have reported that reviewers will request information that has already been submitted in the application – indicating that the reviewers simply haven’t been adequately trained on the format and content of applications. Better training would eliminate these problems. Specifically, the new platform recently introduced by the Commissioner – Knowledge -Aided Assessment & Structured Application (KASA) platform speaks to these concerns. AAM looks forward to working with the Commissioner and the Agency as this platform is introduced.
- Improve communication about deficiencies. The information value of a deficiency is greatly reduced if it is not communicated to all the parties who would benefit from knowing about it. In many cases, a deficiency is observed by multiple reviewers across multiple applications over time. In addition, communicating review problems to applicants on a piecemeal basis does not achieve the joint FDA and industry goal of improving the quality of generic applications.
- A simple solution would be to post changes and additions to data format and content requirements on a central FDA website available for viewing by all generic applicants. The more frequently this list is published, the more helpful it would be; quarterly updates would be helpful and monthly would maximize applicants’ ability to incorporate the new requirements into applications. This would allow both reviewers internally and sponsors externally to see which problems are being identified and to see the recommended resolutions being suggested to the sponsors. In effect this would allow for a peer review of the individual reviewers’ work and provide them a tool to prepare a response when they find a particular deficiency. A tool like this would also help ensure that similarly situated applicants would be treated similarly and help sponsors ensure that their submissions don’t have commonly seen errors, which over time will improve the likelihood of a first-cycle review.

FDA Should Minimize the Impact of Evolving Product-Specific Bioequivalence Recommendations on Generic Drug Availability

FDA often updates ANDA product-specific bioequivalence guidance documents with revisions that provide no added value with respect to demonstrating bioequivalence to the respective RLD. Indeed, a large percentage of product-specific bioequivalence guidance documents FDA issued over the past year revised previous recommendations.⁷⁶ FDA should strive to minimize changes to product-specific bioequivalence guidance when possible.

Each guidance revision can result in long delays in ANDA approvals, can add significant expense to ANDA sponsors and can wreak havoc on a company's portfolio management process because revisions typically add review cycles that further delay approvals or require significant rework of applications already in the process of development. With each guidance revision, there is time associated with, among other things, developing a new protocol and performing a new test. To that end, FDA should conduct a study, using the Regulatory Science Initiative established under GDUFA, to evaluate the impact changes and revisions to product-specific bioequivalence recommendations have on the safety and effectiveness profile of a drug product.

For many products, FDA has issued multiple guidance revisions. With nearly each new bioequivalence recommendation iteration, FDA moves the goalposts to obtain ANDA approval. For example, after initially publishing draft bioequivalence guidance for colesevelam HCl tablets in July 2008, FDA amended the guidance five separate times: December 2009, November 2010, June 2011, November 2013 and September 2015. Similarly, after initially publishing draft bioequivalence guidance for sevelamer carbonate in September 2008, FDA amended the guidance five separate times: July 2009, May 2010, August 2010, May 2011 and September 2015.⁷⁷

AAM recommends that FDA weigh carefully the scientific merit of each change in revised product-specific bioequivalence and evaluate whether such revised standards are necessary to approve pending applications. If a revision has true scientific merit and is critical for determining bioequivalence FDA should require the sponsors of all pending ANDAs for those products to comply with the changes reflected in the revised guidance. But if a revision represents an improvement that is not critical for determining bioequivalence FDA should not require the sponsors of pending ANDAs to comply with the new standards, the agency should instead review all pending ANDAs submitted prior to the revision under the previous

⁷⁶ In October 2016, FDA released 67 product-specific bioequivalence guidances, and 33 (49 percent) were revisions. In January 2017, FDA released 48 product-specific bioequivalence guidances, and 17 (35 percent) were revisions. In May 2017, FDA released 37 product-specific bioequivalence guidances, and 16 (43 percent) were revisions. In July 2017, FDA released 34 product-specific bioequivalence guidances, and 13 (38 percent) were revisions. In October 2017, FDA released 49 product-specific bioequivalence guidances, and 17 (35 percent) were revisions.

⁷⁷ Other examples include: (1) lidocaine topical patch, where FDA's initial December 2006 bioequivalence recommendation was followed by revisions in July 2014, January 2016, and October 2016 where FDA recommended that studies be conducted statistical analysis, adhesion evaluation and bioequivalence with pharmacokinetic endpoints and recommendations on formatting data submissions; (2) rivastigmine extended-release transdermal film, where FDA's initial February 2010 bioequivalence recommendation was followed by revisions in June 2010, November 2010, and October 2016; and (3) lansoprazole delayed-release orally disintegrating tablets, where FDA's initial October 2008 bioequivalence recommendation was followed by revisions in June and October 2016, and where each revision required additional nasogastric administration testing to be conducted in addition to changes in the tubing necessary for the study and the specific procedures for the study to be conducted.

iteration of a product-specific bioequivalence guidance with a post-approval commitment to meet any new tests or procedures. In addition, given the non-binding nature of FDA guidance documents, including product-specific bioequivalence recommendations, AAM recommends that FDA be more open to accepting deviations from published bioequivalence recommendations, provided an ANDA applicant gives scientific justification to support its approach.

FDA Should Provide Greater Transparency of Reference Listed Drug Formulation Changes

Formulation changes to brand-name drugs can unnecessarily frustrate generic competition for those drug products. Often, formulation changes occur without public notice and are discovered only when revised drug product labeling is made available on the NIH DailyMed website. In addition, new formulations may be protected by formulation-specific patents.

FDA's Orange Book does not currently identify when FDA has approved a new formulation and when a previous and superseded formulation has been discontinued. To increase transparency of brand-name formulation changes, and to avoid unnecessary patent certifications and the potential to delay generic competition by the filing of patent infringement litigation triggering a 30-month stay on ANDA approval, FDA should separately identify in the Orange Book formulation changes as different drug products under an approved NDA (e.g., Product 001 and 002), and also identify in the Discontinued Drug Product List section of the Orange Book a discontinued drug product formulation.

FDA has followed such a practice in the past, on occasion, but not consistently. For example, a discontinued formulation of Brevibloc (esmolol HCl) Injection, 10 mg/mL, approved on August 15, 1988 under NDA 019386, is listed in the Discontinued Drug Product List section of the Orange Book as Product 003, while the new formulation, approved on February 23, 2003 under NDA 019386, is listed in the Prescription Drug Product List section of the Orange Book as Product 006. FDA noted this bifurcated listing when the Agency approved an ANDA for a generic version of the original formulation:

We note that Baxter's formulation of Brevibloc Injection, 10 mg/mL, which you have cited as the reference listed drug product is no longer being marketed in the United States. Baxter has replaced this formulation with a new formulation containing sodium chloride as an additional inactive ingredient. The Agency has moved Baxter's original formulation for Brevibloc Injection, 10mg/mL, to the discontinued section of the "Orange Book." However, the Agency has also made the determination that the original formulation was not withdrawn from sale for reasons of safety or effectiveness.⁷⁸

Similarly, when FDA approved a reformulated version of Diprivan (propofol) Injection, 10 mg/mL, on June 11, 1996 under NDA 019627, the Agency assigned the new formulation a separate product number: Product 002. The original and discontinued formulation of Diprivan Injection, 10 mg/mL, approved on October 2, 1989 under NDA 019627, was moved to the "Discontinued Drug Product List" section of the Orange Book where it is identified as Product 001.

⁷⁸ FDA, Approval Letter ANDA 076323, at 2 (Aug. 10, 2004).

More recently, FDA indicated that the Agency would not separately list in the Orange Book a discontinued drug product.⁷⁹ FDA's response, however, does not address previous instances when the Agency has separately listed superseded formulations.

FDA Should Include Date of Patent Listing in the Orange Book

Knowing whether patent information is timely submitted to FDA for Orange Book listing is information critical to ANDA applicants. For example, a company with a pending ANDA is not required to certify to new patent information listed in the Orange Book if such patent information is listed more than 30 days after patent issuance.

We commend FDA for amending the Orange Book to include a new column in the Patent and Exclusivity List that identifies the date on which a particular patent was considered listed in the Orange Book. Supplying such information in a readily accessible document will clarify for ANDA applicants whether a patent is timely listed and must be addressed in a patent certification. However, FDA will undertake this only on a prospective basis and going back to 2013, no doubt as a result of resource constraints. This leaves thousands of patents for which applicants will still have to reach out to FDA for patent submission information, which will involve a great deal of time and effort on the part of both FDA and our members. To efficiently apply these limited resources, we encourage FDA to consider listing patent information retrospectively for those products prior to 2013 at the time FDA receives a request and provides such information to applicants.

FDA Should Improve Pre-Launch Communication

Prior to the enactment of GDUFA, in 2012, the Office of Generic Drugs frequently communicated to generic drug manufacturers when a particular ANDA was being routed through the approval endorsement process. Such information allowed generic drug manufacturers to prepare pre-launch activities in order to market their product at the earliest legally eligible date in case of an FDA approval action. With the enactment of GDUFA, however, FDA abruptly stopped providing ANDA applicants with pre-launch communications.

Such communications are critical for generic applicants because preparing a newly approved product for launch has many moving parts and requires precise planning and coordination. The moving parts range from acquisition and processing of raw ingredients, manufacturing the final product, purchasing the final container and closure systems, packaging, labeling, and quality checks in the form of release testing all the way down to coordinating the logistics for transporting the finished product through the various export/import points, delivery to multiple distribution centers to finally land at the pharmacy. Pre-launch communications provide additional information about the status of an application early enough for the ANDA sponsor to make a better business decision regarding whether to proceed with the launch process to ensure the product would be available to the patient at the earliest legally eligible date. In addition, pre-launch communications were never interpreted by FDA or industry as an official notice of approval.

⁷⁹ See FDA Citizen Petition Response, Docket Nos. FDA-2017-P-1392 and FDA-2017-P-1573, at 11-12 (Aug. 4, 2017).

The FDA Reauthorization Act (FDARA) makes clear that Congress intends that pre-launch communications be reinstated. Section 802 of FDARA amends the FDC Act § 505(j) to provide that “[u]pon the request of an applicant regarding one or more specified pending applications under this subsection, [FDA] shall, as appropriate, provide review status updates indicating the categorical status of the applications by each relevant review discipline.”

In the implementation of this provision, such communications could include the following statement as a means of addressing previous agency concerns, indicating the informal nature of the communication:

This communication is consistent with 21 C.F.R. § 10.85(k) and constitutes an informal communication that represents our best judgment at this time but does not constitute an advisory opinion, does not necessarily represent the formal position of the FDA and does not bind or otherwise obligate or commit the agency to the views expressed. Please be advised that any update given is preliminary and is subject to change at any time.

FDA Should Continue to Prioritize Complex Generics

The development of complex generic products, including generic drug-device combination products, presents unique challenges to both FDA and the regulated industry. Specialty drugs are responsible for more than 40 percent % of total drug spending.⁸⁰ Without sufficient incentives, companies may be reluctant to invest in complex generic programs, which cost significantly more to undertake than investing in the development of a solid oral dosage form. For example, complex generics development includes investment in different manufacturing infrastructure; increased development costs as a result of increased testing and data collection to demonstrate therapeutic equivalence; and investment to design around or challenge patents. These are all sunk costs that cannot be recouped if there is no path forward to the approval of a complex generic ANDA. Uncertainty and delays in complex programs discourage investment.

Commissioner Gottlieb has taken a number of key steps to improve the review and approval of complex generics⁸¹ and prioritize new generic applications through the Drug Competition Action Plan. This includes expediting the review of generic drug applications in markets where there are fewer than three approved generic versions of a given product.⁸² While these steps are important, a recent GAO report highlighted the agency’s lack of clarity and timeliness in working with manufacturers seeking to develop complex generics – particularly with respect to the development and updating of product-specific guidance documents.⁸³

The significant investment required to develop complex products warrants a more collaborative approach between FDA and industry, with ongoing scientific exchange from early development through the approval

⁸⁰ Quintiles/IMS Institute, *Medicine Use and Spending in the U.S.: A Review of 2016 and Outlook to 2021*, April 2017 (. Available at: <https://www.iqvia.com/institute/reports/medicines-use-and-spending-in-the-us-a-review-of-2016...> Accessed: July 5, 2018.

⁸¹ Gottlieb, Scott, M.D., Reducing the Hurdles for Complex Generic Drug Development. (2017) Available at:<https://blogs.fda.gov/fdavoices/index.php/2017/10/reducing-the-hurdles-for-complex-generic-drug-development/>. Accessed: July 5, 2018.

⁸² Prioritization of the Review of Original ANDAs, Amendments, and Supplements, FDA Manual of Policies and Procedures (2017). Available at: <https://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ManualofPoliciesProcedures/UCM407849.pdf>. Accessed: July 5, 2018.

⁸³ Government Accountability Office, FDA Should Make Public Its Plans to Issue and Revise Guidance on Nonbiological Complex Drugs. (2017) Available at: <https://www.gao.gov/assets/690/689047.pdf>. Accessed: July 5, 2018.

process. Timely access to guidance for complex products will encourage development and outline clear standards.

Congress recognized this need in FDARA. Section 803 of FDARA amends the FDC Act to add Section 506H, titled “Competitive Generic Therapies,” and authorizes FDA to designate a drug as a “competitive generic therapy” upon request by the applicant when there is “inadequate generic competition;” that is, when there is no more than one approved ANDA for its corresponding reference product listed in the Orange Book (not including discontinued products).⁸⁴ A generic drug manufacturer who obtains designation of a drug as a “competitive generic therapy” is eligible for certain benefits, including enhanced communications with FDA officials and advice from the Agency.⁸⁵ While FDARA Section 803 and the processes established in the GDUFA II Goals Letter are a good start, there may be additional opportunities to engage in ongoing scientific dialogue that will allow prompt approval of complex generics. AAM believes that the biosimilar program provides a useful model for FDA/industry collaboration. AAM looks forward to working with FDA to achieve these goals.

FDA Should Maintain Incentives for First Generics

FDA should continue to prioritize the review of first generics. AAM appreciates FDA’s efforts in addressing many of the challenges that face generic companies, including the issuance of the November 9, 2017 MaPP entitled “Prioritization of the Review of Original ANDAs, Amendments, and Supplements” (MaPP 5240.3 Rev. 4), recognizing that, in addition to prioritizing the review of first filers, the first three filers should also be prioritized. All the priorities reflected in the MaPP are equally important. First generics should not become de-prioritized as part of FDA’s efforts to approve additional generics and improve competition.

FDA Should Prevent Unnecessary Approval Delays Through Better Coordination in Evaluating GMP Issues

FDARA Section 806 requires FDA to develop and implement within six months of FDARA’s enactment “a protocol for expediting review of timely responses to reports of observations from an inspection under [FDC Act § 704].” This FDA protocol will apply to inspection report responses pertaining to NDAs and ANDAs “for which the approval is dependent upon remediation of conditions identified in the report,” “for which concerns related to observations from an inspection . . . are the only barrier to approval” and “where the drug that is the subject of the application is a drug (i) for which there are not more than 3 other approved [ANDAs] that reference the same listed drug and for which there are less than 6 [ANDAs] tentatively approved; or (ii) that is included on [FDA’s drug shortage list].”⁸⁶ In addition, FDA’s protocol will address expedited facility re-inspection and will establish a 6-month timeline for completion of review of inspection report responses. AAM looks forward to working with FDA to implement this provision of FDARA in a manner that renders the inspection process more efficient, allowing patients to gain access to

⁸⁴ FDC Act § 506H(b)(3), as amended by FDARA § 803(a).

⁸⁵ See FDC Act § 506H(c), as amended by FDARA § 803(a).

⁸⁶ FDARA Section 806.

affordable medications sooner. Further, AAM looks forward to additional guidance to further assist understanding of the protocol to ensure there are not unnecessary delays in the approval of ANDAs.

FDA Should Withdraw the Proposed Rule, “Supplemental Applications Proposing Labeling Changes for Approved Drugs and Biological Products,”

AAM reiterates its request that FDA withdraw as drafted its Proposed Rule, “Supplemental Applications Proposing Labeling Changes for Approved Drugs and Biological Products,” and ensure that FDA pre-approves all safety-related labeling changes for multi-source products. As AAM has previously noted, the Proposed Rule creates a scenario where disparate and potentially conflicting information from multiple manufacturers for single medicines could be widespread, causing confusion and putting patient safety, access and savings at risk. A report by Matrix Global Advisors finds that spending on generic drugs could increase by \$4 billion per year.⁸⁷ Of this, government health programs could pay an additional \$1.5 billion and private health insurance \$2.5 billion for generic drugs.

HHS and FDA Should Modernize Health Care Prescribing Information

Prescribing information provides health care professionals the information necessary for the safe and effective use of pharmaceuticals. Currently, the prescribing information (dosage and administration) is distributed in paper form on or within the package from which a prescription drug is dispensed. The same information is currently also available electronically through various sources.

In 2014, the FDA released a proposed rule to transition prescribing information from the traditional paper-reliant system to a modern electronic system.⁸⁸ AAM recommends that the FDA move forward with its efforts to modernize health care prescribing information, enhance patient safety with real-time updates and reduce health care costs through improved efficiency. Implementing the proposed rule would save up to \$164 million, according to the FDA. This estimate, however, is probably low as the FDA proposed rule did not attempt to quantify the public health benefits of improved patient safety.

Generic and biosimilar manufacturers currently submit and update prescribing information to FDA (labels.fda.gov) every time there is a change in labeling. This ensures that the most up-to-date version of the prescribing information is available to health care professionals. Approximately 500 safety labeling changes are made each year. With a greater reliance on real world evidence, the frequency and importance of label changes will only increase.

Paper distribution of prescribing information is an outdated system. Under a paper-based system, multiple versions of the prescribing information can exist throughout the health care system for years. This creates confusion and may provide outdated information for health care professionals when counseling patients on medicines and treatments. It is important to note that the proposal would not affect information provided to patients when medication is dispensed.

⁸⁷ Brill, A. “FDA’s Proposed Generic Drug Labeling Rule: An Economic Assessment.” Available at: <https://bit.ly/2tXBVzM>. Accessed: July 5, 2018.

⁸⁸ FDA. “Electronic Distribution of Prescribing Information for Human Prescription Drugs, Including Biological Products” Proposed Rule. Available at: <https://bit.ly/2tXokbA>. Accessed: July 5, 2018.

Electronic distribution of prescribing information improves patient safety by ensuring that health care professionals have the most current prescribing information. Thus, while the FDA estimated savings of up to \$164 million four years ago⁸⁹, the savings to the health care system through increased adherence and compliance could be substantial, both in terms of costs and lives. It is well documented that adverse drug reactions cost the health care system \$136 billion each year and result in 100,000 deaths annually.⁹⁰ Real-time information reduces the potential for drug-related medical errors.

For these reasons, AAM reiterates the importance of the FDA moving forward with implementation of the 2014 proposed rule to modernize health care prescribing information.

Abuse of the Patent System Keeps Patient Costs High by Delaying Generic and Biosimilar Competition

AAM's members support and engage in innovation. Without innovation there could be no generic pharmaceutical or biosimilar medicines for patients. However, AAM is concerned that all too often some brand-name drug companies attempt to patent features of drugs that do not represent true innovation and are therefore not worthy of patent protection. Brand-name drug companies often attempt to bury competition from generic and biosimilar drugs indefinitely by finding ways to re-package existing inventions in later patents. These later patents are often not innovative, meaning they are likely invalid.

Recent research shows the brand-name pharmaceutical industry is manipulating this system by obtaining dozens of potentially non-innovative patents to extend its market exclusivity farther than policymakers initially intended, a ploy known as building "patent thickets."⁹² In these instances, branded biologic manufacturers are attempting to accumulate patents not because they are innovative, but rather to increase litigation and development costs for potential would-be biosimilar competitors. These patent thickets chill competition by discouraging competitors from entering a market because of the exorbitant cost of litigating meritless patents.

Sometimes, as the original patent on a lucrative drug is close to expiring, a brand-name drug company will seek a new patent for a minor change such as changing from a pill to a gelcap and call this a new innovation worthy of a new, multi-year monopoly protection from the government.

When the U.S. Patent & Trademark Office (PTO) grants pharmaceutical patents that do not represent innovation, drug costs remain high due to the prevention of generic drug competition. In this way, the PTO has an important role in the cost of prescription drugs.

Patent gamesmanship by some originator pharmaceutical companies is an enormous problem that drives up prescription drug costs to patients and consumers.

⁸⁹ FDA. "Electronic Distribution of Prescribing Information for Human Prescription Drugs, Including Biological Products" Proposed Rule. Available at: <https://bit.ly/2tXokbA>. Accessed: July 5, 2018.

⁹⁰ <https://www.fda.gov/Drugs/Developmentapprovalprocess/Developmentresources/Druginteractionslabeling/ucm110632.htm> htmhtmFDA. "Preventable Adverse Drug Reactions: A Focus on Drug Interactions." Available at: <http://bit.ly/2unFwaH>.

⁹¹ <https://www.ncbi.nlm.nih.gov/pubmed/27485605> "Improving drug safety: From adverse drug reaction knowledge discovery to clinical implementation." 2016 Nov 1;110:14-25. doi: 10.1016/j.ymeth.2016.07.023. Epub 2016 Jul 30.

⁹² Feldman, Robin and Wang, Connie, May Your Drug Price Be Ever Green (October 29, 2017). UC Hastings Research Paper No. 256. Available at: SSRN: <https://ssrn.com/abstract=3061567>. Accessed: April 30, 2018.

HHS Should Support Maintaining a Strong IPR Process to Lower U.S. Drug Prices

One of the key ways to stem these abuses is to maintain a strong inter partes review (IPR) process at the PTO. IPR is an important tool that Congress enacted as a bi-partisan solution to allow the PTO to eliminate bad patents efficiently. Congress established the IPR process, because the PTO grants a very high percentage of patents that do not represent patentable innovation. Patent examiners face heavy caseloads and, as a result, typically spend an extremely limited amount of time sifting through an enormous expanse of prior art while reviewing dozens of complex and technical claims in each patent application. Researchers have found that patent examiners spend an average of just 19 hours on each patent application in an attempt to review and analyze countless pages of references.⁹³

There are many advantages to allowing the PTO to police its own patent-granting decisions: PTO reexamination of granted patents is cheaper, faster and benefits from the greater technical expertise PTO holds to review patents than generalist judges. When IPR eliminates an invalid patent, it cancels a government-granted monopoly and allows free market competition to lower prices.

To achieve the goal of lowering drug prices in the U.S., this Administration should resist efforts to weaken the IPR process, as well as support the USPTO's mission of furthering science and the useful arts by protecting true innovation. HHS should support the USPTO's implementation of a more arduous patent examination regime and support examiners so they may be able to spend more time researching and analyzing the art prior to patent issuance. . Legislation is pending in Congress today—the STRONGER Patents Act as well as the “Hatch-Waxman Integrity Act”—that would undermine the bipartisan goals of the America Invents Act. This Administration should oppose the advancement of those bills. On the other hand, the Administration should support passage of the PACED Act, which would close a loophole that would permit brand companies to escape the IPR process, leaving drug prices higher for patients, for longer periods of time.

HHS Should Support Congressional Action to Provide a Date Certain for Generic and Biosimilar Entry

There are other potential steps that could be taken to address the abuses that threaten the generic and biosimilars markets. Secretary Azar has correctly described the policy that Congress intended in enacting the Hatch-Waxman Amendments and the BPCIA: Congress rewarded brand pharmaceutical companies with a set period for monopoly patent protection and, upon expiration of that time period, competition should begin.⁹⁴ As Secretary Azar has observed, that is not the state of the market today.

Therefore, in the biosimilars arena, Congress could take steps to provide a date certain for biosimilar competition upon expiration of BPCIA market exclusivity by, for example, ensuring that patents do not create a bar to biosimilar competition upon expiration of the 12-year term of exclusivity. Congress could also take steps to ensure that the so-called “patent dance” commences earlier and so that biosimilars developers must not wait for the filing of a biosimilars application to commence patent litigation that

⁹³ Melissa D. Frakes & Melissa F. Wasserman, Is the Time Allocated to Review Patent Applications Inducing Examiners to Grant Invalid Patents?: Evidence from Micro-Level Application Data, Nat'l Bureau of Econ. Research (July 2014). Available at:<http://www.nber.org/papers/w20337.pdf>. Accessed: July 5, 2018.

slows biosimilar market entry. For example, Congress could allow for the initiation of patent litigation at the point when a developer has a Type III development meeting with FDA. This would accelerate the timeline of litigation and permit biosimilars to be marketed sooner, speeding their cost-savings to patients.

Congress could also harmonize the Hatch-Waxman system with the IPR process, by treating a final written decision of the PTAB as equivalent to a court decision for key Hatch-Waxman purposes. Hatch-Waxman was written at a time when most invalidity decisions came from courts. Accordingly, the 30-month stay dissolves only when there is a *court* decision finding the asserted Orange Book patents invalid or not infringed. An IPR decision does not have the same effect. Similarly, if a generic company loses in district court, the FDA is precluded from approving that company's ANDA until the patent expires, unless an appellate court reverses the district court's judgment. The statute does not provide for lifting that injunction if the patent is declared to be invalid by the PTO through an IPR, although courts may assert discretion to do so. The patent litigation provisions in Hatch-Waxman could be updated to reflect the reality that many Orange Book patents are also challenged in post-grant proceedings, and PTAB decisions are even more likely to be affirmed than district-court decisions. A patent that has been held invalid in an IPR should no longer be the basis for a stay on FDA approval.

Another issue generics and biosimilars developers face is that brand companies often hold some patents in reserve as a means of threatening generic and biosimilar companies with litigation carrying the possibility of massive damages liability later in the process. Congress could enact legislation that forces brand companies to assert all relevant patents promptly.

Trade Agreements Should Enhance Generic and Biosimilar Competition

The RFI rightly notes that "greater generic competition is associated with lower prices." Accordingly, the United States Trade Representative (USTR) should pursue efforts to strengthen generic drug and biosimilar competition to enhance patient access to more affordable treatments. USTR efforts to delay generic drug and biosimilar competition globally hurts the one industry that actually lowers prescription drug prices for patients here in the U.S.

HHS Should Urge USTR to Resist Efforts to Expand Brand Name Drug Monopoly Protection at the Expense of Generic and Biosimilar Competition

President Trump has called prescription drug prices "out of control" and has promised to take action to lower them. Policies that promote the growth of generics and biosimilars in both the U.S. and abroad are key to attaining that objective. As is the case for many goods, high saturation in the U.S. generics market has driven an increasing need to expand abroad for future growth opportunities. The Department of Commerce's 2016 "Top Markets" report for pharmaceuticals estimated that "U.S. generic drug sales reached an estimated \$70 billion, representing a quarter of the global market, due to a large number of drugs going off-patent and health care reforms favoring generics."⁹⁵ This report also predicted that growth

⁹⁵ Department of Commerce. "2016 Top Markets Report Pharmaceuticals." Available at: <https://bit.ly/2IUU0TO>. Accessed: July 5, 2018.

in generics “is driving, and will continue to drive, most of the projected growth in emerging markets over the coming decade.” Many countries, including Japan and other OECD countries, have low generic utilization rates, in some cases as low as 10 percent.⁹⁶ Balanced intellectual property policies in U.S. trade agreements will help level the playing field, allowing the U.S. to maximize exports of both originator and generic/biosimilar pharmaceutical products and satisfy the demand for safe and more-affordable prescription drugs.

Growing export markets for generic and biosimilar products is in our national interest. Given the low profit margins for many widely used generic medicines, any increase in their cost of production must be passed on to patients in the form of higher drug prices if companies are to continue to manufacture such drugs. Being able to sell newly developed products in markets beyond the U.S. allows the fixed costs of developing these products to be spread over a much broader patient base.

AAM opposes the inclusion in U.S. trade agreements of provisions that would expand patent or exclusivity protection for brand-name pharmaceuticals, including longer marketing or data exclusivity periods or mandates to extend a patent term based on delays in granting the patent or obtaining marketing approval. Such provisions would harm exports of generic and biosimilar medicines and raise drug prices in the U.S. Pressing countries to adopt years-long periods of exclusivity removes the flexibility needed to keep pace with changes in the sector in the years ahead and could needlessly delay access for generic and biosimilar products in export markets.

Moreover, establishing a mandatory years-long period of exclusivity for biologics in an internationally binding treaty limits U.S. sovereignty and removes the ability to make changes to U.S. law in the future, when it becomes clear that the market can sustain greater competition.⁹⁷ Increasing branded company exclusivities that block market access to more affordable biosimilar products slows U.S. innovation in the growing biosimilar market and keeps costs for these important medicines high. This would also be expected to have strong negative effects on drug pricing for patients in the U.S., and AAM would therefore oppose such provisions.

The problem with current trade proposals supported by brand-name pharmaceutical companies is that the carrot of delaying global biosimilar and generic competition does not include any stick for bringing brand-name drug prices under control in our country. USTR should not be advocating for the global export of a patent system that President Trump himself complained can be “used as a shield to protect unfair monopolies.”⁹⁸

Rather than export a U.S. pharmaceutical patent system that has often been abused and has allowed, through such “unfair monopolies” that President Trump has mentioned, U.S. drug prices to become the most expensive on Earth, our trade agreements can bring down prices by enhancing generic and biosimilar competition with brand name pharmaceuticals.

⁹⁶ OECD. “Pharmaceutical Market Statistics.” Available at: https://stats.oecd.org/Index.aspx?DataSetCode=HEALTH_PHMC. Accessed: July 5, 2018.

⁹⁷ OECD. “Tackling Wasteful Spending on Health. Highlights”, January 2017. Available at: <https://bit.ly/2MP6XAS>. Accessed: July 5, 2018.

⁹⁸ Remarks by President Trump on Lowering Drug Prices. Available at: <https://bit.ly/2lavgvh>. Accessed: July 5, 2018.

HHS Should Support U.S. Trade Policy that Lowers Drug Prices for Patients in the U.S.

AAM supports provisions in U.S. trade agreements that balance the interests of branded pharmaceutical companies and promote access to medicine and the substantial cost savings that generic and biosimilar pharmaceuticals provide. This balance is reflected in both the intellectual property rights negotiating objectives in the Bipartisan Agreement on Trade Policy (May 10 Agreement) provisions regarding IPR and public health. These principles strike the appropriate balance between promoting innovation and fostering access to affordable medicines.

Instead of increasing exclusivity protection for brand-name pharmaceuticals through trade agreements, USTR's policy should align with the President's Blueprint to enhance generic drug and biosimilar competition. AAM supports the trade policies below to achieve this goal:

- Enhance generic competition by requiring an incentive to challenge patents/exclusivities and granting a reward to those that do so. Trade agreements should require full transparency and a public registry for all patents and exclusivities granted to a drug. Currently, the U.S. is one of the only countries in the world that has an intellectual property framework that includes a reward to promote generic competition. This framework has served as a successful incentive to challenge the validity or applicability of weak patents, thus helping to ensure the expedited entry of generic drugs to the market for the benefit of patients, insurers and U.S. taxpayers. This mechanism, which is often referred to as "paragraph IV 180-day exclusivity," has been, since its implementation, a driver of early generic access and has contributed greatly to the number of patent challenges. Establishing a formal system, akin to 180-day exclusivity in the U.S., would enhance the market for U.S.-made generic medicines in other countries. In addition, there should be a transparent system with a public listing of all patents. Such a system would be facilitated by the creation of a public registry of applicable pharmaceutical patents akin to the U.S. FDA's Orange Book.
- Regulatory Review ("Bolar") Provision. Consistent with U.S. law, a regulatory review clause in trade agreements allows generics and biosimilars manufacturers to use a patented invention during the period of the patent term without the consent of the patent holder for the purposes of developing information to obtain marketing approval from health regulatory authorities. The regulatory review clause is an important provision that facilitates the production and introduction of generics and biosimilars manufacturers into the market on the date of patent expiry. Inclusion of such a provision in trade agreements will allow for the more rapid development of generics and biosimilars and sales with our trading partners. Trade agreements should expressly provide for mandatory and broad Bolar provisions to ensure the expedited launch of generics and biosimilars.
- Best Mode. According to the Trade-Related Aspects of Intellectual Property Rights (TRIPs) Agreement⁹⁹, patent authorities may require the applicant to indicate the best mode for carrying out the invention known to the inventor at the filing date or, where priority is claimed, at the

⁹⁹ World Trade Organization. "Agreement on Trade-Related Aspects of Intellectual Property Rights." Available At: <https://bit.ly/2hfZzQR>. Accessed: July 5, 2018.

priority date of the application. Therefore, under the “best mode” requirement, if there are several ways in which the invention may be put into practice, the applicant can be required to disclose that which is most practicable. Trade agreements patent provisions should make disclosure of the best mode mandatory.

HHS Should Support USTR Efforts to Address Technical and Regulatory Barriers to Trade in Pharmaceuticals

The pharmaceutical sector is global in nature and U.S. companies are currently unable to leverage fully their global supply chains when seeking to bring new generic or biosimilar medicines to market. The regulatory environment for generic medicines has not kept pace with the market-driven globalization of pharmaceutical supply chains. Trade agreements present an opportunity to address technical and other regulatory barriers that restrict market access for U.S. exports of generic and biosimilar products. Specifically, trade agreements should incorporate provisions to address:

- **Regulatory Harmonization and Recognition.** The inclusion of regulatory harmonization provisions in trade agreements to facilitate a single development program and decrease the burden of redundant inspections by regulators will expedite development and trade in prescription medicines generally.
- **Regulatory Approval Backlogs for Generic Drugs.** Regulators should address any approval backlogs for generic medicines with special emphasis on expediting the approval of “first generics” – instances where there is no generic competition with the branded drug.

Balanced trade agreements can help ensure a robust global generic and biosimilar industry to bring safe, affordable, FDA-approved generic and biosimilar medicines to patients.

Conclusion

AAM and the Biosimilars Council commend the Administration’s consideration of policy options in the context of the entire pharmaceutical ecosystem, including regulatory, reimbursement and market-access incentives. Changes to one area or program must take into account potential impacts to other programs or parts of the drug system to mitigate unintended consequences. To that end, we encourage the Administration to maintain this system-wide perspective as comments are considered and incorporated into future policy proposals.

Appendix 1

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