

July 16, 2018

**VIA ELECTRONIC SUBMISSION** at [www.regulations.gov](http://www.regulations.gov)

The Honorable Alex Azar  
Secretary  
Department of Health and Human Services  
200 Independence Avenue, S.W.  
Washington, D.C. 20201

**Re: HHS Blueprint to Lower Drug Prices and Reduce Out-of-Pocket Costs (RIN 0991- ZA49)**

Dear Secretary Azar:

Novartis Services, Inc. is submitting this letter on behalf of Novartis Pharmaceuticals Corporation (NPC), Sandoz Inc. (Sandoz) and Alcon Laboratories, Inc. (Alcon). We refer to NPC, Sandoz, and Alcon collectively herein as “Novartis.” We appreciate the opportunity to provide comments in response to the *HHS Blueprint to Lower Drug Prices and Reduce Out-of-Pocket Costs* Request for Information (RFI) issued on May 16, 2018 by the Department of Health & Human Services (HHS or the Department).

NPC researches, develops, manufactures, and markets innovative medicines aimed at improving patients’ lives. We offer a broad range of medicines for cancer, cardiovascular disease, inflammatory disease, infectious disease, neurological disease, eye disease, organ transplantation, respiratory disease, and skin conditions.

Sandoz is a leader in generic pharmaceuticals and biosimilars, providing access to a broad portfolio of high-quality, cost-effective prescription drugs. Sandoz launched the first biosimilar approved under the Biologics Price Competition and Innovation Act (BPCIA) pathway in the United States.

Alcon is a leader in the research, development, manufacturing, and marketing of eye care products, including surgical devices and vision care products.

Our mission is to discover new ways to improve and extend people's lives. We use science-based innovation to address some of society's most challenging healthcare issues. We discover and develop breakthrough treatments and find new ways to deliver them to as many people as possible.

## I. Overarching Topics

Novartis believes that prescription drug reimbursement in the United States (U.S.) should be modernized to account for the highly innovative drugs currently coming onto the market, including future pipelines of cell and gene therapies and other high value, innovative treatments that offer the potential to cure illnesses, as well as biosimilars and generics that offer the opportunity to increase patient access and reduce costs across the healthcare system. While we have commented below on various, specific aspects of the RFI, Novartis believes the following key policy initiatives should be central to any HHS modernization effort with regard to U.S. drug payments:

- Shift the U.S. healthcare system to value-based pricing principles for pharmaceuticals and other healthcare services;
- Remove regulatory barriers and encourage the Center for Medicare & Medicaid Innovation (CMMI or Innovation Center) to test specific value-based models, including indication—based pricing, that appropriately hold the healthcare system accountable for outcomes while providing incentives to reinvest in innovation;
- Promote innovation and competition through biosimilars, and ensure appropriate access to these products while reinvesting the savings from their use into future innovation;
- Ensure modernization of Part B drug reimbursement, including appropriate payment for high value, innovative products, such as cell and gene therapies;
- Modernize the Part D rebate system, including ending the gaming associated with this structure by ensuring the value of rebates are passed on to beneficiaries to the maximum extent possible and protecting the innovation that brings highly ground-breaking products to market;
- Reduce beneficiary out-of-pocket costs in Medicare Part D by updating regulatory requirements to put more accountability on plans;
- Facilitate Medicaid participation in value-based initiatives without tightening formularies in a way that diminishes beneficiary access to needed therapies;
- Refocus the 340B Drug Discount Program to better align with the program's original intent and serve vulnerable patients;
- Advance policies that prevent the use of Risk Evaluation and Mitigation Strategies (REMS) to block generic drug development and improve the Food & Drug Administration's (FDA's) Reference Listed Drug (RLD) site to provide more context for information presented; and
- Incorporate digital technology to improve quality while lowering costs.

While this is an appropriate time to modernize and account for changes in how prescription drugs are provided to Medicare and Medicaid beneficiaries, any changes must be phased-in, with a mechanism for evaluating adverse or unintended impacts to access or beneficiary out-of-pocket costs. Both incremental changes, especially in respect to Part B medications, and broader changes, should be studied, and an appropriate process should be created to allow results to be incorporated before widespread change. Changes should be implemented across the entire healthcare spectrum, not just prescription drugs, so that the significant savings from appropriate

medication usage can be captured in other payment systems, as opposed to evaluation only in a siloed manner. Transparency should exist across all healthcare services, especially in the context of value-based models, with information provided that can assist beneficiaries in fully understanding the cost of their healthcare and improve their general understanding of the various therapy options available in some relative way.

All changes must be implemented in a way that does not compromise access or increase beneficiary out-of-pocket costs. The Centers for Medicare & Medicaid Services (CMS) must focus on broad changes in behavior, such as instructing CMMI to develop value-based models that fundamentally change the way that products are provided and billed. By way of example, an indication-based pricing pathway for certain products would be a fundamental shift in providing broader access to high value, innovative products such as cell and gene therapies, and would generate savings for Medicare.

Lastly, the significant savings from biosimilar use must be appropriately encouraged across the entire healthcare spectrum, so that the meaningful savings from these products can be captured and reinvested in innovation. A recent report from the RAND Corporation suggests the potential savings from biosimilars could be significant - \$54 billion in direct spending on biologic drugs from 2017-2026 with a range of \$24 to \$150 billion.<sup>1</sup> Recent reimbursement changes for biosimilars are a strong start, but more needs to be done to spur greater use of these products. Biosimilars are an example of an area ripe for a CMMI pilot. As discussed further below, a pilot could test savings to be gained from programs such as a copay sharing approach that would incentivize greater use of biosimilars and provide broader savings to the Medicare and Medicaid programs.

Novartis welcomes the opportunity to work collaboratively with HHS on the many recommendations and potential solutions outlined in this document and partner in evolving the U.S. pharmaceutical pricing and reimbursement system.

## **II. Overview of Novartis Comments**

Novartis appreciates the opportunity to provide feedback as HHS considers numerous proposals aimed at lowering drug prices and out-of-pocket costs for beneficiaries. We believe all patients deserve access to needed prescription medicines that can improve, sustain, and save their lives. Prescription drugs contribute significant value to the health care system when utilized appropriately. We encourage HHS to pursue policies that preserve or expand the access to, and affordability of, prescription drugs and be mindful of the possible unintended consequences of new policies as the Department moves forward.

Below is a brief summary of certain key aspects of our comments:

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<sup>1</sup> Andrew W. Mulcahy et al., Biosimilar Cost Savings in the United States: Initial Experience and Future Potential, RAND Corporation (2017), *available at* [https://www.rand.org/content/dam/rand/pubs/perspectives/PE200/PE264/RAND\\_PE264.pdf](https://www.rand.org/content/dam/rand/pubs/perspectives/PE200/PE264/RAND_PE264.pdf).

- **Shifting the U.S. Healthcare System to Value-Based Pricing Principles:** Novartis has long supported the use of value-based pricing principles in the U.S. healthcare system. Current healthcare system limitations have restricted the use of true value-based pricing or contracting approaches for pharmaceuticals. We encourage CMS and other U.S. healthcare stakeholders to collaborate in shifting to a value-based pricing approach that can ensure patient access to innovative medicines that are priced based on the value they deliver, with reasonable patient out-of-pocket costs. While taking time to transition to this new approach, we see near-term promise in value-based tools and models such as indication-based pricing that align value and remove barriers to access. Any new value-based model should be tested through a demonstration that is voluntary, narrow in scope and scale, includes all necessary waivers, and is only launched after sufficient opportunity for stakeholder input. Importantly, value should be measured by determining the total benefit of the product, including improvements in patient outcomes, as well as related cost savings that benefit the healthcare system and society as a whole.
- **Biosimilars:** We support HHS' efforts to increase the use of biosimilars. To date, several policies have already changed to enable a more level playing field between biosimilars and biologics but further action could do more to incentivize the use of biosimilars. To that end, among other steps, we encourage CMMI to enable value-based arrangements designed to spur the use of these products and provide additional incentives to help lower patient cost in Part D. We have provided comments on interchangeability, as well as comments on ways to improve the development and review process, steps to enhance the Purple Book, and further education efforts needed for providers and patients.
- **Part B:** We support modernizing the Part B drug reimbursement program by moving certain products, when appropriate, from Part B to Part D and/or utilizing a properly designed Competitive Acquisition Program (CAP). As discussed more fully below, we believe any change to Part B must be phased-in slowly with adequate time to study the impact of the changes and adjust accordingly. For purposes of moving drugs from Part B to D, it is critical to identify the most appropriate drugs for this policy shift. We recommend beginning with a subset of products and have provided below some criteria for CMS to consider as it determines which drugs may be viable candidates for such a move. For purposes of CAP, we have identified below several characteristics we believe are important for a successful launch of this program, including starting with a phased-in approach, providing adequate physician incentives, ensuring beneficiary access to necessary drugs, and appropriate selection of products for the program.
- **Part D:** The Part D program has been a success since its enactment over a decade ago, enabling beneficiary access to a wide range of prescription therapies. We urge HHS not to take any action that would diminish the value of the program for the seniors it serves. That said, we support modernizing the Part D program as long as beneficiary access to prescription drugs is not compromised. We are supportive of any efforts to improve cost predictability and affordability for seniors, including

through establishment of an out-of-pocket spending maximum, provision for sharing point-of-sale rebates, and increased transparency throughout the Part D program. We are concerned that proposals that would increase costs for beneficiaries or limit access, such as any effort to erode the current Part D protected classes, exempt manufacturer coverage gap discounts from true out-of-pocket spending (TrOOP), and eliminate the two drug per class requirement would yield detrimental consequences for beneficiaries.

- **Medicaid:** We support updating the Medicaid program to better meet the needs of patients, while preserving access to necessary therapies. We oppose any lifting of the inflationary rebate cap, which ultimately could affect the availability of drug products to government purchasers and others. We urge HHS to consider policies that would facilitate state participation in value-based initiatives; permit appropriate access to supportive services for certain products and services to encourage medication adherence; and, for purposes of new drugs, encourage state Medicaid programs to engage in early communication with manufacturers to promote better planning and ensure timely access to newly approved, innovative therapies. We are concerned about policies that would allow states to tighten formularies in a way that diminishes patient access to needed therapies. While this state flexibility may be intended to lower the cost of prescription drugs, we believe many patients would be denied appropriate access to life-sustaining or life-saving treatments, which would harm beneficiaries and, ultimately, lead to increased costs for the system as a whole.
- **340B Drug Discount Program:** We support refocusing the 340B Drug Discount Program (340B program or 340B) to better align with its original intent and serve vulnerable patients. We encourage HHS to reconsider several 340B policies of concern including those related to penny pricing, netting of over and under charges, the definition of patient, contract pharmacies, and child sites.
- **Risk Evaluation and Mitigation Strategies Distribution Restrictions:** As a leading manufacturer of generics, Novartis supports policies that prevent the use of REMS to block generic drug development. We are concerned that the structure and content of FDA's RLD site leads the public, including patients and providers, to believe that all manufacturers listed on the site have participated in "gaming" tactics to delay generic competition. We urge FDA to provide more context for the information presented on the site and, additionally, provide notice to manufacturers of any complaint so there is an opportunity to investigate the issue internally and potentially bring resolution.

### III. Response to Solicitation of Comments

HHS presents a variety of wide-ranging proposals and questions in the RFI. We appreciate the Department's interest in exploring many different policies that may help to achieve its aim. Below we have focused our comments on those where we, as a company, have insight given the nature of our products and our experience in the market.

## **A. Shifting the U.S. Healthcare System to Value-Based Pricing Principles**

### **1. General Comments**

Pharmaceutical innovation has provided tremendous value to society. For example, medicines have accounted for 50-60 percent of the increase in cancer survival rates and have reduced mortality associated with heart disease.<sup>2</sup> Rheumatoid arthritis patients experienced a 50 percent chance of complete clinical remission after 52 weeks of treatment when treated with a combination therapy consisting of both a new and older medicine, compared with 28 percent when treated with only the older medicine.<sup>3</sup> Further, innovative medicines have been critical to effectively managing chronic illnesses such as a diabetes and hypertension.<sup>4</sup>

To continue this progress, we need to ensure access to innovation in a way that is sustainable for health systems. However, changing demographics are putting health systems around the world under immense budget pressure. The CMS Office of the Actuary expects U.S. national health spending to grow at an average rate of 5.5 percent annually over the period of 2017 through 2026, accounting for nearly 20 percent of the Gross Domestic Product by 2026.<sup>5</sup> Key drivers of these projected increases are an expected enrollment growth in Medicare due to an aging population, and increased per beneficiary spending in both the Medicare and Medicaid programs.

The current complicated model of drug pricing and patient access in the U.S. is reaching an inflection point. While industry critics focus on the rise in wholesale acquisition price (WAC) or gross drug prices, the reality is that pharmaceutical manufacturers receive an ever-decreasing portion of the price they charge when selling their products. In 2017, only 56 percent of the list price of branded drugs were received by manufacturers with the rest of the price funding discounts and rebates to other stakeholders, such as pharmacy benefit managers (PBMs), wholesalers, health plans and government payers while real net per capita spending on medicines continued to decrease for the third year

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<sup>2</sup> Frank Lichtenberg, The Expanding Pharmaceutical Arsenal in the War on Cancer, National Bureau of Economic Research Working Paper 10328 (February 2004), *available at* <http://www.nber.org/papers/w10328.pdf>; and Earl S. Ford et al., Explaining the Decrease in U.S. Deaths from Coronary Disease, 1980–2000, *New Eng J Med* (2007), *available at* <https://www.nejm.org/doi/full/10.1056/NEJMsa053935>.

<sup>3</sup> Joel Kremer, “COMET’s Path, and the New Biologicals in Rheumatoid Arthritis,” 372 *The Lancet* 347-348 (August 2008), *available at* [https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(08\)61001-6/abstract](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(08)61001-6/abstract).

<sup>4</sup> Denys Lau and David Nau, Oral Antihyperglycemic Medication Nonadherence and Subsequent Hospitalization Among Individuals With Type 2 Diabetes, 27 *Diabetes Care* 2149 (September 2004), *available at* <http://care.diabetesjournals.org/content/27/9/2149.full-text.pdf>; and David Cutler, et al., The Value of Antihypertensive Drugs: A Perspective On Medical Innovation, 26 *Health Affairs* 97 (January/February 2007), *available at* [http://www.chcanys.org/clientuploads/downloads/Clinical\\_resources/Clinical%20Articles/CVD\\_ValueofAntiHypertensiveDrugs.pdf](http://www.chcanys.org/clientuploads/downloads/Clinical_resources/Clinical%20Articles/CVD_ValueofAntiHypertensiveDrugs.pdf).

<sup>5</sup> Gigi A. Cuckler et al., National Health Expenditure Projections, 2017-26: Despite Uncertainty, Fundamentals Primarily Drive Spending Growth, 37 *Health Affairs* 482(2018), *available at* <https://www.healthaffairs.org/doi/pdf/10.1377/hlthaff.2017.1655>.

in a row.<sup>6</sup> At Novartis, while increasing our gross prices across our U.S. pharmaceutical portfolio by 5.4 percent in 2017, our net prices actually decreased by 2.1 percent driven by the continued increase of rebates and discounts to 49.5 percent.

The continuing gap between the gross and net prices in the U.S. fuels increasing confusion on the real price paid for pharmaceuticals by the healthcare system. Patients are seeing more administrative barriers such as prior authorization or step therapy that limit their access to the medicines prescribed by their physicians. In 2016, 82 percent of the 52,082 U.S. employers with 200 or more employees required prior authorization for medicines.<sup>7</sup> At the same time, patients utilizing specialty products with ever-increasing coinsurance benefits do not see the benefit of the lower net prices, but have their out-of-pocket costs calculated based on the higher gross price.

This antiquated system has resulted in minimal transparency as to the price that all stakeholders pay for a pharmaceutical product, and requires a variety of temporary “fixes” to overcome current barriers to access. Escalating rebates and contractual commitments fuel gross price increases that still result in low, or in recent years, negative net price increases. Pharmaceutical companies provide financial assistance, when permitted, through a variety of programs to qualified patients with no insurance or poor insurance coverage with insufficient benefits requiring high out-of-pocket costs. Patients require assistance with navigating the complex approval process for specialty products to ensure coverage by their insurer.

We call for a radically different system that values and rewards what matters most – the best outcomes for patients. This approach, widely known as value-based healthcare, is one of the solutions to delivering sustainable healthcare. In value-based healthcare, all stakeholders are incentivized to deliver the best possible outcomes for patients, healthcare systems, and society. This naturally improves the efficiency of health systems, by shifting resources away from wasteful medical interventions to those that add the most value. This will result in a system that better supports patients, protects their access to medicines, and provides overall savings to the healthcare system; while ensuring fair reimbursement for medicines and enabling the continued support of ongoing research and development for new innovative, life-saving treatments.

At Novartis, we want to accelerate society’s shift to value-based healthcare through a commitment to value-based pricing. We commit to transparently assess the value of our medicines (e.g., with a comprehensive definition of value across four pillars: clinical, patient, system and societal value). When pricing new products in that value-based manner, we call for a system that affords broad access to patients with minimal benefit design barriers (e.g., minimal use of prior authorization and step edit methodologies; reasonable patient out-of-pocket costs).

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<sup>6</sup> Medicine Use and Spending in the U.S.: A Review of 2017 and Outlook to 2022; IQVIA Institute (2018), available at <https://www.iqvia.com/-/media/iqvia/pdfs/institute-reports/medicine-use-and-spending-in-the-us-a-review-of-2017-and-outlook-to-2022.pdf>.

<sup>7</sup> James Robinson et al., Value-Based Pricing and Patient Access for Specialty Drugs, 21 JAMA 2169 (2018), available at <https://jamanetwork.com/journals/jama/fullarticle/2680859>.

In this way, drugs that can demonstrate value and are priced according to that value are unhindered in their ability to deliver that value. Models like this would encourage the use of drugs with a discernable benefit to the system, which would improve patient outcomes and increase the sustainability of the healthcare system as a whole. When partnered with useful programs and interventions, such as digital technologies, these models could have a dramatic beneficial effect on the system, including better patient health and lower costs.

As the payment and reimbursement systems evolve, many of the temporary “fixes” applied to the system in recent years would similarly evolve:

- The payment of ever-increasing rebates to middlemen and other stakeholders would be eliminated to deliver instead value-based prices directly to the market and patients.
- With the overall health system committing to more affordable patient out-of-pocket costs, insured patients would no longer require significant financial support programs funded by the pharmaceutical industry.
- With increased access to the treatments prescribed by their physician, patients would no longer need advisors to help them secure reimbursement through their insurers.

As we continue to focus our research and development efforts on the outcomes that matter most for patients, we seek solutions for diseases with high unmet need or illnesses where patient quality of life can be significantly improved. We will continue to identify partnership opportunities with government and commercial health systems to demonstrate, measure, and improve patient outcomes in diseases where we have expertise, building on our recent successes with innovative solutions for Entresto® and Kymriah®.

We encourage CMS and other U.S. healthcare stakeholders to collaborate with us in shifting to this new value-based system. Novartis commits to working closely with all stakeholders to bring this vision to a reality.

## **2. Advancing Value-Based Tools**

We recognize that the U.S. healthcare system will take time to evolve to this new model. Thus, during this transition, we see the need for additional value-based tools and models such as indication-based pricing (discussed further below) that can be tested more immediately and will begin to better align value and remove barriers to access.

We have long supported moving toward value-based tools as HHS evaluates ways to reward value rather than simply making payments based on the volume of services provided. We look forward to working with CMS on implementing the most promising approaches in ways that will most likely ensure success. We have previously engaged with CMS and the private sector on developing innovative approaches to pricing, which has afforded us the opportunity to understand first-hand many of the challenges and

opportunities associated with pursuing various value-based approaches. We understand how complex these models can be and have insight into structures and approaches that make these efforts effective and worthwhile.

As an initial matter, for any value-based initiative, it is critical to determine how value will be measured. Care must be taken to ensure value frameworks are not misused in ways that impose centralized, one-size-fits-all policies, impede patients' and physicians' ability to tailor care to individual needs and preferences, and hinder progress against unmet medical need. If not thoughtfully designed, value frameworks can produce output that is confusing for users, lack patient-centeredness, rely on limited evidence and data, and generally focus on pharmaceuticals rather than on the broad range of treatments and healthcare services.

In determining value for drugs, it is important to measure value by the impact of the product to the healthcare system as a whole. Holistic models allow drugs to reflect their value by offsetting other aspects of the healthcare system. Thus, for instance, in some cases, the cost of a product may be high but the net effect of that product may be to reduce overall costs to the system (e.g., by alleviating the need for care in an institutional setting; eliminating the chronic use of other medications). While it can be difficult to quantify, it is critical to look at the impact to the system as a whole in making any value determination.

Value-based purchasing arrangements generally require new models of reimbursement. As CMS looks to construct models, we encourage the agency to work collaboratively with manufacturers in doing so. For instance, there may be situations where it is appropriate and advantageous to provide manufacturers with historical data (e.g., relating to patient experience with the therapy) so manufacturers can assist CMS in crafting a demonstration that is both viable and likely to achieve success for all stakeholders. As discussed more thoroughly below, value-based models should be tested first through, for example, a voluntary demonstration program. Any demonstration should provide sufficient opportunity for stakeholders, including patients, providers, and manufacturers, to gather ample data and provide targeted feedback before pursuing such demonstrations. It should also be voluntary (with sufficient incentives to attract meaningful participation) and first tested on a narrow scope<sup>8</sup> and scale to rigorously evaluate the impacts on patients and ensure quality of care is never compromised. CMS will also need to ensure that all appropriate waivers are provided for any value-based pricing model as failing to do so could have unintended consequences on other aspects of drug payment policy and price reporting. Thus, for instance, as explained in more detail below, value-based contracts incorporating specific outcome guarantees should be excluded from the calculation of Best Price and other government reporting requirements (e.g., average sales price (ASP), 340B etc.). With these changes, manufacturers can take on more financial outcomes risk in these arrangements without the negative potential of inadvertently setting a new Best Price. In addition, CMS will

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<sup>8</sup> While we are proponents of testing on a narrow scope to identify and rectify any issues before launching more broadly, we balance this with understanding the need to have enough participation to adequately evaluate and measure the impact.

need to provide a waiver from the Anti-Kickback Statute where appropriate to alleviate potential compliance concerns that have discouraged manufacturers from successfully pursuing alternative payment arrangements in the past.

Several approaches could yield results in significantly reducing Medicare and Medicaid expenditures or improving quality, or both. Specifically, Novartis believes that any CMS demonstration must be focused on broadening access and realizing the significant cost savings high value, innovative products could impart across the healthcare system as a whole. Oftentimes, the additional expenditures for these products are small in comparison to the significant savings across the healthcare delivery spectrum, and the material improvements in quality of care and quality of life. Kymriah® is an example of a product that is priced at value compared to alternative treatments, and that generates remarkable improvements in care, quality of life, and longevity for certain patients. As an FDA-approved one-time administration innovative therapy that is manufactured specifically for each patient, Kymriah® and similar products provide a unique opportunity to implement a pilot around value-based care. Novartis submits the below examples of potential pilots to consider:

- CMS should encourage a new Part D approach for specific therapeutic areas linking price and access that allows manufacturers that price products at or below a determined “value-based” benchmark level (meeting criteria for rigor and independence) to receive limited (none or highly streamlined) prior authorization, step therapy and cost sharing requirements (or other utilization management controls) than those prevalent for other non-value-based price products. Drugs priced above the value-based benchmark could continue to encounter more stringent requirements. Such a model would incentivize manufacturers to price products according to the value delivered, and offset lower price points with appropriate utilization management controls. In other words, drugs charging value-based prices should be placed in an open access framework with highly limited utilization management controls and reasonable out-of-pocket costs for clinically appropriate patients.
- A pilot focused on a biosimilar copay sharing arrangement where part of the copay is waived for beneficiaries or carried by the health plan in order to incentivize use compared to higher cost innovator products.
- Pilots that combine adherent drug use with digital technologies to establish the evolved value proposition of coordinated care options available through new capabilities;
- Ophthalmology also offers CMS a unique opportunity for consideration of value-based approaches. Physician administered drugs for age-related vision conditions are among the top Part B pharmaceutical expenditures, and as the population continues to age, Medicare spending in this therapeutic area is expected to continue to grow. Alternative payment models specific to treatments for age-related vision conditions may offer the opportunity for savings to the federal government. The implementation of such models would be furthered by

the measurability of changes in disease activity and the ability to link such changes to the administration of treatment.<sup>9</sup>

- The management of heart failure (HF) is a major healthcare issue associated with a high mortality rate, frequent hospitalizations, and poor quality of life and is also an area prime for a pilot.<sup>10</sup> In the U.S., approximately 6.5 million patients aged ≥20 years have HF, with 960,000 new cases diagnosed each year (data from 2005 to 2013).<sup>11</sup> Heart failure among populations enrolled in Medicare is highly prevalent and has a tremendous impact on resource consumption. The prevalence of HF is about 11 percent among Medicare beneficiaries, but these patients with HF account for 34 percent of Medicare spending.<sup>12</sup> The high prevalence, significant disease burden and costs of HF in the elderly population with limited improvement in HF management highlights the need to focus on HF care in the Medicare population. In 2013, the American College of Cardiology (ACC)/American Heart Association (AHA) Task Force on Practice Guidelines published a comprehensive evidence-based guideline for the evaluation and management of HF patients, including managing chronic HF and managing hospitalized patients.<sup>13</sup> In 2016, the Heart Failure Society of America (HFSA) partnered with the ACC and AHA to provide coordinated guidance on the management of HF.<sup>14</sup> Accelerating the adoption of guideline directed medication therapy (GDMT) in clinical practice is critical to improve patient care. Optimizing GDMT could reduce total healthcare costs, improve quality metrics (e.g.,

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<sup>9</sup> Paul B. Ginsburg, Treatment-specific payment approaches: The case of macular degeneration, USC-Brookings Schaeffer on Health Policy (November 2017), *available at* <https://www.brookings.edu/blog/usc-brookings-schaeffer-on-health-policy/2017/11/27/treatment-specific-payment-approaches-the-case-of-macular-degeneration/>.

<sup>10</sup> Kenneth Dickstein et al., ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2008: The Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2008 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association of the ESC (HFA) and endorsed by the European Society of Intensive Care Medicine (ESICM), 29 Eur Heart J, 4388 (October 2008), *available at* <https://academic.oup.com/eurheartj/article/29/19/2388/2398014>.

<sup>11</sup> Emelia J. Benjamin et al., Heart Disease and Stroke Statistics – 2017 Update, A Report from the American Heart Association, J Am. Heart Ass'n (March 7, 2017), *available at* <http://circ.ahajournals.org/content/early/2017/01/25/CIR.0000000000000485/>.

<sup>12</sup> Kathryn Fitch et al., The High Cost of Heart Failure for the Medicare Population: An Actuarial Cost Analysis, Millman (February 2015), *available at* <http://www.milliman.com/uploadedFiles/insight/2015/heart-failure-cost-medicare-analysis.pdf>.

<sup>13</sup> Clyde W. Yancy et al., 2013 ACCF/AHA Guideline for the Management Of Heart Failure: A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, J Am. Heart Ass'n (June 5, 2013), *available at* <http://circ.ahajournals.org/content/early/2013/06/03/CIR.0b013e31829e8776>.

<sup>14</sup> Clyde W. Yancy et al., 2016 ACC/AHA/HFSA Focused Update on New Pharmacological Therapy for Heart Failure: An Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America, J Am Heart Ass'n (September 27, 2016), *available at* <http://circ.ahajournals.org/content/134/13/e282>.

reduction of 30-day hospital readmissions)<sup>15</sup>, and reduce mortality.<sup>16</sup> However, current infrastructure at the institution and physician-level present significant barriers on the use of GDMT, leading to disparities in care and unintended consequence of patient outcomes. As novel therapies are being integrated into routine practice, implementing evidence-based algorithms and evaluating the impact of GDMT on total cost of care and quality metrics is critical. We propose a demonstration project that would evaluate how optimal HF with reduced ejection fraction treatment, defined as per the 2017 ACC/AHA/HFSA Focused Update,<sup>17</sup> impacts the quality of care provided to Medicare beneficiaries and economic costs to the Medicare program.

### 3. Current Nature and Use of Value-Based Arrangements

Value-based arrangements are voluntary arrangements between manufacturers and other entities, such as health plans or risk-bearing providers, in which the price or price concession for a prescription medicine is linked to value as determined by the contracting entities.<sup>18</sup> Generally, the contracting parties agree to a payment structure tied to a set clinical goal or objective allowing the payer and manufacturer to share financial risk for failed treatment.<sup>19</sup> These arrangements allow manufacturers to show the effectiveness of their prescription medicine, which can be particularly important in the case of an innovative, high-value drug, and they allow payers to reduce uncertainty regarding clinical value, performance and financial impact.<sup>20</sup>

Value-based arrangements can take many forms and encompass many types of contracting strategies. Outcomes-based contracts (OBCs) typically include a rebate or discount that is provided by the manufacturer to the payer if a drug does not achieve the agreed upon clinical outcomes. As interest in moving the healthcare system from volume to value has increased, participation in value-based agreements has continued to rise in the United States. From 2015-2017, 16 risk-sharing contracts were publicly announced

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<sup>15</sup> Clyde W. Yancy et al., 2013 ACCF/AHA Guideline for the Management Of Heart Failure: A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, *J Am Heart Ass'n* (June 5, 2013), *available at* <http://circ.ahajournals.org/content/early/2013/06/03/CIR.0b013e31829e8776>.

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

<sup>17</sup> Clyde W. Yancy et al., 2017 ACC/AHA/HFSA Focused Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America, *J Am Heart Ass'n* (April 28 2017), *available at* <http://www.ahajournals.org/content/early/2017/04/26/CIR.0000000000000509>.

<sup>18</sup> Michelle Drozd, PhRMA Perspective: Government Policies to Support Innovative Contracting Approaches, *PhRMA*, 22 (October 2016), *available at* [http://www.cbiret.com/sites/default/files/files/Drozd\\_Michelle\\_pres\(1\).pdf](http://www.cbiret.com/sites/default/files/files/Drozd_Michelle_pres(1).pdf).

<sup>19</sup> Rewarding Results: Moving Forward on Value-Based Contracting for Biopharmaceuticals, Network for Excellence in Health Innovation (March 2017), *available at*, [https://www.nehi.net/writable/publication\\_files/file/rewarding\\_results\\_moving\\_forward\\_on\\_value\\_based\\_contracting\\_for\\_biopharmaceuticals\\_copy1.pdf](https://www.nehi.net/writable/publication_files/file/rewarding_results_moving_forward_on_value_based_contracting_for_biopharmaceuticals_copy1.pdf).

<sup>20</sup> Jeff Micklos and Caitlin Sweany, Economic Investment and the Journey to Health Care Value — Part II: Health Care Payers, 9 *New Eng J Med* 95, 95 (November 2017), *available at*, [https://ajpblive.s3.amazonaws.com/media/pdf/AJPB\\_0506\\_2017\\_NPC\\_Leonard.pdf](https://ajpblive.s3.amazonaws.com/media/pdf/AJPB_0506_2017_NPC_Leonard.pdf).

for drugs used in treating a variety of conditions including hepatitis C, diabetes, and cholesterol.<sup>21</sup> In 2016, the number of U.S. pharmaceutical outcomes-based deals grew by 254 percent, as compared per annum to arrangements put into effect from 2012-2015.<sup>22</sup> As of August 2017, there were 184 publicly announced value-based payer-provider contracts among the top five commercial payers.<sup>23</sup>

#### 4. Benefits of Value-Based Arrangements

Value-based arrangements are beneficial to manufacturers, payers, patients, and the healthcare system overall. In these arrangements, the manufacturer and payer are able to agree upon the expected health outcomes associated with use of a drug and if the drug does not produce those results, the manufacturer will provide a discount, rebate or refund to the payer. These arrangements allow for distribution of risk between payers and pharmaceutical manufacturers and provide transparency related to the value of a medication to patients.<sup>24</sup> As a result, value-based arrangements are able to facilitate patient access to therapies by providing a mechanism through which payers will agree to cover a manufacturer's drug while minimizing the payer's financial risk.<sup>25</sup> Value-based arrangements can be particularly helpful in securing access to therapies where clinical value has not yet been fully demonstrated.<sup>26</sup>

Importantly, value-based arrangements are able to improve patient outcomes while reducing costs for both patients and the healthcare system as a whole. For example, they improve patient outcomes by incentivizing payers to provide broader access to medicines that will benefit patients, regardless of cost, since the financial risk is balanced by the assurance that the payer will receive a discount if the medicine does not achieve the appropriate clinical outcomes. Value-based arrangements can also lower costs throughout the healthcare system by facilitating the use of cost-effective therapies that, when used, are able to save money by reducing the need for more expensive care, such as hospitalizations. A recent study found that payers who have implemented OBCs reported that the arrangements reduced patient costs and budget uncertainty.<sup>27</sup>

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<sup>21</sup> Justin S. Yu et al., Performance-Based Risk-Sharing Arrangements for Pharmaceutical Products in the United States: A Systematic Review, 23 J Manag Care Spec Pharm 1028 (October 2017), available at <https://www.jmcp.org/doi/pdf/10.18553/jmcp.2017.23.10.1028>.

<sup>22</sup> Ray Pressburger et al., No Time to Waste, Accenture (2017), available at [https://www.accenture.com/t00010101T000000Z\\_w\\_/gb-en/acnmedia/PDF-58/Accenture-no-time-waste-value-based-care-POV.pdf](https://www.accenture.com/t00010101T000000Z_w_/gb-en/acnmedia/PDF-58/Accenture-no-time-waste-value-based-care-POV.pdf).

<sup>23</sup> Id.

<sup>24</sup> Value-based pricing for pharmaceuticals: Implications of the shift from volume to value, Deloitte (2012), available at <https://www2.deloitte.com/us/en/pages/consulting/articles/value-based-pricing-for-pharmaceuticals.html>.

<sup>25</sup> Ashley Noble Value-Based Purchasing for Prescription Drugs, National Conference of State Legislatures (November 9, 2017), available at <http://www.ncsl.org/blog/2017/11/09/value-based-purchasing-for-prescription-drugs.aspx>.

<sup>26</sup> Tara Nazareth et al., Outcomes-Based Contracting Experience: Research Findings from U.S. and European Stakeholders, 23 J Manag Care Spec Pharm 1018 (October 2017), available at <https://www.jmcp.org/doi/pdf/10.18553/jmcp.2017.23.10.1018>.

<sup>27</sup> Id. at 1024.

In addition, by participating in these arrangements, pharmaceutical companies may be able to better understand value and direct research efforts to develop, more efficiently, products that are targeted at providing greater benefit to patients and payers. Also, the analysis of value-based arrangements could strengthen the data available for the purposes of post-market surveillance and the early identification of potential safety concerns with use of a particular product.<sup>28</sup> The information provided through the testing of these arrangements could also allow pharmaceutical companies to use the results from these arrangements to differentiate their products from those of their competitors to provide greater value and, in doing so, foster more meaningful innovation.<sup>29</sup>

## **5. Potential Value-Based Purchasing Models**

### **a. Indication-Based Pricing**

Fundamentally, an indication-based pricing model would evaluate how a therapy performs for one approved indication relative to another approved indication. Under this model, in concept, a baseline benchmark payment would be established for the therapy, providing a higher rate of reimbursement when the therapy performs better for a particular indication (relative to its other approved indications).

We view indication-based pricing as a promising value-based tool when used for appropriate products within a well-defined distribution structure to ensure accurate application of pricing. However, Novartis believes that while indication-based pricing might be an appropriate approach for certain products and therapeutic areas, it is not a broad based solution for system-wide challenges. For example, we recently adopted an indication-based pricing approach for Kymriah® with the approval of the second indication for DLBCL (Diffuse large B-Cell lymphoma), by lowering the WAC price for the new indication based on different patient outcomes in DLBCL. Novartis believes this was the correct approach for this highly innovative product with a well-defined distribution system based on an individualized therapy for a targeted patient set. The targeted nature of this approach and significant distinctions in price by indication will provide material value back to the broader healthcare system. However, this is not an approach that can be implemented across all products, based on the lack of well-defined and well-controlled distribution systems.

As researchers learn more about cancer and the pathways that allow cancers to grow, it has become increasingly more frequent that a combination of treatment modalities are employed in order to increase the chances for a successful response (e.g., treatment with chemotherapy and radiation, or a combination/cocktail of more than one infused chemotherapy agent). Additionally, combinations of predominantly oral therapies are becoming a vital part of cancer treatment. In some cases, a second, new drug is required because the cancer has become resistant to the initial drug when given alone. In other

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<sup>28</sup> Value-based pricing for pharmaceuticals: Implications of the shift from volume to value, Deloitte (2012), available at <https://www2.deloitte.com/us/en/pages/consulting/articles/value-based-pricing-for-pharmaceuticals.html>.

<sup>29</sup> Id. at 12.

instances, a patient's clinical and/or disease status may prohibit administration of the therapeutic dose due to toxicity concerns; yet, the drug could be effective at a lower dose if combined with a second therapy. In still other situations, two drugs given together have been found to be more effective than either drug given alone as initial treatment, resulting in the co-administration of both products in order to yield an optimal response. The value of combination therapies is also recognized in other disease areas, including rheumatoid arthritis, hypertension, and Crohn's disease.

Under the current system, combination oral cancer therapy usually requires separate prescriptions and separate patient cost sharing. In many cases, the oral therapies needed are available only as branded drugs (the patent has not yet expired), and cost-sharing under commercial plans and public programs would require the patient to pay separate cost-sharing for each drug. The WAC of oral drugs is assigned based on the National Drug Code. Changes to pricing metrics, government price calculations, and billing would be required in order to enable manufacturers the flexibility to assign different pricing to branded drugs when they are used in combination, either with another drug from the same manufacturer, or with a branded drug from a different manufacturer. The assigned prices should be able to reflect the value of the combination therapy to the patient, healthcare system, and society. More broadly, current government price reporting and other Medicare administrative limitations exist that can create financial disincentives for providers of products with indication-based pricing and limit the value for Medicare. Therefore, we call for a demonstration model to test modifications to the Medicare Part B reimbursement system that would seek to establish new government price reporting methodologies and appropriate financial incentives for providers who embrace indication-based pricing. Novartis has invested significant resources in evaluating a potential indication-based pricing pathway, and believes that implementation of such a pathway will lead to greater beneficiary access to highly innovative products while generating considerable savings for CMS.

In initiating this sort of model, we recommend CMS select the specific drugs involved by soliciting proposals from manufacturers on a voluntary basis. This will allow the market to determine which drugs are most suitable, as not all drugs are. The market should also determine the price of each indication; an indication-specific price should not be set by government. In addition, the confidentiality of net prices and other proprietary information should be maintained. When evaluating indication-based prices, plans should use the full range of available evidence, including real-world evidence, for the product. This sort of model should be tested on a small scale first – targeting only limited type(s) of drugs and/or providers and the agency should determine the implications before expanding this concept more broadly. From an operational standpoint, for this model, we encourage CMS to issue J codes for products on an indication-specific basis so that manufacturers can price and track product usage on such basis.

We understand that any indication-based model could have significant operational and implementation challenges, including concerns around government price reporting and beneficiary cost-sharing. As mentioned above, this model would likely require changes in coding (or creation of additional codes). In addition, measures would need to be taken

to protect against abuse (e.g., providers buying the product for the lower priced indication but then billing for the higher priced indication). However, if structured appropriately, indication-based pricing has the capacity to lead to a more effective marketplace, one that provides greater access to drugs and savings to CMS.

### **b. Long-term Financing Models**

In light of typical state budgeting processes, long term financing models are being proposed to help states, insurers, and consumers pay for high cost treatment by spreading payments over a number of years. The RFI contains a number of questions about these models, including their impact on manufacturer development decisions and barriers that might limit the applicability of these arrangements in the private sector. While our view on these models is dependent upon a number of factors, as a general matter, we support efforts to make payments for high value, innovative products, such as cell and gene therapies, more predictable for states and other payers. Further, we could support, where appropriately structured, financing/insurance/reinsurance concepts to address affordability for patients and other key market stakeholders.

Novartis believes that these models could provide significant benefits to state Medicaid programs in both flexibility and predictability of payments, and also significantly improve patient access to high value, innovative therapies. Additionally, creative financing alternatives such as long-term financing models could potentially encourage innovation and patient access, while making high value, innovative products sustainable for payers and Medicaid programs. However, manufacturers and payers should tailor solutions to specific disease and therapy characteristics to be effective.

Further, Novartis believes that to be implemented correctly, these models need to adjust for the inevitable movement of beneficiaries across healthcare plans, and that controls and contingencies would have to exist within these approaches. For example, it would be crucial to account for the cost of disease cured by a therapy paid for by another payer. Another example is how to account for beneficiary movement across healthcare plans or Medicaid programs. Additionally, many therapies have financial costs and benefits at different times, creating gaps between initial and downstream payers when patients switch payers between the initial therapy payment and subsequent cost effects. A model that separates the total cost of a specific drug into discrete milestones, in which the milestones follow the patient across multiple payers and over time while tracking health outcomes, could neutralize any negative impact to payer long-term savings from their payment for these products from insurer or Medicaid changes.

As we have recommended previously in testing any new reimbursement model, any long-term financing model should be voluntary and tested on a small scale to fully understand the implications and unintended consequences of such an arrangement. As in other value-based models, CMS should consider the barriers that could disincentivize participation in long-term financing models, such as the Anti-Kickback Statute and price reporting requirements. However, Novartis supports consideration of this and other creative alternative financing solutions, and believes that well-designed mechanisms

could help ensure economic incentives for future drug development, ensure appropriate patient access, and provide a payer value proposition.

## 6. Guiding Principles for CMMI Demonstrations

Since we anticipate CMS may test certain value-based purchasing models through CMMI, we highlight below comments we have previously provided to the agency on guiding principles for CMMI demonstrations.<sup>30</sup> However, we note, and discuss more fully below, that CMMI often may not be an appropriate place to test value-based arrangements. CMMI does not have authority to adequately address certain issues that serve as barriers to these arrangements, including issues related to Medicaid Best Price. That said, for purposes of any demonstrations implemented through CMMI, we believe any new model should be voluntary, reduce burdensome requirements, and be tested on a small scale first. For purposes of small scale testing, we encourage the agency to limit any new models both in terms of scope (e.g., number of beneficiaries included) and duration.

Importantly, we encourage CMS to formalize guiding principles for CMMI demonstrations in regulation prior to issuing new models. These principles are critical to ensuring predictability for stakeholders and will assist in gaining interest from the private sector. They would also help guard against unintended consequences for beneficiaries. In addition, in any such rulemaking, we encourage CMS to include further detail about CMMI's process for model development and stakeholder engagement, as well as anticipated utilization of information gained through demonstrations to work with Congress in more broad reforms to the Medicare and Medicaid programs. Establishing through regulation a more predictable and consistent format for CMMI initiatives would be useful as the private sector seeks to engage with the agency on these issues.

Below are a few guiding principles applicable across a variety of models that we encourage CMS to incorporate as it considers new models to test through CMMI:

- **Ensure Beneficiary Access to Care:** Changes in reimbursement can impact incentives and behavior. In developing new models, we encourage CMS to consider first whether the model is likely to compromise beneficiary access to care. Innovative therapies are an important tool in improving beneficiary outcomes and lowering overall costs. CMMI should ensure that any new model maintains or improves access to such therapies. This issue of access to care underscores the need to test on a small scale initially.
- **Drive Improvements in Quality:** Any new model should maintain or improve quality. To that end, we encourage CMS to use well-developed, scientifically sound, valid, reliable outcome measures that can demonstrate improved quality. Alongside outcome measures, we encourage use of thoughtful process measures that closely tie to the desired clinical outcomes whereby the processes support achievement of

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<sup>30</sup> Novartis comment letter submitted on November 20, 2017 in response to Innovation Center New Direction RFI (September 20, 2017).

the desired outcome. Such measures should also provide meaningful and actionable information to providers so that they are able to identify how to improve the quality of care they are rendering. Furthermore, we encourage use of measures that apply across a wide patient population, both prevalent conditions and those less common, as a means of evaluating quality and ensuring that patients of all types are receiving the best possible care. In addition, any quality measures used should be consistent with applicable treatment guidelines issued by relevant medical societies. If such treatment guidelines recommend certain therapies, then the use of the treatment should count toward fulfilling the quality measure.

- **Seek Sufficient Stakeholder Input:** The specifics of any proposed model are important and stakeholders need those details in order to provide CMS with a thoughtful assessment. We encourage CMS to consistently solicit input from stakeholders through a meaningful process, such as a request for applications or a proposed rule, before implementing any new model.
- **Provide Necessary Waivers:** Certain new models may require waivers from existing laws. For instance, as explained in more detail below, we believe it is particularly important to provide waivers from the Anti-Kickback Statute when necessary and exclude value-based prices from Best Price and other government reporting requirements (e.g., ASP, 340B etc.). We encourage the Innovation Center to consider these and additional laws that need to be waived within the context of any model design and to seek additional waiver authority where necessary. We caution, however, that the agency's waiver authority should not be used as a means to make de facto changes in law (which could happen, for instance, if the waiver is applied on a nationwide basis). In addition, as discussed below, the Administration should consider a new safe harbor that includes clear standards to protect value-based arrangements. Providing a specific safe harbor would encourage greater participation in these novel arrangements, and facilitate the healthcare system's movement towards improving patient outcomes, while reducing healthcare costs.
- **Consider New Model Interaction with Existing Models:** Prior to implementing any new model, we encourage the Innovation Center to consider how that model will interact with existing models and/or other applicable payment reforms. Ultimately, overlapping requirements and increased administrative burdens can impact quality of care. Combined implementation can also make it difficult to test each of the individual models.
- **Preserve Positive Aspects of the Existing Medicare and Medicaid Programs:** In designing new models, we encourage the agency to retain positive aspects of the existing Medicare and Medicaid programs, particularly those that foster market-based competition (such as the noninterference clause) or ensure patient access to treatment (such as the Part D protected classes policy).
- **Establish A Consistent, Predictable, and Reliable Mechanism for Evaluating Models:** For new models, we encourage CMS to provide interim reporting during the

course of any demonstration, provide transparency on the impacts observed, and include a process by which the demonstration can be halted or restricted if harmful consequences are observed (e.g., measurably diminished access to treatment).

## 7. Barriers to Value-Based Arrangements

The current regulatory environment was not designed with value-based arrangements in mind. As a result, several barriers<sup>31</sup> exist presently that inhibit value-based arrangements in both the private sector and federal healthcare programs, including Medicaid Best Price, the Anti-Kickback Statute, and certain price reporting requirements.<sup>32</sup> We discuss each of these issues more fully below:

- **Medicaid Best Price:** The issue of Medicaid Best Price presents a number of challenges within the context of value-based arrangements. For instance, depending on the nature of the agreement, product provided at low or no cost in certain instances (e.g., due to a poor outcome) can set a lower best price. It can also lower the 340B ceiling price, which furthers the financial exposure for the manufacturer. There are also more technical reporting questions that arise. For example, a manufacturer may not know a drug's final price when the quarterly best price reporting is due. In addressing these issues, we encourage HHS to ensure that a poor outcome does not set a new price for Medicaid. For purposes of reporting, we encourage HHS to keep the reporting as simple and straightforward as possible. Manufacturers should continue to have the ability to make reasonable assumptions in their price reporting, which enables a more equitable and nimble system.

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<sup>31</sup> Gregory Daniel et al., *Overcoming the Legal and Regulatory Hurdles to Value-Based Payment Arrangements for Medical Products*, Duke-Margolis Center for Health Policy, 35 (December 2017), available at [https://healthpolicy.duke.edu/sites/default/files/atoms/files/overcoming\\_legal\\_and\\_regulatory\\_hurdles\\_to\\_value\\_based\\_payment\\_arrangements\\_for\\_medical\\_products.pdf](https://healthpolicy.duke.edu/sites/default/files/atoms/files/overcoming_legal_and_regulatory_hurdles_to_value_based_payment_arrangements_for_medical_products.pdf); Alison Ward et al., *Regulatory, Legal Uncertainties Are Barriers to Value-Based Agreements*, Health Affairs Blog (November 2016, available at <https://www.healthaffairs.org/doi/10.1377/hblog20161104.057443/full/>); Academy of Managed Care Pharmacy, *AMCP Partnership Forum: Advancing Value-Based Contracting*, 23 J Manag Care Spec Pharm 1096 (November 17, 2017), available at <https://www.jmcp.org/doi/abs/10.18553/jmcp.2017.17342>; *Rewarding Results: Moving Forward on Value-Based Contracting for Biopharmaceuticals*, Network for Excellence in Health Innovation (March 2017), available at <https://www.nehi.net/publications/76-rewarding-results-moving-forward-on-value-based-contracting-for-biopharmaceuticals/view>

<sup>32</sup> We appreciate the recent issuance from the FDA of the final payer guidances that address manufacturers' communications with payers for value-based arrangement. *Drug and Device Manufacturer Communications with Payers, Formulary Committees, and Similar Entities — Questions and Answers Guidance for Industry and Review Staff*, FDA (June 2018), available at <https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM537347.pdf>; and *Medical Product Communications That Are Consistent with the FDA-Required Labeling — Questions and Answers Guidance for Industry*, FDA (June 2018), available at <https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM537130.pdf>.

- **Anti-Kickback Statute:** It is commonly understood that the Anti-Kickback Statute discourages widespread adoption of value-based arrangements. This statute is broad and contains serious ramifications for any violations.<sup>33</sup> The Anti-Kickback Statute was designed to prevent fraud and abuse in a fee-for-service reimbursement system and, therefore, does not adequately address the unique nature of new, value-based arrangements. As a result, manufacturers and payers are deterred from engaging in value-based arrangements due to the fear of inadvertently violating the Anti-Kickback Statute. The current regulatory framework must reflect the changing healthcare system that increasingly seeks to reward value. We urge HHS to work with the Office of Inspector General (OIG) to adopt a safe harbor designed specifically for value-based arrangements focused on manufacturers, payers, and large integrated healthcare systems, as this would encourage greater participation in such arrangements and potentially increase appropriate patient access to high value, innovative products.
- **Price Reporting:** There are a complex set of government price reporting rules for calculating ASP in Medicare Part B and Best Price in Medicaid. These detailed and highly technical reporting rules were put in place before the advent of innovative reimbursement approaches. While manufacturers are permitted to make reasonable assumptions, there is often ambiguity about how to capture certain aspects of innovative pricing methods for purposes of these calculations. We encourage HHS to continue to permit reasonable assumptions but also to provide clarity where needed.

Finally, we also encourage HHS to remove barriers to value-based arrangements in Medicare Advantage, Medicare Part D, and Medicaid. Improved use of value-based agreements in these programs could help reduce costs to both beneficiaries and taxpayers.

## 8. Value-Based Insurance Design Generally

In the context of value-based purchasing, we wanted to comment briefly on value-based insurance design (VBID) more generally. There are several principles we believe are important as CMS considers VBID. When establishing VBID cost-sharing it should be based on an appropriate assessment of value, not solely based on cost. Value should include benefits to patients, such as improved quality of life or allowing for a more productive life, as well as the reduction and prevention of more costly medical interventions, such as hospitalizations. Value should incorporate relevant clinical and quality measures and account for changes in evidence, clinical practice and innovations. Any assessment of value should be based on the full range of available evidence. Importantly, VBID should not lead to higher cost-sharing or fewer benefits for patients. As with any value-based design, we encourage CMS to ensure the model consistently enables patient access to therapies, including prescription drugs that meet their needs. We support CMS's efforts to advance VBID models and encourage the agency to continue to seek stakeholder feedback as it moves forward.

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<sup>33</sup> See 42 USC § 1320a-7b.

The Medicare Advantage Value-Based Insurance Design (MA-VBID) test is an opportunity for Medicare Advantage Organizations (MAOs) to offer supplemental benefits or reduced cost sharing to enrollees with CMS approved chronic conditions, focused on the services that are of highest clinical value to them. Specifically, the model is testing whether the additional flexibility provided to MAOs to develop and offer interventions can improve health outcomes and lower expenditures for MA enrollees. As the system continues to develop, it is important that VBIDs recognize the value of new prescription drugs and that the designs enable patient access to therapies that meet their needs.

Novartis supports policies recently finalized by CMS that enable greater flexibility under the uniformity requirements.<sup>34</sup> We believe this additional flexibility will ensure that VBID in Medicare Advantage is able to better align incentives, leading to care that is higher in value. We appreciate CMS's efforts to ensure the additional flexibility does not result in discriminatory benefit designs and urge the agency to take proactive steps to prevent and identify potential discrimination that would undermine the goals of VBID. For purposes of monitoring compliance with the non-discrimination responsibilities, we encourage the agency to collect relevant data from plans that would assist the agency in protecting beneficiaries from discriminatory practices. Such data could include beneficiary cost sharing amounts and the rationale for additional benefits along with the impact of those benefits on quality, outcomes, costs, and overall value.

## **B. Biosimilar Development, Approval, Education, and Access**

The Novartis portfolio includes both branded and biosimilar biopharmaceuticals, which requires us to consider both types of products when advocating for policy issues. The Novartis perspective is that novel and biosimilar biopharmaceuticals have important and complementary roles to play in healthcare: novel biologics bring new and innovative treatment options for patients, while high-quality biosimilars provide less costly alternatives to already established treatments, thereby increasing patient access to these therapies. This unique perspective positions Novartis as a credible source of scientific information on both novel biologics and biosimilars.

We appreciate the measures HHS has taken to improve the use of biosimilars and commend the Administration for continuing to look for additional ways to do so. Many of these measures have helped to level the playing field between biosimilars and biologics, but there is more that needs to be done to truly incentivize the use of biosimilars. The Medicare program will help shape the use of biosimilars in other markets, including the utilization of these products by commercial plans. For this reason, it is critical that CMS work to remove barriers to access in Medicare and Medicaid and take steps to incentivize

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<sup>34</sup> Medicare Program; Contract Year 2019 Policy and Technical Changes to the Medicare Advantage, Medicare Cost Plan, Medicare Fee-for-Service, the Medicare Prescription Drug Benefit Final Rule, 83 Fed. Reg. 16440 (April 16, 2018); and Announcement of Calendar Year (CY) 2019 Medicare Advantage Capitation Rates and Medicare Advantage and Part D Payment Policies and Final Call Letter, CMS (April 2, 2018).

the use of these products. As a company, we have invested heavily in biosimilar research and development, as well as regulatory and payment policy, and understand the positive impact that can flow from a healthy biosimilar market, both in terms of patient access to life-saving therapies and lower costs to patients and payers. A well-functioning generics and biosimilars market frees up resources to pay for new, cutting edge innovative treatments and therapies.

The emerging biosimilars market in the United States holds great potential to increase patient access to life-saving therapies, lower patient costs and bring savings to the healthcare system broadly. The importance of this market is particularly relevant now at a time when government programs are strained with growing healthcare costs and an aging population. A recent report from the RAND Corporation, a nonprofit research organization, estimates that biosimilars will lead to a reduction of “\$54 billion in direct spending on biologic drugs from 2017-2026, or about 3 percent of total estimated biologic spending over the same period with a range of \$24 to \$150 billion.”<sup>35</sup> The actual savings hinge on a variety of factors, including regulatory and policy decisions that shape the biosimilar market. Additionally, according to this RAND report, the “availability of lower-cost biosimilars may help providers respond to cost-control incentives put in place by payment policies and programs.”<sup>36</sup> In this way, biosimilars are an important tool to assist providers in managing patient costs in new payment structures, such as bundled payment models.

Below are several important steps CMS can take to incentivize the use of biosimilars:

- Enable value-based contracting arrangements that include necessary waivers designed to accelerate market entry and spur the use of these products. As mentioned above, we recommend conducting demonstrations to lower patient out-of-pocket costs (such as a copay sharing arrangement) to incentivize the use of biosimilars and test savings relative to innovator products in Part B and Part D;
- Adjust payments in the 340B program post pass through status to ensure biosimilars that have been on the market beyond pass through status are not disadvantaged relative to their reference product;
- Provide additional incentives in Part D, such as extending tiering exceptions for biosimilars on the specialty tier; and
- Assign unique J codes to biosimilars instead of using long-term Q codes for these products (as discussed more fully below under the section entitled, “Modernizing Part B”).

The RFI asks a series of questions relating to improving biosimilar development, approval, education, and access, including questions relating to interchangeability, improving the efficiency of the development and approval process, improving the Purple

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<sup>35</sup> Andrew W. Mulcahy et al., *Biosimilar Cost Savings in the United States: Initial Experience and Future Potential*, RAND Corporation (2017), *available at* [https://www.rand.org/content/dam/rand/pubs/perspectives/PE200/PE264/RAND\\_PE264.pdf](https://www.rand.org/content/dam/rand/pubs/perspectives/PE200/PE264/RAND_PE264.pdf).

<sup>36</sup> *Id.* at 13.

Book, and educating providers and patients. We have provided below more specific and extensive comments to various questions in the RFI related to these issues.

## 1. Interchangeability

Novartis believes that there is no scientific need or even justification for an additional regulatory interchangeability designation after biosimilarity has been established. The introduction of an additional step in the regulatory review process to establish interchangeability adds additional complexity, time, costs – for both manufacturers and regulators – and possible confusion with no established impact on efficacy or safety or relevant benefit to patients.

The additional statutory requirements for interchangeable products expects the product “to produce the same clinical result as the reference in any given patient” and that “for a biological product that is administered more than once to an individual, the risk in terms of safety or diminished efficacy of alternating or switching between use of the biological product and the reference product is not greater than the risk of using the reference product without such alternation or switch.”<sup>37</sup>

Novartis is concerned that the first criteria may imply that biosimilar products are of lower quality than interchangeable products and that as a consequence they are not considered to be equally safe or effective as the reference product in every patient. This is not correct as all approved biosimilar medicines in the U.S. have to meet the FDA's requirements, demonstrating there are no clinically meaningful differences in terms of purity, potency or safety to the reference medicine. This potentially confusing consideration is contributing to the misperception of biosimilars in the U.S. as described in the following section on education.

The second requirement is related to hypothetical increased risk of alternating or switching between the biosimilar and the reference medicine compared to the risk of using the reference medicine only. The cumulative data available from over 90 biosimilar single switch studies to date as well as three multiple switch studies does not support this potential concern.<sup>38</sup>

While Novartis does not support the separate status of interchangeable from biosimilar, we do believe that treatment decisions should be made by the treating physician and the patients. Further, Novartis believes that the currently available data support the safety of switches between a reference product and a biosimilar, or across biosimilar products.

It is of note that almost a decade after the enacting of the legislation, no products to date have been successfully developed/approved as interchangeable. Sandoz provided detailed comments on the draft interchangeability guidance and related challenges for

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<sup>37</sup> 42 U.S. Code § 262(k)(4).

<sup>38</sup> Hillel P. Cohen et al., Switching Reference Medicines to Biosimilars: A Systematic Literature Review of Clinical Outcomes, 78 *Drugs* 463 (2018), available at <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5854749/>.

industry, which may, at least in part, explain the current situation where no interchangeable biosimilars have been approved.

Based on the above, and considering that no product has been successfully developed/approved to date as interchangeable; Novartis continues to believe that there is no scientific justification for an additional interchangeable designation beyond approval of biosimilarity.

As mentioned above, should the HHS and the FDA consider maintaining the interchangeable status, Novartis would like to emphasize comments we provided on this topic through our Sandoz Division on March 22, 2016 (FDA-2015-P-4935-003) in which we commented on a Citizen Petition submitted to the Agency by AbbVie.<sup>39</sup> We also submitted detailed comments on May 10, 2017 on the draft interchangeability guidance and on the two questions posed in the associated Federal Register Notice (FDA-2017-D-0154-0024 and FDA-2017-D-0154-0023).<sup>40,41</sup> We reference each of these three submissions as an integral portion of this comment letter, along with all cross-references contained therein. The main challenges raised by the draft interchangeability guidance are related to:

- The recommended design of the switching study;
- The requirement to use U.S. reference product only in the trial(s); and
- The statistical evaluation of comparative use human factors studies.

Novartis has very specific concerns about these three challenges and is proposing steps that can be taken to rectify these shortcomings. Further details on these three topics are provided in Appendix A, entitled “Additional Comments on Interchangeability.”

## **2. Development and Review Challenges**

In the RFI, HHS states that FDA prioritizes efforts to improve the efficiency of the biosimilar and interchangeable product development and approval process. HHS is interested in specific types of information resources or development tools that would be most effective in reducing the development costs for biosimilars and interchangeable products.

### **a. Full Implementation of Biosimilar User Fee Act I and II**

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<sup>39</sup> Novartis comment letter comment letter submitted on March 22, 2016 in response to Citizen's Petition (Docket No. FDA-2015-P-4935), *available at* <https://www.regulations.gov/document?D=FDA-2015-P-4935-0003>.

<sup>40</sup> Novartis comment letter comment letter submitted on May 10, 2017 in response to FDA's Draft Guidance entitled, Considerations in Demonstrating Interchangeability with a Reference Product (Docket No. FDA-2017-D-0154), *available at* <https://www.regulations.gov/document?D=FDA-2017-D-0154-0024>.

<sup>41</sup> Novartis comment letter comment letter submitted on May 10, 2017 in response to two “Topics for Comment” in the FDA's Draft Guidance entitled, Considerations in Demonstrating Interchangeability with a Reference Product (Docket No. FDA-2017-D-0154), *available at* <https://www.regulations.gov/document?D=FDA-2017-D-0154-0023>.

According to FDA's Biosimilar User Fee Act (BsUFA) reports<sup>42</sup>, FDA has had mixed results with regard to its BsUFA performance. For example, in FY 2016, FDA met 12 of the 20 performance goals and in FY2017, FDA met 11 of the 19 performance goals – with similar performances in previous years. Of note, FDA has a 40 percent first cycle approval rate versus 60 percent first cycle complete response letters (CRLs) for biosimilar products. Additionally, while 140 of the 155 allocated Center for Drug Evaluation and Research (CDER) biosimilar positions have been filled (72 percent), only one of 15 positions allocated to guidance development and education has been filled. We would have hoped to have seen greater improvement in performance and hiring given the \$28.8M in BsUFA fees collected in FY 2017 and \$26.9M in FY 2016 (with \$48.6M carryover as of the conclusion of FY 2017).<sup>43</sup>

While we understand that the hiring challenges are not specific to the biosimilar program, we believe that further delays in hiring staff related to the review of biosimilar applications and biosimilar policy could further compound missed BsUFA goals and further hamper FDA policy efforts. It is critical that FDA fill these positions to ensure that the Agency can meet its BsUFA II goals, ensure that important biosimilar policies are implemented and conduct important education activities for patients and providers. Additionally, we believe FDA should prioritize hiring of the remaining BsUFA positions within CDER to ensure that the program as envisioned under BsUFA II will be implemented efficiently such that the enhanced communication, touchpoints and other milestones associated with sponsor-FDA interactions can be realized.

Lastly, the hiring of staff for biosimilar policy and education is of particular importance at this time given the ongoing misinformation campaigns that are detrimental to the acceptance of biosimilars in the U.S, and that are described below. Hiring for these positions is also critical in order for FDA to continue setting forth biosimilar policies, specifically finalizing and implementing many of the guidances that FDA has committed to in this space (e.g., equitable application of the biologics naming guidance to all biologics, including reference products for which biosimilars are already approved and are being marketed).

## **b. Use of Global Comparator Product**

The increasing number of countries developing biosimilar regulations shows their belief in the role of biosimilars in supporting the sustainability of healthcare systems. However, nearly all national or regional biosimilar regulations require the biosimilar to generate the comparability data (including clinical data) with the reference product licensed in the respective country or region. Practically, this often requires that a biosimilar

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<sup>42</sup> BsUFA Performance Reports, FDA, *available at* <https://www.fda.gov/AboutFDA/ReportsManualsForms/Reports/UserFeeReports/PerformanceReports/ucm384244.htm> (last updated April 25, 2018).

<sup>43</sup> BsUFA Financial Reports, FDA, *available at* : <https://www.fda.gov/AboutFDA/ReportsManualsForms/Reports/UserFeeReports/FinancialReports/BsUFA/default.htm> (last updated April 29, 2018).

manufacturer must repeat elements of the development program in each country where approval is sought.

Some streamlining efforts were already achieved when the FDA included in biosimilar guidance documents the possibility to accept certain development data for biosimilars generated with reference (comparator) product versions licensed outside their own jurisdiction, provided the reference (comparator) product is authorized in a jurisdiction with similar high scientific and regulatory standards (e.g. by the European Medicines Agency of the E.U.) and appropriate bridging data are provided. Biosimilar sponsors must submit an acceptable analytical and clinical bridge between the reference (comparator) product used during the biosimilar development and the US-licensed reference product to stay within the legal/regulatory framework. The studies establishing this bridge are not legally required and are at the discretion of the FDA.

A 3-way pharmacokinetic (PK) comparison (e.g. Biosimilar – U.S. -licensed reference product– EU-licensed reference product) typically requires 50-100 additional subjects in a clinical pharmacology study, which adds \$5-10 million in additional costs. Due to the multiplier effect of required repetition of these comparative studies by each biosimilar applicant and for the same US-licensed reference product, their collective costs are substantial and would not only be financially unsustainable but also ethically questionable. It is our view that these required clinical bridging studies do not bring any added scientific value, nor do they increase the safety of the biosimilar product or of the patient.

Bridging between comparator products sourced from various jurisdictions and reference products potentially exposes subjects to unnecessary, and therefore unethical, clinical trials. For example, a 3-way human bioequivalence-comparison as recommended by the FDA exposes additional subjects to potent drugs that often carry side effects.

Revisiting the requirement of these clinical bridging studies would be an important and effective tool in reducing the development costs for biosimilars and interchangeable products: access to these life-saving innovative medicines could be improved.

The bridge between the US-licensed reference product version and the reference (comparator) product version can indeed be established in most cases without clinical bridging studies while remaining within the current biosimilars framework. Therefore, we invite FDA to reconsider these biosimilar regulatory requirements and adopt criteria as described below for waiving these clinical bridging studies.

- 1. Initial criteria for the choice of the reference product (comparator product)**

- The chosen comparator product must be authorized by a Stringent Regulatory Authority (SRA)<sup>44</sup> (i.e., “in the jurisdiction that has a well-established regulatory framework and principles, as well as considerable experience of evaluation of the biotherapeutic products and post-marketing surveillance activities.”)<sup>45</sup>
- This means that the comparator product should be from “a jurisdiction that has formally adopted International Conference on Harmonization (ICH) guidelines. This criterion ensures that any comparability studies that have been conducted to support manufacturing changes of the reference have been conducted according to an internationally accepted process and standard, and also that the reviewing authority is experienced in operating this standard.”<sup>46</sup>
- The comparator product “should have been approved with a complete registration dossier, including safety and efficacy studies in each therapeutic indication. It should be fully identifiable (e.g. brand/invented/trade name, pharmaceutical form, formulation, strength, origin, lot number, number of batches, age of batches).”<sup>47</sup>
- A public assessment report must be available for a comparator product that was approved outside of the U.S. (e.g., European Public Assessment Report or the Summary Basis of Approval).

## **2. Initial criteria for waiving the bridging studies between the U.S. licensed Reference Product and the chosen comparator product**

The chosen comparator product must:

- meet the criteria of the comparator product as described above;
- have the same pharmaceutical form and route of administration as the U.S.-licensed reference product;
- have the same active pharmaceutical ingredient (API) as the U.S.-licensed reference product;
- have the same composition of excipients as the U.S.-licensed reference product;
  - if the compositions of excipients are different, data should show that the differences are without clinical effects.

This new scientific approach would also be in line with the FDA’s extensive engagement in robust regulatory and scientific discussions with other health authorities to support global development of biosimilars.

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<sup>44</sup> We note that the World Health Organization (WHO) is transitioning to new terminology and will assess Regulatory Authorities based on the WHO Global Benchmarking Tool. This transition may require further consultation on this topic.

<sup>45</sup> WHO Questions and Answers: Similar Biotherapeutic Products, WHO (December 2017), *available at* [http://www.who.int/biologicals/QA\\_for\\_SBPs\\_HK\\_12\\_Dec\\_2017\\_\(2\).pdf](http://www.who.int/biologicals/QA_for_SBPs_HK_12_Dec_2017_(2).pdf).

<sup>46</sup> Christopher Webster and Gillian Woollett, A ‘Global Reference’ Comparator for biosimilar development, 32 *BioDrugs* 279 (May 19, 2017), *available at* <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5541093/>.

<sup>47</sup> WHO Questions and Answers: Similar Biotherapeutic Products, WHO (December 2017), *available at* [http://www.who.int/biologicals/QA\\_for\\_SBPs\\_HK\\_12\\_Dec\\_2017\\_\(2\).pdf](http://www.who.int/biologicals/QA_for_SBPs_HK_12_Dec_2017_(2).pdf).

The use of a global reference standard is essential to support global regulatory convergence and sustainability of biosimilar development.

### **c. Enhanced Biosimilar Development Transparency**

In terms of facilitating development for biosimilar manufacturers, we request FDA to pool its knowledge from reference product reviews and approvals into a single, publicly available place that identifies FDA's current thinking on tiered critical quality attributes for reference products and on clinical study endpoint(s), either surrogate pharmacodynamic (PD) endpoint(s) or where it is not possible clinical endpoint(s), considered most sensitive for relevant indications (e.g., reference product snapshots available on FDA's website). This information could be created at two levels:

1. Generalizable to all potential biosimilars, and
2. Specific to a reference product.

FDA could place this information on its website in a transparent manner which would greatly streamline early biosimilar development. Additionally, it would potentially enable sponsors to identify the most appropriate analytical and functional parameters, improving the efficiency and the robustness of biosimilar development. Similarly for the clinical development of biosimilars, it would be quite valuable if the FDA could leverage the totality of the information it has access (and/or possibly in partnership with academic institutions or other organizations) to help identify the most sensitive endpoints (acceptable PD markers or where not possible clinical endpoints) for the purpose of biosimilarity evaluations in a relevant indication. We note that the FDA has done this via guidance (e.g., "FDA Guidance Pathological Complete Response in Neoadjuvant Treatment of High-Risk Early-Stage Breast Cancer: Use as an Endpoint to Support Accelerated Approval"), where it has used its experience reviewing applications for products to facilitate the development of new molecular entities in a specific indication. In total, this information would significantly streamline and increase the quality of biosimilar development and help to realize the potential of biosimilars to increase access and decrease costs for patients.

In addition, it has been observed for several reference products that drifts/shifts in critical quality parameters have been a serious challenge to biosimilar developers. When a biosimilar developer is forced to "chase" a moving target as the reference products shifts and drifts over time, this can be a dramatic obstacle to demonstration of biosimilarity, in particular in fulfilling FDA's stringent statistical requirements. Novartis welcomes the recent FDA decision to withdraw its draft guidance on "Statistical Approaches to Evaluate Analytical Similarity." Further, we acknowledge the Agency's intent to issue a new draft guidance that will include considerations about the appropriate methods to analyze analytical data to account for potential lot-to-lot variability of the reference product and the intent to provide appropriate flexibility for sponsors in order to help spur the efficient development of biosimilars without compromising the agency's rigorous scientific standards. This issue represents a major challenge that adds significant uncertainty in

the development of biosimilars. Novartis looks forward to the re-issued draft guidance and proposals on how to effectively mitigate this issue during the development.

### 3. Improving the Purple Book

The Purple Book provides information about reference products, biosimilars, and interchangeable products. HHS is interested in how the Purple Book could be more useful to providers, patients and manufacturers.

Novartis considers the Purple Book to be a valuable resource for patients, physicians, pharmacists, as well as industry. We believe it mostly contains the important information needed to achieve its purpose and that its current scope is sufficient and should not be unnecessarily expanded. However, Novartis would like to suggest several straightforward recommendations to improve the usability of this tool:

- **Conversion of static tables into a functional spreadsheet:** At present, the Purple Book consists of two static tables. We recommend that the Purple Book be provided in functional database in which it would be possible to search (ex.: INN or brand name). If the current format is retained, then we suggest adding the functionality to sort the available information (e.g., reorder information in columns).
- **Identify the reference product:** We recommend that an additional column be added to the Purple Book to capture the identity of the reference product used in development of a biosimilar or interchangeable biologic. This information would be useful to pharmacists to identify the reference medicine for which an interchangeable biologic can be substituted without the intervention of the prescribing physician.
- **Integrate the two Purple Book tables into one:** The listing of CDER and the Center for Biologics Evaluation and Research (CBER) products in different tables allows the responsibility for updating each table to be undertaken by each respective FDA division. However, this separation is not useful for physicians, pharmacists, and patients. In addition, individuals from these groups may not know that it is necessary to search both tables. We recommend that the two tables that currently comprise the Purple Book be at least integrated into a single table, or preferably a single, searchable database. If the FDA believes it is important to differentiate between CBER and CDER products that could be done easily by adding a column to capture this information.
- **Create a preamble to the Purple Book:** The Orange Book contains a very useful Preamble and Introduction that provides relevant basic information. We suggest a Preamble and Introduction be provided to the Purple Book as well to explain the basis for the Purple Book as well as key definitions. The inclusion of key term definitions should be based upon statutory definitions, but in formats that are easily understood by patients and healthcare providers. Parallel to the key terms in the Orange Book we recommend:

- **Clinically equivalent:** A biological product is considered clinically equivalent to the reference biologic if it meets the following criteria:
  - The biological product is highly similar to the reference product notwithstanding minor differences in clinically inactive components and that there are no clinically meaningful differences between the biological product and the reference product in terms of safety, purity and potency;
  - It has the same dosage form and route of administration, and is identical in strength or concentration;
  - The biological product is manufactured in compliance with Current Good Manufacturing Practice guidelines; and
  - They are adequately labeled.
  
- **Interchangeably equivalent:** Biosimilar products:
  - that are clinically equivalent to the reference biologic;
  - can be expected to produce the same clinical result as the reference biologic in any given patient; and
  - if the biologic product is administered more than once to the individual, the risk in terms of safety or diminished efficacy of alternating or switching between use of the biologic product and the reference biologic is not greater than the risk of using the reference biologic without such alteration or switch.

Novartis is aware of discussions advocating for the extension of the scope of the Purple Book. We respectfully consider that it is important to keep the Purple Book within its original intent and not aim to transform it beyond this purpose. The Purple Book was designed to identify the date a product was licensed and to identify “whether a biological product licensed under section 351(k) of the PHS Act has been determined by FDA to be biosimilar to or interchangeable with a reference biological product (an already-licensed FDA biological product).”<sup>48</sup>

For example, Novartis considers that **the Purple Book should not be used as a vehicle to differentiate indications** that were studied during the biosimilars development program versus those approved on the basis of extrapolation. In granting approval of a biosimilar for an extrapolated indication, the FDA determined based on firm scientific data that a biosimilar is as safe and effective for an extrapolated indication as the reference product.<sup>49</sup> Differentiating between studied and extrapolated indications is a thinly veiled effort to insinuate that use of a biosimilar to treat an extrapolated indication

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<sup>48</sup> Purple Book: Lists of Licensed Biological Products with Reference Product Exclusivity and Biosimilarity or Interchangeability Evaluations, FDA, *available at* <https://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/TherapeuticBiologicApplications/Biosimilars/ucm411418.htm> (last updated July 2, 2018).

<sup>49</sup> Guidance for Industry - Scientific Considerations in Demonstrating Biosimilarity to a Reference Product (April 2015), *available at* <https://www.fda.gov/downloads/drugs/guidances/ucm291128.pdf>.

may not be as safe or effective as use of the reference product for that purpose. The FDA should not be a party to requests that can and likely would be used to disparage biosimilars.

Unlike the Orange Book, the Purple Book does not contain patent information. This reflects differences in the Hatch-Waxman Patent Term Restoration Act of 1984 that authorized generic drugs and the BPCIA that authorized biosimilars.<sup>50</sup> Novartis believe this is appropriate and that **patent details should not be included in the Purple Book** as this lies outside of the mandate of this resource. In addition, creating and maintaining patent information would be very challenging given that patent estates for biologics are frequently very large and are frequently the subject of intensive litigation.

#### 4. Education for Providers and Patients

In the RFI, HHS recognizes the importance of physician and patient confidence in biosimilar and interchangeable products to increased acceptance of these products in the market. FDA intends to build on past education efforts by developing additional resources for providers and patients. HHS is interested in the types of information that would be most useful to providers and patients to promote understanding of these products.

The FDA has made great strides on biosimilar education. We note the important steps FDA has already taken to help educate patients and prescribers, notably creating a single website that contains videos, facts sheets, infographics and other helpful materials. Additionally, FDA has placed print ads in medical journals focusing on arthritis, rheumatology, dermatology, gastrointestinal disorders, cancer and hematology.

While we applaud FDA for the work it has accomplished and look forward to additional planned outreach activities, we believe more education is needed in light of ongoing campaigns to disparage biosimilar products, examples being:

- Alliance for Safe Biologic Medicines submitted a letter to the editor of the Vancouver Sun entitled: “Opinion: Patients on biologics need to be wary of substitutions.”<sup>51</sup>
- The Patients For Biologics Safety & Access website states “FDA must require that manufacturers of both innovator biologics and biosimilars conduct rigorous clinical testing to prove that their product works safely and effectively in each and every condition and distinct patient population for which it is approved for use. Failure to perform adequate testing in each group of patients and disease states puts patients at risk.” The same website states: “There must be no automatic substitution of biosimilars for biologics. The choice of products should not be

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<sup>50</sup> Compare Public Law 98-417 with Public Law 111–148, 124 Stat. 119.

<sup>51</sup> Michael Reilly, Opinion: Patients on biologics need to be wary of substitutions, Vancouver Sun (December 25, 2017), available at <https://vancouversun.com/opinion/op-ed/opinion-patients-on-biologics-need-to-be-wary-of-substitutions>.

determined by a pharmacist, regulator, or insurer but by a physician in consultation with his or her patient; over a biosimilar.”<sup>52</sup>

- A detailed campaign entitled “Finely Tuned” was established to “educate” patients about Remicade<sup>®</sup> and biosimilars. This campaign conflates the concept of interchangeability with the possibility of being prescribed a biosimilar infliximab. The website states: “In order for the FDA to deem a biosimilar interchangeable with Remicade that biosimilar must show that it will work the same as Remicade for anyone who takes it – **no infliximab biosimilar has yet proven this. ... Are you being asked to switch to a biosimilar? Then make your voice heard!**” (Emphasis included in the website.)<sup>53</sup>

Current arguments used in the debate about biosimilars often resemble those used in the 1980's when generic versions of chemically synthesized medicines entered the market. As was seen during the establishment of the European biosimilar pathway, opponents of biosimilars adapt their argumentation and their target audience as the biosimilar debate and the regulatory pathway mature, which further emphasizes the importance of the FDA's efforts for accurate information. All argumentation against biosimilars essentially develops from the premise that biosimilars are "only similar, but not identical."

Solutions that we recommend are:

- a. FDA education continues to stress that:
  - Biosimilars are designed to match the structure and function of the reference biologic.
  - 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.
  - FDA conducts rigorous and thorough evaluation to ensure that all biosimilars and interchangeable biologics meet the FDA's high standards for approval.
  - The introduction of biosimilars is anticipated to lower cost burdens for the U.S healthcare System and may help expand earlier and more consistent access to biological innovative medicines.
- b. The FDA publish “Setting the Record Straight” or “The Truth about Biosimilars” education that specifically addresses the facts about biosimilars that have consistently been misrepresented in misinformation campaigns.
- c. The terms that are used to describe biosimilars can be confusing to the average patient. While not a term explicitly written in BPCIA legislation, we believe that use of positive wording such as “clinically equivalent” is easier for patients and the public to understand and will be more readily accepted as opposed to “no

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<sup>52</sup> Biosimilars Overview, Patients for Biologics Safety & Access, *available at* <http://www.biosimsafety.org/biosimilars-overview/> (last visited July 10, 2018).

<sup>53</sup> Finely Tuned, Janssen Biotech, Inc., *available at* <https://www.finelytuned.com/> (last updated March 24, 2017).

clinically meaningful differences” which is a positive concept couched in negative verbiage.<sup>54</sup>

### **C. Incentivizing the Use of Generics**

In the RFI, HHS seeks comments on whether government programs contain the correct incentives to obtain affordable prices on safe and effective drugs or cause underpricing of generic drugs, and thereby reduce generic competition. Novartis appreciates HHS’ interest in encouraging a robust market for generic drugs and, in turn, increasing choice for beneficiaries and lowering costs. Generics medicines saved \$253 billion in 2016, and over the past decade have saved the U.S. healthcare system \$1.67 trillion.<sup>55</sup>

#### **1. Conditions on First Generic Exclusivity**

The President’s fiscal year (FY) 2019 budget proposal (the “Budget”) included a proposal that would, effective 2019, 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 a final approval, a trigger of the first applicant’s 180-day exclusivity.<sup>56</sup> This means the period of exclusivity would immediately begin for the first filer even though that first filer is not yet entitled to market its generic drug. According to the Budget, the proposal is intended to enhance competition and facilitate more timely access to generic drugs.

Novartis supports efforts to encourage generic development and innovation. However, we are concerned that this policy would weaken an important incentive for pharmaceutical companies to study, prepare and submit generic applications as soon as feasible upon expiration or dispute of existing innovator patents. Under current policy, a pharmaceutical company that is first to file an abbreviated new drug application (ANDA) which contains a paragraph IV certification and is substantially complete, but which cannot be fully approved because the company is being sued by the innovator for challenging existing patents, triggering a 30-month stay on FDA final approval, will be granted a 180-day exclusivity as a reward for defending legal challenge. This delicate legal balance is important to allow generic companies the opportunity to position themselves to enter the market immediately after patent expiration, or invalidation, and increase market competition.<sup>57</sup>

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<sup>54</sup> Public Law 111–148, 124 Stat. 119.

<sup>55</sup> Generic Drugs Access & Savings in the U.S., Association for Accessible Medicines (2017), available at <https://accessiblemeds.org/sites/default/files/2017-07/2017-AAM-Access-Savings-Report-2017-web2.pdf>.

<sup>56</sup> The President’s FY 2019 Budget Proposal for HHS, 68 (February 12, 2018), available at <https://www.hhs.gov/sites/default/files/fy-2019-budget-in-brief.pdf>.

<sup>57</sup> 21 U.S. Code § 355; and Guidance for Industry 180-Day Exclusivity: Questions and Answers, FDA (January 2017), available at <https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM536725.pdf>.

While this proposal may target some deficient ANDA's that are filed inappropriately to gain exclusivity, current law provides effective safeguards to prevent abuse of the 180-day exclusivity incentive. Specifically, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 identified the following circumstances under which an ANDA's 180-day exclusivity eligibility would be forfeited: (1) failure to market the drug; (2) withdrawal of the application; (3) amendment of the certification; (4) failure to obtain tentative approval; (5) entry into agreement with another applicant, the listed drug application holder, or a patent owner; and (6) all of the patents as to which the applicant submitted a certification qualifying it for the 180-day exclusivity period have expired.<sup>58</sup> For these reasons, we urge the FDA to continue to promote generic competition by maintaining its current policy. The Administration's proposal could disrupt this delicate commercial balance by penalizing the first filer for delays beyond its control and for which it may not be responsible. Any regulatory action would likely be challenged in court successfully under the terms and intent of the Hatch-Waxman Patent Term Restoration Act.<sup>59</sup>

## **2. Guidance on Complex Generics**

Earlier this year, the FDA announced its 2018 Strategic Policy Roadmap, which outlines a comprehensive approach to increasing competition under the FDA's Drug Competition Action Plan.<sup>60</sup> In connection with these efforts, the FDA has recognized the importance of complex generic drugs to patients and to the "economic health" of the generic market.<sup>61</sup> The FDA has also recognized the need for regulatory clarity with respect to complex generic drugs.<sup>62</sup>

We appreciate and support the FDA's focus on providing greater scientific and regulatory clarity on the development and approval of complex generics. However, there is a need for additional regulatory clarity for complex products. In particular, we strongly encourage the FDA to expedite the issuance of product-specific guidance for complex products.

### **D. Modernizing Part B**

Novartis appreciates CMS' efforts to improve the quality of healthcare, achieve better patient outcomes, and lower costs in the healthcare system. As part of these efforts, we are supportive of the agency's interest in modernizing the reimbursement for drugs in Part B. Part B is a complex benefit, covering a range of pharmaceuticals that treat a variety of diseases. The design of the current payment system impacts a host of stakeholders, including beneficiaries, providers, and manufacturers. We support modernizing the Part B drug reimbursement program by moving certain products, when

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<sup>58</sup> Pub. L. No. 180-173 § 1102.

<sup>59</sup> Public Law 98-417.

<sup>60</sup> Healthy Innovation, Safer Families: FDA's 2018 Strategic Policy Roadmap, FDA (January 2018), available at <https://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Reports/UCM592001.pdf>.

<sup>61</sup> Commissioner Scott Gottlieb, MD, Reducing the Hurdles for Complex Generic Drug Development, FDA (October 2, 2017), available at <https://blogs.fda.gov/fdavoices/index.php/2017/10/reducing-the-hurdles-for-complex-generic-drug-development/>.

<sup>62</sup> Id.

appropriate, from Part B to Part D and/or utilizing a properly designed CAP. We caution the agency to take actions in a measured and thoughtful way to ensure meaningful access to prescription drugs is retained.

Below we have provided more detailed comments regarding moving certain drugs from Part B to Part D and implementing a Part B CAP. We have also included recommendations for modernizing the Healthcare Common Procedure Coding System (HCPCS) coding process. Further, as CMS looks for ways to improve the Part B system, we encourage the agency to provide updated guidance regarding assumptions for calculating ASP.

## 1. Moving Certain Drugs from Part B to Part D

The President's Budget requested authority to move some Part B drugs to Part D and the RFI requests comment on this policy, including information on which drugs or classes of drugs would be suitable candidates for such a change.

The Part B Program has changed considerably since its inception and we understand the reimbursement policies for this program must evolve as well. If HHS were to move drugs from Part B to Part D as part of that evolution, the success of such a change would be dependent on identifying the most appropriate products to move. Importantly, CMS should use a phased-in approach over time, studying the impact along the way to ensure no unintended consequences occur (e.g., diminished access, higher out-of-pocket costs) and, if they do, to have the time and ability to correct those more immediately.<sup>63</sup> Further, the current protected classes in Part D should remain intact and include products moving from Part B to Part D.

We recommend beginning with a select category of products, such as oral solids, self-administered products, or other drugs currently covered by both Part B and Part D. Additional products should be phased-in only when there is sufficient experience with the initial implementation of the policy to ensure appropriate, safe, and continued access for beneficiaries. In considering which drugs to move, we recommend adhering to the following:

- Eligible drugs should require simple administration and straightforward dosing.
- Products that require administration by a healthcare provider are not appropriate to move to Part D.<sup>64</sup>

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<sup>63</sup> HHS previously released a report evaluating the difficulties of moving drugs from Part B to Part D. The report is outdated as the benefit has changed considerably over time, but many of the concepts discussed in the report remain relevant. See Former HHS Secretary Michael O. Leavitt, Report to Congress: Transitioning Medicare Part B Covered Drugs to Part D, Department of Health and Human Services (2005), available at [https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/Reports/Downloads/RtC\\_PtbtoPtD\\_2005\\_4.pdf/](https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/Reports/Downloads/RtC_PtbtoPtD_2005_4.pdf/).

<sup>64</sup> See Grecia M. Marrufo et al., Estimating the Effects of Consolidating Drugs under Part D or Part B, Acumen, LLC (September 2011), available at [https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/Reports/downloads/Acumen\\_B\\_to\\_D\\_Final\\_Report\\_2011.pdf](https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/Reports/downloads/Acumen_B_to_D_Final_Report_2011.pdf); see also Former HHS Secretary Michael O. Leavitt, Report to Congress: Transitioning Medicare Part B

- The appropriateness for movement of the class should be determined based on the characteristics of the most complex drug(s) in the class.

The design of Part B and Part D differ in critical ways, including reimbursement and product distribution and delivery to patients.<sup>65</sup> Medicare pays for most Part B drugs based on the ASP plus six percent.<sup>66</sup> The pricing set for drugs under Part D is based on multiple factors and is typically comprised of the following three components: (1) the cost of the drug itself (i.e., the ingredient cost charged by the manufacturer or wholesaler); (2) the pharmacy dispensing fee; and (3) sales tax.<sup>67</sup> Additionally, Part D plans negotiate prices and the ultimate price of a therapy differs from plan to plan as a result of these negotiations. With respect to beneficiary cost sharing, beneficiary out-of-pocket-costs are calculated differently under Part B and Part D. Part B beneficiary cost sharing is usually 20 percent of the cost of a drug (often covered by Medigap insurance) with limited variation related to factors such as premium and cost-sharing subsidies.<sup>68</sup> Comparatively, Part D cost sharing is dependent on a wide array of factors that result in greater variation throughout the Part D benefit. The most influential factors dictating cost sharing under Part D include: (1) the Part D plan type; (2) the tier on which the drug is placed on the Part D plan's formulary; and (3) the beneficiary's coverage phase (i.e., a beneficiary's out-of-pocket costs will differ when a beneficiary is in the catastrophic phase of the benefit).<sup>69</sup> Further, Part D plans are given significant flexibility in determining which drugs to include and how drugs will be placed on their formularies.<sup>70</sup>

Given the significant differences in benefit design, it is critical to adhere to a measured, phased-in approach for any changes. As noted above, there is a complex interplay of a variety of factors that impact beneficiary out-of-pocket costs in such a change, including a beneficiary's income level, availability of supplemental coverage, drug price, and type of drugs used by the patient. According to a recent Avalere analysis, in 2016, "average out-of-pocket costs were about 33 percent higher for Part D-covered new cancer therapies (\$3,200) than for those covered in Part B (\$2,400)."<sup>71</sup> Further, the analysis concluded that if any high-cost drug therapies (in addition to cancer therapies) are

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Covered Drugs to Part D, Department of Health and Human Services (2005), *available at* [https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/Reports/Downloads/RtC\\_PtBtoPtD\\_2005\\_4.pdf/](https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/Reports/Downloads/RtC_PtBtoPtD_2005_4.pdf/).

<sup>65</sup> Grecia M. Marrufo et al., Estimating the Effects of Consolidating Drugs under Part D or Part B, Acumen, LLC (September 2011), *available at* [https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/Reports/downloads/Acumen\\_B\\_to\\_D\\_Final\\_Report\\_2011.pdf](https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/Reports/downloads/Acumen_B_to_D_Final_Report_2011.pdf).

<sup>66</sup> Medicare Part B drug payment policy issues, Medicare Payment Advisory Commission, 33 (June 2017), *available at* [http://medpac.gov/docs/default-source/reports/jun17\\_ch2.pdf?sfvrsn=0](http://medpac.gov/docs/default-source/reports/jun17_ch2.pdf?sfvrsn=0). However, given the impact of sequestration the amount realized is actually less.

<sup>67</sup> Grecia M. Marrufo et al., Estimating the Effects of Consolidating Drugs under Part D or Part B, Acumen, LLC, 5 (September 2011), *available at* [https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/Reports/downloads/Acumen\\_B\\_to\\_D\\_Final\\_Report\\_2011.pdf](https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/Reports/downloads/Acumen_B_to_D_Final_Report_2011.pdf).

<sup>68</sup> Id.

<sup>69</sup> Id. at 10.

<sup>70</sup> Id. at 38.

<sup>71</sup> Matt Brow and Richard Kane, Avalere Analysis Highlights Complexities of Transitioning Medicare Part B Drugs into Part D, Avalere (May 21, 2018), *available at* <http://avalere.com/expertise/life-sciences/insights/avalere-analysis-highlights-complexities-of-transitioning-medicare-part-b-d>.

switched from Part B to D, many patients would pay more out-of-pocket since they typically purchase supplemental coverage for Part B and are not eligible for low income subsidies in Part D. However, there are instances when Medicare patients do not have supplemental coverage in Part B and, as a result, would pay less out-of-pocket from a switch to Part D, especially to the extent they are eligible for the low income subsidy.<sup>72</sup> Thus, the transition of drugs from Part B to Part D is complex and may impact each beneficiary differently, depending on the particular circumstances.<sup>73</sup> This reality underscores the need for a measured, phased-in approach.

In implementing this policy, which involves a fundamental re-design of the Medicare benefit for the impacted products, CMS should allow beneficiaries who do not have Part D coverage, which was nearly 30 percent of Medicare beneficiaries in 2017,<sup>74</sup> to obtain it without a late enrollment penalty for a specified period of time (and after an enrollment education campaign for beneficiaries). Otherwise, such beneficiaries may experience higher out-of-pocket costs or, even worse, no coverage that could lead to issues with medication adherence and, ultimately, higher costs to the system. In addition, moved drugs should be placed on a designated tier in Part D with a maximum 20 percent coinsurance and zero dollar deductible. CMS should ensure Medigap is made available to interested beneficiaries (at least for a specified period) for coverage of coinsurance for this tier, consistent with the allowance for drugs remaining in Part B.

CMS should take deliberate steps to ensure patient choice for drugs moved to Part D. More broadly, the agency should make certain that meaningful access is provided to such products on all formularies (especially when those products are not in a protected class). CMS should also consider operational issues that will arise with the change, including supply chain issues relating to distribution and the need for certain stakeholders to change existing, or enter into new, contractual arrangements. For instance, generic manufacturers, including Sandoz, do not have direct Medicare Part D contracts with payors/plans. In addition, pharmacies may not have the resources to accommodate the demand for a product that is moved from Part B to Part D. Specifically, stocking and dispensing therapies to beneficiaries may require more space and resources than is available.<sup>75</sup> Further, there may be challenges associated with the processing and billing of claims for drugs that are moved into Part D.<sup>76</sup> These examples demonstrate just a few of the complexities involved in moving drugs from Part B to D and underscore the need for a slow, deliberative process before undertaking the endeavor.

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<sup>72</sup> Id.

<sup>73</sup> Id.

<sup>74</sup> MedPAC Report to the Congress: Medicare Payment Policy, Chapter 14, p. 397 (March 2018), available at [http://www.medpac.gov/docs/default-source/reports/mar18\\_medpac\\_ch14\\_sec.pdf](http://www.medpac.gov/docs/default-source/reports/mar18_medpac_ch14_sec.pdf).

<sup>75</sup> Grecia M. Marrufo et al., Estimating the Effects of Consolidating Drugs under Part D or Part B, Acumen, LLC, 33-34 (September 2011), available at [https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/Reports/downloads/Acumen\\_B\\_to\\_D\\_Final\\_Report\\_2011.pdf](https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/Reports/downloads/Acumen_B_to_D_Final_Report_2011.pdf).

<sup>76</sup> Former HHS Secretary Michael O. Leavitt, Report to Congress: Transitioning Medicare Part B Covered Drugs to Part D, Department of Health and Human Services, 5 (2005), available at [https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/Reports/Downloads/RtC\\_PtbtoPtD\\_2005\\_4.pdf](https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/Reports/Downloads/RtC_PtbtoPtD_2005_4.pdf).

## 2. Part B Competitive Acquisition Program

In the RFI, HHS seeks comments on a CAP for Part B drugs. In particular, HHS is interested in ways to more successfully implement this program relative to the 2006-2008 implementation.<sup>77</sup> The 2006-2008 program was particularly hindered by providers electing not to continue in the program;<sup>78</sup> therefore, physician satisfaction and incentives for physician participation are critical for success of a future CAP for Part B drugs.<sup>79</sup> Lack of vendor participation and initial payments for the cost of drugs administered through the CAP which exceeded ASP reimbursement also contributed to the failure of the earlier program.<sup>80</sup>

For CAP to succeed, it is paramount that physicians be incentivized to participate and that patient access to prescribed medications be protected. Therefore, the following criteria should guide the program:

- **Phased-in Approach:** As with any other change to Part B drug payment, we encourage CMS to adopt a phased-in approach, starting first with a narrow subset of products. The agency should study the impact of the program to ensure it is functioning appropriately and without unintended consequences before expanding the CAP to more products.
- **Adequate Physician Incentives:** CMS needs to provide adequate incentives for provider participation.<sup>81</sup> Payment to physicians could include a reasonable and meaningful fixed fee, removing beneficiary copay amounts, allowing shared savings, or enabling a tiered payment approach that differs based on the cost of the product. It is important to acknowledge that, currently, the Part B physician payment amount may often offset losses to those providers in other areas. Thus, CMS should be mindful of attempting any change that would further exacerbate that issue. In addition, CMS should guard against any CAP design that would impose additional financial risk on providers relating to the cost of the product.
- **Program Design Must Ensure Access:** We recommend a CAP design that does not enable vendors to curtail access to needed therapies. As such, the program

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<sup>77</sup> Edward M. Drozd et al., Evaluation of the Competitive Acquisition Program for Part B Drugs: Final Report, RTI International (December 2009), available at [https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/Reports/downloads/CAPPartB\\_Final\\_2010.pdf](https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/Reports/downloads/CAPPartB_Final_2010.pdf) (report analyzes the challenges that were encountered during the 2006-2008 CAP implementation and identifies potential solutions to improve the CAP in the future).

<sup>78</sup> Id. at 12 (report finds that the CAP program had a significant provider attrition rate with 45 percent of practices participating in the CAP in 2006 opting not to participate in 2007 and 53 percent of practices participating in 2007 opting not to participate in 2008).

<sup>79</sup> Id. at 12, 78-79 (report finds that long-term viability of the CAP, may be strongly influenced by physicians' satisfaction with the program and that if physicians are dissatisfied with the program, they may not participate in CAP, and future rounds of bidding for CAP vendors will fail to attract bidders).

<sup>80</sup> Id. at 73-76.

<sup>81</sup> Id. at 12, 78-79.

should not contain formularies or utilize tools that delay patient access or interferes with clinical decision-making.

- ***Selection of Impacted Products:*** It is important that CMS carefully consider the products included within the CAP. To ensure competition and a level playing field, we believe CMS must mandate the whole class of drugs participate such that all relevant manufacturers are included. In addition, when some drugs used to treat a condition are covered by the CAP and others are not, CMS should guard against financial incentives that could adversely affect physician decision-making and patient choice.

### **3. Institute a More Efficient, Timely Coding Process**

The current process for obtaining a HCPCS code for new Part B drugs is often lengthy and time consuming, leading to the slow uptake of new drugs in many instances. At present, with limited exceptions, CMS assigns new HCPCS codes on an annual basis every January 1. As a result, new drugs and technologies introduced after January 1 are paid based on a “miscellaneous” code. Because these codes are not specific to a single drug or technology, they must be processed manually, leading to delays and uncertainty among providers, and occasionally negatively impacting patients’ access. In total, the process can often take up to 21 months after FDA approval until a code for a new drug takes effect (but could be accomplished in a quarter).<sup>82</sup> We recommend modernizing the coding process such that codes are issued on a quarterly, rather than annual, basis.

In addition to issuing codes on a quarterly basis, as mentioned above in the section entitled “Shifting the U.S. Healthcare System to Value-Based Pricing Principles,” we recommend CMS issue J codes for sole sourced products on an indication-specific basis to allow manufacturers the option of pricing and tracking product usage on such basis.

Finally, we urge CMS to assign unique J codes to biosimilars such that the Q codes would convert to J codes within the standard cycle (which, as mentioned above, we believe should be quarterly as opposed to annually). This change is important to ensuring a sustainable marketplace for biosimilars. Currently, biologics transition from Q codes to J codes. Assigning biosimilars a long-term Q code reflects a lack of parity with biologics and, as a result, creates confusion for the physician community and suggests instability around reimbursement for biosimilars. Assigning a J code for biosimilars will bolster the physician community’s view of these products and provide greater certainty. In addition, Q codes can be challenging for regional payers and state Medicaid agencies to process. For these reasons, we encourage CMS to assign unique J codes to biosimilars, consistent with the current practice for biologics.

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<sup>82</sup> The delay in assigning a code is often impacted by factors such as the timing of FDA approval and the deadline for the coding application.

## **E. Modernizing Part D**

### **1. General Comments**

The Part D program has been a success since its enactment over a decade ago, enabling beneficiaries to access a wide range of prescription therapies.<sup>83</sup> However, due to a variety of factors, Part D beneficiaries are increasingly absorbing more of the costs of this benefit.

Part D plan benefit design changes have imposed higher and more unpredictable cost sharing on patients, largely through the use of coinsurance and increasingly complex formularies. A recent study found that seniors with four or more chronic conditions reported higher rates of cost-related nonadherence in 2011 compared to 2007, partially due to changes in Part D benefit design.<sup>84</sup> The increase in complex formularies has played a significant role in pushing more cost sharing responsibilities onto patients. Currently, almost all stand-alone Part D plans have a formulary with five tiers and some plans even have six tiers. At the same time, plans have begun to include less brand name drugs on their preferred tier. These changes are significant because most plans have shifted to charging tiered copayments or varying coinsurance amounts for covered drugs rather than charging a fixed copayment rate. Further, a substantial majority of prescription drug plans use specialty tiers for high-cost medications.<sup>85</sup>

Coinsurance, as opposed to a fixed copayment, can be problematic for beneficiaries as it can often make it more difficult for beneficiaries to anticipate cost sharing for a specific product. Further, coinsurance is based on the list price of the drug, which does not account for the discounts and/or rebates that the plan receives for the drug. Unfortunately, Part D plans have been utilizing coinsurance to a greater extent in recent years. The average percentage of covered drugs facing coinsurance rose from 35 percent in 2014 to 58 percent in 2016 among Part D plans.<sup>86</sup> As a result, Part D enrollees often face high cost-sharing for brand and non-preferred drugs. In 2017, all of the top 10 Part D plans used coinsurance rather than fixed dollar copayments for medications on non-preferred drug tiers and charged 30 percent to 50 percent coinsurance.<sup>87</sup>

The trends in the way Part D plans utilize coinsurance and tiering may significantly impact beneficiary access to affordable medicines. Studies have shown that patients are

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<sup>83</sup> Jack Hoadley et al., *Launching the Medicare Part D Program: Lessons for the New Health Insurance Marketplaces*, Georgetown University Health Policy Institute (June 2013), available at <https://www.rwjf.org/content/dam/farm/reports/reports/2013/rwjf406589> (report discusses the successful launch of the Part D benefit and acknowledges the overall success of the program).

<sup>84</sup> Naci Huseyin et al., *Medication Affordability Gains Following Medicare Part D Are Eroding Among Elderly with Multiple Chronic Conditions*, 33 *Health Affairs* 1435 (August 2014), available at <https://www.healthaffairs.org/doi/pdf/10.1377/hlthaff.2013.1067>.

<sup>85</sup> *The Medicare Part D Prescription Drug Benefit*, Kaiser Family Foundation (October 2017), available at <https://www.kff.org/medicare/fact-sheet/the-medicare-prescription-drug-benefit-fact-sheet/>.

<sup>86</sup> Caroline Pearson, *Majority of Drugs Now Subject to Coinsurance in Medicare Part D Plans*, Avalere Health (March 2016), available at <http://avalere.com/expertise/managed-care/insights/majority-of-drugs-now-subject-to-coinsurance-in-medicare-part-d-plans>.

<sup>87</sup> *MedPAC Report to the Congress: Medicare Payment Policy*, Chapter 14, p. 397 (March 2017).

less likely to adhere to their medications when faced with high cost-sharing.<sup>88</sup> Patient nonadherence can result in significant health consequences that are ultimately more costly to the patient and the healthcare system.<sup>89</sup> Importantly, patients using high-cost therapies are not benefitting from rebates and discounts that are provided to plans by manufacturers. While Medicare Part D premiums have remained relatively stable, beneficiaries are subject to high out-of-pocket costs that are often unpredictable despite the substantial rebates that plans receive from manufacturers. Rather than share those rebates with patients at the pharmacy counter, plans typically retain those rebates and, at times, use them to reduce premiums. This practice may help keep premiums low, but patients consistently taking one or more therapies, such as chronically ill beneficiaries, are negatively impacted, and may experience barriers to access as a result.

The changes in benefit design not only affect the financial burden for beneficiaries and the costs to the healthcare system as a whole, but also the trajectory for innovation. Currently, manufacturers are not incentivized to launch products highly dependent on Part D, as it is often difficult to recoup the costs of product development. For example, cardiovascular drug development is in decline, despite the widespread prevalence of cardiovascular disease. One of the significant factors impacting the decline of innovation in this area is plan resistance to paying for these therapies. According to a recent piece in JAMA Cardiology, insurers generally avoid paying for new cardiovascular drugs using a variety of tools, including delaying or blocking the addition of new drugs to formularies, prior authorization and fail first tactics.<sup>90</sup> The author indicates it is “difficult to understand how the development of new cardiovascular drugs will continue.”<sup>91</sup> To the extent plans permit manufacturers to price a new cardiovascular drug “only marginally higher than a generic drug, manufacturers will be only able to recoup their development costs if they can be assured of rapid and widespread adoption.”<sup>92</sup> Given the current tools available to plans in limiting access, manufacturers know from experience that rapid and widespread adoption is far from assured. As a result, development of these products has declined significantly and we believe will continue to do so. Thus, as CMS evaluates refinements to Part D, we urge the agency not to adopt additional plan tools that lead to access issues for beneficiaries and, ultimately, a lack of incentive to innovate in important disease states.

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<sup>88</sup> Stacie Dusetzina et al., Cost sharing and adherence to tyrosine kinase inhibitors for patients with chronic myeloid leukemia, 32 J Clin Oncol. 306 (February 1, 2014), *available at* [https://www.ncbi.nlm.nih.gov/pubmed/?term=J+Clin+Oncol.+2014+Feb+1%3B32\(4\)%3A306-118](https://www.ncbi.nlm.nih.gov/pubmed/?term=J+Clin+Oncol.+2014+Feb+1%3B32(4)%3A306-118); and Jalpa Doshi et al., Impact of cost sharing on specialty drug utilization and outcomes: a review of the evidence and future directions. 22 Am J Manag Care. 188 (March 2016), *available at* [https://www.ncbi.nlm.nih.gov/pubmed/?term=Am+J+Manag+Care.+2016+Mar%3B22\(3\)%3A188-97](https://www.ncbi.nlm.nih.gov/pubmed/?term=Am+J+Manag+Care.+2016+Mar%3B22(3)%3A188-97).

<sup>89</sup> Leonard Egede, et al., Longitudinal effects of medication nonadherence on glycemic control. 48 Ann Pharmacother 562 (May 2014), *available at* <https://www.ncbi.nlm.nih.gov/pubmed/24586059>; and Aurel O Luga and Maura J McGuira, Adherence and health care costs. 7 Risk Manag Healthc Policy 35 (2014), *available at* <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3934668/>.

<sup>90</sup> Milton Packer, The Imminent Demise of Cardiovascular Drug Development, 2 JAMA Cardiol. 1293 (December 2017), *available at* <https://jamanetwork.com/journals/jamacardiology/article-abstract/2661162>.

<sup>91</sup> Id. at 1294.

<sup>92</sup> Id. at 1294.

Novartis is supportive of efforts to modernize Part D as long as beneficiary access to prescription drugs is not compromised. We urge HHS not to take any action that would diminish the value of the program for the seniors it serves. We are particularly supportive of any efforts to improve cost predictability and affordability for seniors such as: (1) establishing a maximum annual out-of-pocket cap on beneficiary spending, and (2) applying a share of negotiated rebates at the point-of-sale. We are concerned that beneficiaries would be adversely impacted by proposals limiting access or increasing costs for beneficiaries such as: (1) eroding the protected classes; (2) excluding manufacturer coverage gap discounts from the calculation of TrOOP spending; and (3) eliminating the two drug per class requirement.

## **2. Positive Measures to Address Patient Cost-Sharing Amounts**

### **a. Annual Out-of-Pocket Cap on Beneficiary Spending**

Novartis believes that a cap on beneficiary out-of-pocket costs should be explored to ensure that beneficiaries can continue to access and afford their medications. As it is, Part D formularies are not as generous as commercial formularies given out-of-pocket costs and, as a result, when individuals become eligible for Medicare they often lose the financial security that is offered by commercial plans through an annual cap on out-of-pocket costs. Establishing an annual out-of-pocket cap would also better align the Part D benefit with Medicare Advantage (MA) where a maximum out-of-pocket (MOOP) limit applies for Medicare Parts A and B healthcare services.

CMS has the authority to establish a Part D MOOP for beneficiaries. In creating a Part D MOOP, the agency can rely on the statutory authority in Part D that mirrors the MA authority the agency used to establish the Part A/B MOOP for local MA plans. When CMS established the MA MOOP, the agency relied on the prohibition on discriminatory MA benefit design<sup>93</sup> stating that the new MOOP requirement was necessary to ensure plans did not discriminate against beneficiaries who utilize higher than average healthcare services.<sup>94</sup> CMS further indicated that establishing the MA MOOP was consistent with its authority to add “necessary and appropriate” contract terms to agreements with MA plans.<sup>95</sup> Both of the statutory provisions that CMS relied on in establishing the MA MOOP have counterparts in Part D.<sup>96</sup>

Further, under SSA § 1860D-21(c)(2), the Secretary may waive Part D provisions “to the extent the Secretary determines that such provisions duplicate, or are in conflict with, provisions otherwise applicable to the organization or plan under part C or as may be

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<sup>93</sup> SSA § 1852(b)(1)(A).

<sup>94</sup> Medicare Program; Policy and Technical Changes to the Medicare Advantage and the Medicare Prescription Drug Benefit Programs Final Rule, 75 Fed. Reg. 19678, 19710-11 (April 15, 2010); and Medicare Program; Policy and Technical Changes to the Medicare Advantage and the Medicare Prescription Drug Benefit Programs Proposed Rule, 74 Fed. Reg. 54634, 54657 (Oct. 22, 2009).

<sup>95</sup> SSA § 1857(e)(1).

<sup>96</sup> SSA § 1860D-11(e)(2)(D) (prohibiting benefit designs that are likely to substantially discourage enrollment by certain part D eligible individuals under the plan); and SSA § 1860D-12(b)(3)(D) (allowing CMS to add additional contract terms that the Secretary deems necessary and appropriate).

necessary in order to improve coordination” between Part D and MA. The lack of a Part D MOOP, given the presence of the Part A/B MOOP, can create perverse incentives. For instance, the current design may lead beneficiaries with high healthcare costs to use Part B drugs even when there are Part D drugs that would be better from a clinical standpoint and more cost effective to the system as a whole.

A recent analysis conducted by one of the top independent actuarial firms in the country found that patients with heart failure (HF) entered the catastrophic phase of the benefit at much higher rates than all Part D enrollees. Only 5 percent of all non-LIS Part D enrollees entered the catastrophic phase in 2017, but 16 percent of non-LIS HF enrollees and 23 percent of HF patients on Entresto® entered the catastrophic phase. This suggests that beneficiaries with more chronic conditions have increased costs, resulting from them spending more in the catastrophic where they are subject to a 5 percent coinsurance. A Part D MOOP would be vital to ensuring access to innovative medicines for these beneficiaries. If CMS creates a Part D MOOP, the agency must then critically evaluate subsequent plan designs to ensure that plans are not discriminating against high cost beneficiaries.

We encourage the agency to use the authority discussed above to reduce beneficiary financial burden and uncertainty and improve patient access to needed therapies by establishing a Part D MOOP. This would protect patients from unduly burdensome out-of-pocket costs, create needed parity in benefit design between MA and Part D, and ensure beneficiaries are able to access appropriate therapies at the appropriate time. While we believe a Part D MOOP and the other reforms discussed in this section are the best approach for addressing affordability challenges in Part D, allowing manufacturers to voluntarily offer cost-sharing assistance could provide another alternative for reducing some seniors’ out-of-pocket costs.

#### **b. Applying a Share of Negotiated Rebates at the Point-of-Sale**

HHS requests information on rebates in Part D, including what CMS should consider doing to restrict or reduce the use of such rebates. We encourage CMS to implement a requirement that sponsors include a minimum percentage of manufacturer rebates and discounts in the drug’s negotiated price at the point of sale in order to lower patient costs and better align incentives. When Part D was created, it was anticipated that plan sponsors would share a portion of the rebate savings with beneficiaries. However, as CMS has recently acknowledged, rarely, if ever, are rebate savings passed on to beneficiaries.<sup>97</sup> We believe this change alone could result in materially lower costs for millions of seniors and significant savings to taxpayers. Ensuring that beneficiaries receive the benefit of rebates is one of the most direct, visible, and tangible ways to lower costs for seniors.

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<sup>97</sup> Medicare Program; Contract Year 2019 Policy and Technical Changes to the Medicare Advantage, Medicare Cost Plan, Medicare Fee-for-Service, the Medicare Prescription Drug Benefit Programs, and the PACE Program, 82 Fed. Reg. 56336, 56419 (November 28, 2017).

While the sum of manufacturer rebates and discounts has greatly risen, currently amounting to over \$100 billion per year, the price that patients pay for their prescription medicines has not comparably decreased.<sup>98</sup> In addition, the share of gross drug expenditures realized by non-manufacturer entities such as plan sponsors has increased. These expenditures are largely composed of the rebates and discounts paid by manufacturers.<sup>99</sup> In 2017, only 56 percent of the list price of branded drugs was received by manufacturers with the rest of the price funding discounts and rebates to other stakeholders, such as pharmacy benefit managers, wholesalers, health plans and government payers while real net per capita spending on medicines continued to decrease for the third year in a row.<sup>100</sup> Rebates can reduce the net cost of certain diabetes, asthma, high cholesterol, and hepatitis therapies by up to 30 percent to 55 percent.<sup>101</sup> However, patients are typically paying cost-sharing amounts based on the list price of the drug, which does not take into account these substantial discounts.

Novartis, like many other pharmaceutical manufacturing companies, negotiates with sponsors to provide rebates and price concessions on our products, which are intended to benefit the patient. At Novartis, while increasing our gross prices across our pharmaceutical portfolio by 5.4 percent in 2017, our net prices actually decreased by 2.1 percent driven by continued increase of rebates and discounts to 49.5 percent. This difference was largely the result of the rebates and price concessions that were negotiated by sponsors and other stakeholders in the supply chain. In the U.S., the total amount of annual rebates and discounts on Novartis products increased from 38 percent in 2012 to 49.5 percent in 2017.<sup>102</sup> Unfortunately, patients are not receiving a corresponding discount when they pay for their prescription medicines.

As a step to lower costs for patients, we encourage CMS to require plan sponsors to include a minimum percentage of manufacturer rebates and discounts in the drug's negotiated price at the point of sale. We believe this change could result in significant savings for beneficiaries and taxpayers. Importantly, as CMS explores this policy more fully, we urge the agency to ensure it maintains the confidentiality of proprietary information provided to it, and avoids cross-subsidization of competing medicines, as we believe these requirements are critical to preserving competition. We appreciate that, in prior rulemaking, CMS appeared to understand the concerns and indicated an interest in protecting the confidentiality of such information, including the manufacturer/sponsor/PBM pricing relationship with respect to an individual product. In

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<sup>98</sup> The Pharmaceutical Supply Chain: Gross Drug Expenditures Realized By Stakeholders, Berkeley Research Group (January 2017), *available at* [https://www.thinkbrg.com/media/publication/863\\_Vandervelde\\_PhRMA-January2017\\_WEB-FINAL.pdf](https://www.thinkbrg.com/media/publication/863_Vandervelde_PhRMA-January2017_WEB-FINAL.pdf).

<sup>99</sup> *Id.*

<sup>100</sup> Medicine Use and Spending in the U.S.: A Review of 2017 and Outlook to 2022, IQVIA Institute (2018) *available at* <https://www.iqvia.com/-/media/iqvia/pdfs/institute-reports/medicine-use-and-spending-in-the-us-a-review-of-2017-and-outlook-to-2022.pdf>

<sup>101</sup> Estimate of Medicare Part D Costs After Accounting for Manufacturer Rebates. QuintilesIMS (October 2016), *available at* <https://www.iqvia.com/-/media/iqvia/pdfs/institute-reports/estimate-of-medicare-part-d-costs-after-accounting-for-manufacturer-rebates.pdf?la=en&hash=C2AE92B591D0E059BDC9D90FE526E23E73493F84>.

<sup>102</sup> Novartis 2017 U.S. Transparency and Patient Access Report, *available at* <https://www.novartis.com/sites/www.novartis.com/files/us-transparency-patient-access-report-2017.pdf>.

the future, we are hopeful the reimbursement model will evolve into a value-based system where rebates are unnecessary.

In the RFI, HHS requests comment on whether it would be advisable to remove the discount safe harbor in an effort to restrict the use of rebates. We oppose any effort to narrow the safe harbor as that would further limit contracting ability and curtail innovative efforts to lower prices through negotiation. Even as crafted today, the Anti-Kickback Statute is deterring manufacturers from engaging in value-based arrangements because of fears of inadvertent violations. We believe there are far superior ways to re-direct the value of rebates, including through providing some portion of the rebate to beneficiaries at the point of sale (as discussed above).

### **3. Proposals That Would Limit Access and/or Increase Costs**

In the RFI, HHS references the 5-part plan to modernize the Part D program contained in the President's FY 2019 Budget. HHS notes that the 5-part plan is intended to be implemented together, as "eliminating even one piece of the package significantly changes the proposal's impacts."<sup>103</sup> While we agree with modernizing the Part D program, we strongly disagree that the 5-part plan must be implemented as a whole. Several of the proposals in the 5-part plan, as well as others in the RFI, would raise costs and limit access to life-saving therapies for beneficiaries, particularly those who are most vulnerable. We discuss below our concerns with several of these proposals.

#### **a. Erosion of the Part D Protected Classes**

In Section II of the RFI, entitled "Responding to President Trump's Call to Action," HHS mentions providing plans "full flexibility to manage high cost drugs that do not provide Part D plans with rebates or negotiated fixed prices, including in the protected classes." In addition, in Section III of the RFI, HHS asks whether the protected class policy should be used in a way that helps to discourage price increases. We believe price transparency is a better way to manage price increases, and we are particularly supportive of greater transparency throughout the healthcare system as a whole, including for products in the Part D protected classes.<sup>104</sup> Novartis publishes key financial information annually in its Form 20-F, Annual Report and Transparency and Patient Access Report. Such information includes annual gross and net price increases, total rebates and discounts, research and development costs, total gross and net sales.

Novartis appreciates the challenge in achieving a balance between ensuring beneficiary access to therapies and controlling costs to the Medicare program and beneficiaries.

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<sup>103</sup> HHS Blueprint to Lower Drug Prices and Reduce Out-of-Pocket Costs Request for Information. 83 Fed. Reg. 22692, 22693 (May 16, 2018).

<sup>104</sup> Jim Stergios and Gregory Sullivan, Are Drug Prices Driving Healthcare Cost Growth? Pioneer Institute, 12 (April 2016), available at <https://pioneerinstitute.org/healthcare/are-drug-prices-driving-healthcare-cost-growth/> (report recommends advancing regulatory actions to enforce existing provisions in legislation to expand healthcare pricing transparency as consumers would benefit most from policies that ensure all transactions for health-related services and products are subject to high standards of transparency).

However, we are concerned with any policy that would erode the protection provided to beneficiaries by the protected classes. Attempting to control costs at the expense of limiting beneficiary access to needed therapies will only increase costs to the system as a whole. Beneficiaries served by the protected classes are often among the most vulnerable. If such beneficiaries are not able to receive their therapies in a consistent and timely way, they may be admitted for expensive health complications or become otherwise dependent on more costly services that would not have otherwise occurred. Therefore, it would be best to manage price increases through price transparency rather than by limiting patient access to medicines.

CMS originally developed the protected class policy in 2005 to “ensure that Medicare beneficiaries reliant upon these drugs would not be substantially discouraged from enrolling in certain Part D plans, as well as to mitigate the risks and complications associated with an interruption in therapy for these vulnerable populations.”<sup>105</sup> This policy has served an important role for millions of beneficiaries for more than a decade. Each time the protected class policy has been addressed in statute or regulation, Congress and CMS have reaffirmed the policy and the need for the purpose it serves.

Currently, plan sponsors have appropriate tools to manage access to drugs in the protected classes. For instance, plans are permitted to exclude products from their formularies including, multi-source brands, extended release products, and certain medication forms and dosages.<sup>106</sup> In addition, plans are permitted to apply utilization management tools, such as prior authorization and step therapy, in appropriate circumstances.<sup>107</sup> The use of these tools and others have enabled plans to be very effective at managing competitive pricing for drugs in the protected classes. As evidence of this, a recent MedPAC report indicates that from 2006 to 2014, prices for protected class drugs grew more slowly than Part D prices overall.<sup>108</sup> In addition, according to a recent analysis, the generic utilization rate in the protected classes is higher than for non-protected classes.<sup>109</sup>

We respectfully disagree with the assertion that Part D plans are unable to negotiate discounts for drugs in the protected classes. Notably, a 2016 report by the QuintilesIMS Institute, now IQVIA, found that plan sponsors successfully negotiate significant cost reductions for medicines most commonly used by Part D beneficiaries, including medicines in two of the protected classes.<sup>110</sup> Across the 12 most commonly used

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<sup>105</sup> Centers for Medicare and Medicaid Services, Medicare Benefit Policy Manual, Chap. 6, Sec. 30.2.5 (Rev. 18, 01-15-16), available at <https://www.cms.gov/Medicare/Prescription-Drug-Coverage/PrescriptionDrugCovContra/Downloads/Part-D-Benefits-Manual-Chapter-6.pdf>.

<sup>106</sup> Id.

<sup>107</sup> Id.

<sup>108</sup> MedPAC Report to the Congress: Medicare Payment Policy, Chapter 14, 412 (March 2017).

<sup>109</sup> Policy Proposal: Revising Medicare’s Protected Classes Policy, The PEW Charitable Trusts (March 2018), available at [http://www.pewtrusts.org/-/media/assets/2018/03/dsri\\_policy\\_proposal\\_revising\\_medicares\\_protected\\_classes\\_policy.pdf](http://www.pewtrusts.org/-/media/assets/2018/03/dsri_policy_proposal_revising_medicares_protected_classes_policy.pdf), citing Centers for Medicare & Medicaid Services, “2015 Medicare Drug Spending Data.”

<sup>110</sup> Estimate of Medicare Part D Costs After Accounting for Manufacturer Rebates: A Study of Original Branded Products in the U.S., QuintilesIMS Institute (October 2016), available at <https://www.iqvia.com/>

therapeutic classes of medicines – including antidepressants and anticonvulsants – Part D plan sponsors negotiated an average rebate of 35.3 percent. Accounting for negotiated rebates, the analysis found that the final net costs to the plan sponsor for antidepressants and anticonvulsants were roughly half of the list price. This demonstrates that Part D sponsors are able to negotiate rebates and drive appropriate generic utilization within the protected classes.

Given the nature of the patient population, CMS' current policy relating to the use of utilization management and other tools for protected class drugs strikes the right balance. We believe it would be misguided and potentially more expensive to the system as a whole to attempt to control costs by limiting access to needed therapies for the most vulnerable of beneficiary populations. For these beneficiaries, many therapies are not interchangeable and ostensibly similar patients may experience clinically meaningful differences when treated with different products. A recent article in BMJ underscores the need for patient access to a variety of medications. In particular, the article shows that individual differences in treatment responses are often common and substantial.<sup>111</sup> The article indicates that having a “variety of medication options would be useful to optimize outcomes across all patients...”<sup>112</sup> This need for access to a variety of medication is particularly true for beneficiaries who rely on the therapies covered in a protected class.

The rationale that led CMS to create the protected classes policy is just as relevant today. Any erosion of this policy would expose vulnerable beneficiaries to potentially adverse outcomes resulting from therapy interruption or delays. This, in turn, would lead to higher costs for the system as a whole due to increased use of medical services and, potentially, institutional settings. We urge CMS to maintain the current structure of the protected classes.

#### **b. Excluding Manufacturer Coverage Gap Discounts from TrOOP**

We are particularly concerned about the proposal to exclude manufacturer coverage gap discounts from beneficiaries' TrOOP. This proposal would have negative consequences on patient costs, which would ultimately lead to lower medication adherence and higher costs for the system as a whole.

The calculation of TrOOP generally includes beneficiary out-of-pocket costs, discounts provided by drug manufacturers while the beneficiary is in the coverage gap, and charitable patient assistance. The manufacturer discounts are provided to benefit patients by reducing patient out-of-pocket costs while they are in the coverage gap. The inclusion of these discounts in TrOOP helps patients move through the coverage gap

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[/media/iqvia/pdfs/institute-reports/estimate-of-medicare-part-d-costs-after-accounting-for-manufacturer-rebates.pdf?la=en&hash=C2AE92B591D0E059BDC9D90FE526E23E73493F84.](#)

<sup>111</sup>Gowri Ramen et al., Evaluation of person-level heterogeneity of treatment effects in published multiperson N-of-1 studies: systematic review and reanalysis, 8 BMJ Open (May 26, 2018), *available at* <https://www.ncbi.nlm.nih.gov/pubmed/29804057>.

<sup>112</sup> Id. at 11.

and into the catastrophic phase where beneficiaries pay a maximum of 5 percent cost sharing. Therefore, excluding these discounts from TrOOP would only harm patients by ensuring that high-cost patients stay in the coverage gap for a longer period of time before reaching the catastrophic phase.<sup>113</sup>

An Avalere study previously estimated that under such a proposal Part D beneficiary spending would increase by \$4.1 billion from 2017-2020, which amounts to a per capita annual increase of between \$880 and \$1,080 in each of the four years of the analysis for affected beneficiaries (i.e., those who would have reached the catastrophic phase under the existing policy).<sup>114</sup> Patients with chronic illness who rely on prescription medicines would be disproportionately impacted by this policy as they would no longer be protected from high out-of-pocket costs leading to reduced medication adherence and, in turn, worse health outcomes and higher costs for the system. For these reasons, we urge CMS not to take any steps that would exclude manufacturer coverage gap discounts from the calculation of TrOOP.

### **c. Eliminating the Two Drug Per Class or Category Requirement**

One aspect of the 5-part plan contained in the President's Budget would change the formulary standards in Part D to require a minimum of one drug per category or class instead of two.<sup>115</sup> We strongly oppose any elimination of the current requirement that Part D formularies contain at least two drugs per therapeutic class or category. This proposal would restrict patient access to therapies and, in turn, increase overall healthcare costs (e.g., through increased emergency room visits and hospitalizations). As described more fully below, any action to lower the minimum number of drugs covered in each class would be counter to the needs of patients.

It is critical that physicians and patients have a wide range of treatment options available to treat and manage disease. This is particularly true for those who have chronic conditions. Weakening this critical beneficiary protection would impede beneficiary access to the therapies prescribed by their physicians. For many conditions, treatment is becoming personalized to the individual patient as continued research leads to better understanding of the disease and how to manage it. For conditions with multiple treatment options, it remains important for patients to have access to a variety of therapies because patient reactions to the same medications may differ. Patients often must try multiple treatment options before finding the one that best meets their needs and, in some cases, the best therapy involves a combination of products. Eliminating the

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<sup>113</sup> Juliette Cubanski, Summary of Recent and Proposed Changes to Medicare Prescription Drug Coverage and Reimbursement, Kaiser Family Foundation (February 2018), *available at* <https://www.kff.org/medicare/issue-brief/summary-of-recent-and-proposed-changes-to-medicare-prescription-drug-coverage-and-reimbursement/>.

<sup>114</sup> Miryam Frieder, Proposed Changes to Part D Would Increase Beneficiary Costs, Avalere (March 2016), *available at* <http://avalere.com/expertise/managed-care/insights/proposed-changes-to-part-d-would-increase-beneficiary-costs>.

<sup>115</sup> The President's FY 2019 Budget Proposal for HHS, 62 (February 12, 2018), *available at* <https://www.hhs.gov/sites/default/files/fy-2019-budget-in-brief.pdf>.

two drug per class or category requirement would reduce meaningful access to therapies thereby limiting physician and patient choice and, ultimately, lead to higher costs for the patient and the system.

This proposal may also create challenges with patient continuity of care. It is important that patients who are stabilized on a therapy maintain access to the product to prevent unnecessary, and often costly, complications and diminished outcomes. When patients switch to a chemically distinct but similar medicine for reasons other than lack of clinical efficacy or response, studies have found mostly negative effects among patients who previously had a stable, well-controlled disease.<sup>116</sup> Eliminating the two drug per class or category requirement will mean that many patients would not retain access to therapies that are effectively treating or managing their condition(s).

The financial implications for patients who rely on life-saving or life-sustaining therapies and cannot forgo their medicine are significant. This proposal would result in fewer drugs in each class being covered by Part D plans and patients would then have to pay out-of-pocket for needed medicines -- to the extent, they are able.

Implementing this proposal would be out of step with the current practice of medicine and with the commercial market. Rather than modernizing Part D, it would lead to a more archaic, rudimentary benefit. For these reasons, we urge CMS to maintain the two drug per class or category requirement and preserve patient access to important therapies.

#### **4. Fiduciary Responsibility of Pharmacy Benefit Managers**

HHS is interested in comments on the role of PBMs, including their obligations and the impact of the rebate structure on their incentives. Novartis believes there is a need for greater transparency in the relationship between PBMs and manufacturers.

PBMs should be held to a standard of meaningful transparency and reporting. This entails annual reporting to the federal government the amount of manufacturer rebates received in the aggregate and the amount passed on to consumers in the aggregate. PBMs must be required to maintain confidentiality of manufacturer rebates and not be permitted to specify any manufacturer proprietary pricing or rebating information. PBMs should be required to be transparent with beneficiaries regarding their prescription drug benefits, working with insurers to make cost sharing data available to patients and enabling pharmacies to provide information about all available prescription drug options at the point of sale. Further, PBMs should be required to pass rebates along to patients to the maximum extent possible and to afford patients the full value of third-party cost-sharing payments received on behalf of a patient, such as through manufacturer copay assistance programs.

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<sup>116</sup> Elaine Nguyen et al. Impact of Non-Medical Switching on Clinical and Economic Outcomes, Resource Utilization and Medication-Taking Behavior: A Systematic Literature Review. 32 Current Medical Research and Opinion 1281 (March 24, 2016), *available at* <https://www.tandfonline.com/doi/full/10.1185/03007995.2016.1170673>.

## 5. Part D End of Year Statement on Price Changes and Rebates

Currently, Part D plans provide their members with an explanation of benefits that includes information such as the negotiated price for their prescriptions and how much was paid by the plan and the member. HHS requests comments on, among other things, whether additional information should be added about the rate of change in the prices over the course of the benefit year and how this information should be delivered.

While Novartis supports appropriate transparency of pricing information, we do not believe changes are necessary to the current explanation of benefits. Specifically, we do not see value in adding more information that is complex or, at a minimum, confusing without further context, particularly when such information does not seem useful to beneficiaries. In evaluating this policy, to the extent any changes are made to the statement, we urge CMS to ensure the confidentiality of proprietary information.

## 6. Star Ratings

In Section II of the RFI, HHS mentions updating the methodology used to calculate Drug Plan Customer Service star ratings that are appropriately managing utilization of high-cost drugs. Presently, if a Part D plan issues an adverse redetermination decision, that decision may be appealed to the Independent Review Entity. HHS believes this may discourage plans from appropriately managing high cost products and so is considering a change.

While the proposed policy change and its impact are not entirely clear in this description, we are concerned with any change that would limit beneficiary appeal rights, which, in turn, could limit access. Decisions on managing utilization of high cost drugs should not rest with plans but, rather, should receive full appeal rights before a neutral entity. This is particularly true for certain classes of drugs, including those that treat vulnerable populations.

### F. Incentives to Lower/Not Increase List Price

HHS poses several questions related to incentives and penalties that could be used to curtail price increases over a certain lookback period. This is a complex area and, depending on the particular policy, could have long-term unintended consequences. As indicated above, we believe price transparency is a better way to manage price increases and we are particularly supportive of greater transparency throughout the healthcare system as a whole.<sup>117</sup>

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<sup>117</sup> Jim Stergios and Gregory Sullivan, Are Drug Prices Driving Healthcare Cost Growth? Pioneer Institute, 12 (April 2016), available at <https://pioneerinstitute.org/healthcare/are-drug-prices-driving-healthcare-cost-growth/> (report recommends advancing regulatory actions to enforce existing provisions in legislation to expand healthcare pricing transparency as consumers would benefit most from policies

As an additional item, for purposes of creating incentives to lower or not increase list prices, we encourage CMS to make some changes to the HCPCS coding process. In particular, as mentioned above, the current process for obtaining a HCPCS code for new Part B drugs is often lengthy and time consuming, leading to the slow uptake of new drugs in many instances. At present, with limited exceptions, CMS assigns new HCPCS codes on an annual basis every January 1. As a result, new drugs and technologies introduced after January 1 are paid based on a “miscellaneous” code. Because these codes are not specific to a single drug or technology, they must be processed manually, leading to delays and uncertainty among providers, and occasionally negatively impacting patients’ access. In total, the process can often take up to 21 months after FDA approval until a code for a new drug takes effect (but could be accomplished in a quarter).<sup>118</sup> We recommend modernizing the coding process such that codes are issued on a quarterly, rather than annual, basis. We believe this change could help with initial uptake of a product and, as a result, assist in lowering list prices.

## **G. Medicaid**

### **1. General Direction for Medicaid**

The Medicaid program is essential to ensuring patients served by the program have access to necessary therapies. We support efforts to update the program to better meet the needs of patients, while preserving access to necessary therapies. We are concerned about policies that would allow states to tighten formularies in a way that diminishes patient access to needed therapies. While this state flexibility may be intended to lower the cost of prescription drugs, we believe many patients would be denied appropriate access to life sustaining or life-saving treatments, which could harm beneficiaries and, ultimately, lead to increased costs for the system as a whole. Below are several concepts we urge HHS to consider as it looks for ways to update the Medicaid program:

- ***Value-Based Purchasing Initiatives:*** CMS should incentivize and facilitate ways for states to engage in value-based purchasing initiatives where appropriate. Per the comments above, these initiatives should be voluntary, limited in size and scope, and only launched after ample stakeholder feedback. However, enabling increased use of value-based purchasing would be a way to help modernize the program.
- ***Enable Supportive Services:*** The agency should recognize the benefit of supportive services that assist patients with various aspects of drug therapy, including improving adherence, managing adverse events, and ensuring access. Manufacturers and other stakeholders should be permitted to provide these services when needed in conjunction with a covered outpatient drug. This could help ensure

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that ensure all transactions for health-related services and products are subject to high standards of transparency).

<sup>118</sup> The delay in assigning a code is often impacted by factors such as the timing of FDA approval and the deadline for the coding application.

that access to healthcare is not limited by a patient's socioeconomic status.<sup>119</sup> This could be accomplished through waivers of relevant laws, such as fraud and abuse laws, which may be necessary depending on the circumstances.

- **New Drugs:** In an effort to reduce state budgetary pressures and promote the availability of new drugs, we recommend CMS encourage state Medicaid programs to have discussions with manufacturers well in advance of a new drug entering the market.<sup>120</sup> As is commonly known, most state Medicaid programs have limited budgets and, as a result, can find coverage of new, innovative medicines challenging, even when the therapies offer high value in improving and extending life. Encouraging earlier communication between manufacturers and Medicaid on anticipated new drug therapies would assist states in proactively anticipating and managing budget challenges in order to ensure beneficiary access to groundbreaking therapies.

## 2. Medicaid Drug Rebate Program

The Medicaid Drug Rebate Program (MDRP) is essential to providing patient access to therapies while reducing costs. Under the program, drug manufacturers that have entered into a Medicaid rebate agreement with HHS provide rebates in exchange for state Medicaid program coverage of all the manufacturer's drugs, with some exceptions and limitations.<sup>121</sup> While states may impose utilization management tools, the broad coverage of prescription drugs under Medicaid allows patients to access therapies that best fit their specific needs, including innovative therapies. Importantly, these rebates result in materially lower costs for states and the federal government. Between 2006 and 2009, the Office of the Inspector General (OIG) found that Medicaid recouped between 29 and 38 percent of its expenditures for prescription drugs each year, resulting in an average annual savings of about \$8 billion.<sup>122</sup> The increased access for patients to necessary therapies, along with the significant savings to the government, reflects the value of the MDRP to the healthcare system as a whole.

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<sup>119</sup> Another important consideration in selecting worthwhile supportive services is programs that incentivize medication adherence. Medication adherence ensures that patients are receiving the full benefit of their prescription therapies. When patients are not adherent to their medications, they are more likely to experience health-related complications, which increases costs for both the patient and the healthcare system overall. Donald G. Pittman, et al, Antihypertensive medication adherence and subsequent healthcare utilization and costs, 16 Am J Manag Care, 568 (August 2010), *available at* [https://www.ajmc.com/journals/issue/2010/2010-08-vol16-n08/ajmc\\_10aug\\_pittman\\_568to576](https://www.ajmc.com/journals/issue/2010/2010-08-vol16-n08/ajmc_10aug_pittman_568to576).

<sup>120</sup> We appreciate the recent FDA Guidance on this topic which should enable these conversations to take place and hope CMS will encourage Medicaid programs to begin implementing these discussions in a regular and consistent way. Drug and Device Manufacturer Communications with Payors, Formulary Committees, and Similar Entities — Questions and Answers Guidance for Industry and Review Staff, FDA (June 2018), *available at* <https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM537347.pdf>.

<sup>121</sup> SSA § 1927.

<sup>122</sup> Higher Rebates for Brand-Name Drugs Result in Lower Costs for Medicaid Compared to Medicare Part D. Office of the Inspector General (August 2011), *available at* <https://oig.hhs.gov/oei/reports/oei-03-10-00320.pdf>.

### 3. President's FY 2019 Budget Proposal- Five State Medicaid Drug Coverage Demonstration

The President's Budget includes a proposal that, with new statutory demonstration authority, would provide up to five states with flexibility to negotiate prices with manufacturers, rather than participate in the MDRP, and to make drug coverage decisions that meet the needs of the state.<sup>123</sup> Participating states would determine their own drug formularies and would be required to include an appeals process in an effort to ensure beneficiaries can access non-covered drugs based on medical need.<sup>124</sup> We are concerned that the five state demonstration could be used as a way to permit states to "cherry-pick" the longstanding agreement between CMS, states, and manufacturers to ensure Medicaid recipients have access to innovative medicines. Section 1927 of the Social Security Act (SSA) codifies a carefully-crafted bargain between manufacturers and states: manufacturers provide generous rebates to state Medicaid programs in exchange for the coverage by the state of all of their covered outpatient drugs. Although SSA § 1927 has been amended over the years since the statute's 1990 enactment, that fundamental bargain has endured. The bargain is further memorialized in the rebate agreement that manufacturers enter into with HHS, under which manufacturers agree that, in exchange for federal approval of the payment by state Medicaid programs for their drugs, they will make rebate payments on all of their covered outpatient drugs "for as long as an agreement with the Secretary is in force and State Medicaid Utilization Information reports that payment was made for that drug."<sup>125</sup>

With the recent CMS decision to deny the Massachusetts-proposed closed formulary, we recognize CMS' commitment to the MDRP and the bargain, and appreciate CMS' decision. However, in permitting Massachusetts and potentially other states to negotiate for closed formularies outside of the MDRP, we are concerned that CMS may be inadvertently creating a sub-standard benefit for the country's most needy patient population. We urge CMS to carefully consider whether this is a change that is appropriate, either within the five state demonstration, or within individual states, and to consider protections that should be put in place.

As a vulnerable population, Medicaid patients face many obstacles in accessing and adhering to their health needs, including suffering from multiple chronic conditions, socio-economic barriers to understanding and adhering to healthcare advice and drug regimens, lack of reliable income for food and transportation, and others. Closed formularies present challenges for many patients and could be extremely dangerous for the Medicaid population, unless safeguards are put in place to ensure access to drugs that are not included in the closed formulary. Additionally, innovative medicines must be

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<sup>123</sup> The President's FY 2019 Budget Proposal for HHS (February 12, 2018), *available at* <https://www.hhs.gov/sites/default/files/fy-2019-budget-in-brief.pdf>.

<sup>124</sup> *Id.*

<sup>125</sup> Sample Rebate Agreement between the Secretary of Health and Human Services and the Manufacturer, § II(h), CMS, *available at* <https://www.medicaid.gov/medicaid-chip-program-information/by-topics/prescription-drugs/downloads/samplerbateagreement.pdf>.

readily accessible to these patients, and should not be excluded from a state's closed formulary as a result of a generic drug being available within the class.

In order to ensure that Medicaid patients continue to have access to the drugs they need, we encourage CMS and states implementing a closed formulary to address the following:

- Coverage for drugs that represent a continuity of care should be required when a patient is stable or responding well to a current treatment, regardless of the exclusion of the drug on the closed formulary.
- States implementing a closed formulary must develop an appeals process that ensures that providers, patients, and caregivers understand how to access a drug that is not included on the closed formulary, including information required, review process, and timeline for decision-making. Denials should be in writing, with a specific explanation. Second-level appeals should be required, and these reviews should be conducted by a physician specializing in the patient's specific disease.
- A path to access therapies not on the closed formulary must be created and published, in order to allow patients who have tried and failed on therapies on the closed formulary to have an opportunity at more effective and appropriate treatment of their condition.

We have concerns with CMS' direction to Massachusetts, and with the five state demonstration proposal. While the details of the proposal are unknown, the concept suggests Medicaid beneficiaries would likely experience diminished access to important therapies. Ultimately, we believe this sort of proposal would increase costs to the healthcare system as a whole. We urge CMS and states to recognize the value of innovative therapies and the impact that the right drug for the right patient at the right time can have on overall patient outcomes and healthcare costs. If CMS pursues this sort of model in any form, we encourage the agency to seek stakeholder feedback well in advance of implementation so that its design can guard against unintended consequences.

#### **4. Inflationary Rebate Limits**

In the RFI, HHS states it is concerned that limiting manufacturer rebates on brand and generic drugs in the Medicaid program to 100 percent of calculated Average Manufacturer Price (AMP) allows for excessive price increases to be taken without manufacturers facing the full effect of the price inflationary penalty established by Congress. HHS is concerned this policy may allow for runaway price increases and cost shifting. HHS seeks comment on when this limitation is a valid constraint upon the rebates manufacturers should pay and what impact removing the cap on the inflationary rebate would have on list prices, price increases over time, and public and private payers.

We oppose any lifting of the inflationary rebate cap and, as a general matter, do not believe imposing additional rebate liability on manufacturers would lead to lower costs across the system. Currently, there are two components of calculating the rebate for

innovator drugs under the MDRP: (1) the base rebate and (2) the additional rebate. The base rebate is the greater of 23.1 percent of the AMP or AMP minus Best Price. The additional rebate, also referred to as the "inflationary penalty," may be added if the increase in a drug's AMP exceeds the increase in the Consumer Price Index for All Urban Consumers (CPI-U).<sup>126</sup> The Affordable Care Act established a maximum rebate amount that limits a manufacturer's rebate responsibility for innovator drugs to a maximum of 100 percent of AMP.<sup>127</sup> However, currently, it is the case that, as between Medicaid and Medicaid Managed Care, the rebates can already be over 100 percent. Further, Congress only recently increased manufacturer rebate liability for drugs in government programs.<sup>128</sup> Specifically, the Bipartisan Budget Act of 2018 included provisions that will increase the rebate that manufacturers are required to provide to beneficiaries during the Medicare Part D coverage gap from 50 percent to 70 percent beginning with plan year 2019 and increase rebate liability with respect to line extension drugs.<sup>129</sup>

The Medicaid expansion provision within the ACA has so far resulted in nearly 17 million new patients within Medicaid. Thirty-four states, including the District of Columbia, have expanded Medicaid.<sup>130</sup> Independent analysts estimate that the ACA will increase prescription drug rebates and industry taxes that brand manufacturers pay by almost \$70 billion through 2021.<sup>131</sup> Manufacturer liability increased under the ACA via the creation of additional taxes and rebate requirements, including:

- The Medicaid minimum basic rebate increased from 15.1 percent of AMP to 23.1 percent of AMP;
- Medicaid rebates were extended to Medicaid managed care organizations (MCOs);<sup>132</sup>
- The definition of AMP was altered to increase rebate amounts;
- Medicaid rebates cover a larger number of people due to this extension to Medicaid MCO enrollees plus Medicaid expansion;
- Manufacturers are required to pay rebates of 50 percent in the Part D coverage gap (this has now been increased to 70 percent);
- A new annual fee on brand drug manufacturers sales of drugs that are reimbursed or purchased by certain federal programs (Medicaid, Medicare Part B, Medicaid

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<sup>126</sup> 42 U.S.C. 1396r-8(c).

<sup>127</sup> Pub. L. 111-148 § 2501(e).

<sup>128</sup> Pub. L. 115-123 § 53104 & 53116.

<sup>129</sup> Id.

<sup>130</sup> Status of State Action on the Medicaid Expansion Decision, Kaiser Family Foundation, *available at* <https://www.kff.org/health-reform/state-indicator/state-activity-around-expanding-medicaid-under-the-affordable-care-act> (last updated July 3, 2018).

<sup>131</sup> Implications of the U.S. Supreme Court Ruling on Healthcare, PwC (June 2012), *available at* <https://www.pwc.com/us/en/health-industries/health-research-institute/publications/pdf/implications-of-the-US-Supreme-Court-ruling-on-healthcare.pdf>.

<sup>132</sup> In FY 2016, almost half (49 percent) of all Medicaid expenditures were in Medicaid managed care organizations, up from 24 percent in 2010. Medicaid Managed Care Spending in 2016, Health Management Associates (January 26, 2017), *available at* <https://www.healthmanagement.com/blog/medicaid-managed-care-spending-2016/>.

Part D, and the Department of Veterans Affairs and Department of Defense drug programs);<sup>133</sup> and

- Expansion of 340B pharmacy eligibility.

It is axiomatic that continued mandatory rebating, especially rebates that result in a loss for a drug that costs money to research, develop, approve, produce and market, is not a sustainable long-term pricing model for any industry, particularly an industry as heavily dependent on research and development as the pharmaceutical industry. The removal of the inflationary limit ultimately could impact the availability of drug products to government purchasers and others, and this risk grows as the Medicaid and 340B programs grow.

Novartis invested nearly \$9 billion in research and development in 2017, in search of new cures. We strongly urge the Department to recognize significant savings to government programs due to industry participation in mandated price concessions and rebates, and to balance that with the need for future innovation. Novartis strongly opposes the removal of the limit on the inflationary penalty.

## **5. Inflationary Penalty on Non-Innovator Multiple Source Drugs**

As HHS examines the drug pricing structure more broadly, we wanted to reiterate our concern with the inflationary penalty on non-innovator multiple source drugs. By way of background, the enactment of the Bipartisan Budget Act (BBA) of 2015 included a provision to amend the MDRP by imposing an “inflationary penalty” on non-innovator multiple source drugs, similar to that paid for innovator drugs.<sup>134</sup>

For a number of reasons, it is inappropriate to apply a brand drug policy model to the generic marketplace. The penalty is calculated for price increases above the Consumer Price Index (CPI) for a product compared to its base period AMP.<sup>135</sup> AMPs for generic products fluctuate because multiple manufacturers offer interchangeable products and customers regularly alternate suppliers in search of low prices and supply. Generic AMP price fluctuation can occur due to changes in customer mix and product size mix even when manufacturers do not increase the price to any customer. For example, a decline in sales to (lower-priced) high-volume customers will lead to an increase in AMP because the share of sales to higher-priced customers rises. Furthermore, customers may buy more or less of a product in a given period, which will impact and change the product's AMP (since it is a calculation based on a weighted average and manufacturers do not control the volumes that each customer purchases). AMPs also fluctuate depending on the calculation determination used for the drug which can shift solely due to customer mix in one quarter versus another quarter (i.e., AMP calculations for retail community

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<sup>133</sup> Annual Fee on Branded Prescription Drug Manufacturers and Importers, Internal Revenue Service, available at <https://www.irs.gov/affordable-care-act/annual-fee-on-branded-prescription-drug-manufacturers-and-importers> (last updated February 20, 2018).

<sup>134</sup> Pub. L. No. 114-74.

<sup>135</sup> The Social Security Act defines AMP as: “the term ‘average manufacturer price’ means, with respect to a covered outpatient drug of a manufacturer for a rebate period, the average price paid to the manufacturer for the drug in the United States by—(i) wholesalers for drugs distributed to retail community pharmacies; and (ii) retail community pharmacies that purchase drugs directly from the manufacturer.”

pharmacies versus calculations for drugs that are inhaled, infused, instilled, implanted or injectable). Although the rebate recently went into effect, Sandoz has already begun to pay inflationary penalties on products where we did not increase prices. We encourage the Administration to revisit this inappropriate policy which could negatively affect the continued manufacturing of low-margin, low-cost products.

Additionally, we are concerned about the implementation of related supplemental rebates from the New York Department of Health, which creates an arbitrary penalty that could discourage generic drug manufacturers from participating in or remaining in the Medicaid program and could result in manufacturers discontinuing certain generic drug products.

## **6. Exclusion of Certain Calculations from AMP and Best Price**

HHS requests comment on multiple price reporting questions, including how the inclusion or exclusion of certain discounts, rebates or price guarantees might impact AMP and BP and, as a result, the Medicaid Drug Rebate Program.

The Best Price policy is intended to ensure that Medicaid receives the lowest price for drugs, taking into account all negotiated discounts. Best Price refers to the lowest price provided by manufacturers during the rebate period to any wholesaler, retailer, provider, health maintenance organization, nonprofit entity, or certain governmental entities.<sup>136</sup> Because copay cards are provided to patients and not to any of the entities identified in the statute (e.g., wholesalers, retailers), they do not fall within the statutory definition of Best Price, and it would not be appropriate to include them in the calculation of Best Price.<sup>137</sup> The current regulatory framework on these calculations is working and achieves the desired results.<sup>138</sup> As discussed more fully below, there should be no changes to the current exclusion of copay discount cards from the determination of Best Price and AMP. We are concerned about unintended consequences that may result from changes to the current framework. We encourage HHS to focus on other reforms discussed in the RFI that would have a greater impact on lowering the cost of drugs and patients' out-of-pocket costs.

### **H. Copay Discount Cards**

HHS seeks comment on whether manufacturer copay cards drive up the price of drugs and whether they should be included in Best Price.

#### **1. General Comments**

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<sup>136</sup> 42 U.S.C. § 1396r-8(c)(1)(C)(i).

<sup>137</sup> Id.

<sup>138</sup>The Medicaid Drug Rebate Program, as noted above, has been working successfully for years. Higher Rebates for Brand-Name Drugs Result in Lower Costs for Medicaid Compared to Medicare Part D. Office of the Inspector General (August 2011), available at <https://oig.hhs.gov/oei/reports/oei-03-10-00320.pdf>.

Benefit design in the commercial space is increasingly shifting costs to patients.<sup>139</sup> Between 2012 and 2015, the number of insurance plans that offered benefits with a prescription drug deductible doubled from 23 to 46 percent.<sup>140</sup> High cost sharing amounts in the coverage phase of the plan often limit a patient's ability to obtain necessary therapies.<sup>141</sup> Manufacturer copay cards reduce a patient's out-of-pocket costs and, as a result, improve patient adherence and reduce the level of abandonment from the provider recommended therapy. A recent study found the rate of patient abandonment was 50 percent lower when copay cards were used as compared to what they would have been without copay cards.<sup>142</sup> Copay assistance is critical to patients, particularly those with chronic conditions who require a number of therapies year over year. According to a RAND study, in 2014, 60 percent of U.S. patients had one chronic condition, 42 percent had multiple chronic conditions, and 12 percent had five or more. The segment of the population with chronic conditions averages 20 physician visits a year and 51 prescriptions.<sup>143</sup> As a result of the increased use of services and drugs, patients with chronic conditions are disproportionately impacted by high out-of-pocket costs.<sup>144</sup>

Specialty drugs are complicated therapies that are researched, developed, and approved to treat patients with serious acute and chronic conditions. Some specialty drugs are approved to treat orphan diseases, which is defined by the FDA as diseases

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<sup>139</sup> Anish Mahajan and Robert Brook, High-Deductible Health Plans and Better Benefit Design, 148 Ann Intern Med. 704 (2008), available at <http://annals.org/aim/article-abstract/740856/high-deductible-health-plans-better-benefit-design?volume=148&issue=9&page=704>.

<sup>140</sup> Murray Aitken, Emergence and Impact of Pharmacy Deductibles: Implications for Patients in Commercial Health Plans, IMS Institute for Healthcare Informatics (September 2015), available at <https://www.iqvia.com/-/media/iqvia/pdfs/institute-reports/emergence-and-impact-of-pharmacy-deductibles.pdf?la=en&hash=1D397351342823EDEFDECFC4F119CCBFD56E904F>.

<sup>141</sup> Dana Goldman et al., Pharmacy benefits and the use of drugs by the chronically ill, 291 JAMA 2344 (May 19, 2004)(study finds that doubling co-payments was associated with reductions in the use of eight therapeutic classes and that significant increases in co-payments raise concern about adverse health consequences because of the large price effects, especially among diabetic patients), available at <https://jamanetwork.com/journals/jama/fullarticle/198761>; and Katie Devane et al., Patient Affordability Part Two: The Implications for Patient Behavior & Therapy Consultation, IQVIA (May 2018) (report finds that patients with higher out-of-pocket costs are more likely to abandon their new prescriptions at the pharmacy), available at <https://www.iqvia.com/-/media/iqvia/pdfs/us-location-site/market-access/patient-affordability-part-two---implications-for-patient-behavior-and-therapy-consumption.pdf>.

<sup>142</sup> Katie Devane et al., Patient Affordability Part One: The Implications of Changing Benefit-Designs and High Cost-Sharing, IQVIA (May 2018), available at <https://www.iqvia.com/-/media/iqvia/pdfs/us-location-site/market-access/patient-affordability-part-one---the-implications-of-changing-benefit-designs-and-high-cost-sharing.pdf>; Katie Devane et al., Patient Affordability Part Two: The Implications for Patient Behavior & Therapy Consultation, IQVIA (May 2018), available at <https://www.iqvia.com/-/media/iqvia/pdfs/us-location-site/market-access/patient-affordability-part-two---implications-for-patient-behavior-and-therapy-consumption.pdf>; and Katie Devane et al., Patient Affordability Part Three: The Implications of Co-Pay Cards, IQVIA (May 2018), available at <https://www.iqvia.com/-/media/iqvia/pdfs/us-location-site/market-access/patient-affordability-part-three---the-implications-of-copay-cards.pdf>.

<sup>143</sup> Christine Buttorff et al., Multiple Chronic Conditions in the United States, RAND Corporation (May 31, 2017), available at [https://www.rand.org/content/dam/rand/pubs/tools/TL200/TL221/RAND\\_TL221.pdf](https://www.rand.org/content/dam/rand/pubs/tools/TL200/TL221/RAND_TL221.pdf)

<sup>144</sup> Chronic Diseases: The Leading Causes of Death and Disability in the United States, Centers for Disease Control and Prevention, available at [www.cdc.gov/chronicdisease/overview/index.htm](http://www.cdc.gov/chronicdisease/overview/index.htm) (last updated June 28, 2017).

with fewer than 200,000 patients annually in the US. Specialty drugs present a unique challenge to the healthcare system and the patients who need them. The growth in spending on specialty drugs is driven by various factors, including the aging population, the availability of more treatments to help patients with these diseases, and increased ability to diagnose and treat.<sup>145</sup>

Patient cost-sharing is typically based on the product's list price, even though manufacturers have provided rebates to plans, which significantly reduce that price. Currently, manufacturer rebates are rarely, if ever, passed on directly to the patient. Changes in benefit design have particularly increased the cost burden for patients using specialty drugs. Specialty drugs frequently require coinsurance and patients typically pay a percentage of the pharmacy reimbursed amount, rather than the price of the drug negotiated by the PBM or insurance plan.<sup>146</sup> Out-of-pocket spending for specialty drugs in the coinsurance phase of commercial plans accounted for 58 percent of patient's overall spending, compared to 13 percent for other brand drugs.<sup>147</sup>

Discounts negotiated for prescription drugs by PBMs and plans function differently than discounts negotiated with providers for medical services. When plans negotiate discounted rates for services delivered by providers such as hospitals or physicians, the benefit of those negotiated rates are typically passed on to the patient with patient cost sharing most often as a copay. However, in plans where a coinsurance for provider services is required, the co-insurance percentage is calculated based on the negotiated rate with the provider. In contrast, with PBMs and plans, cost sharing for almost one in five brand prescriptions and more than one-third of specialty prescriptions is based on the list price of the drug, without consideration of negotiated rebates.<sup>148</sup> The difference in these systems underscores the need for copay cards as a mechanism to reduce out-of-pocket costs for patients.

To address the question of the impact of copay cards on drug prices, a recent study found that while some copay cards may raise prices (those offered when an FDA-approved generic is available), copay cards offered when there is not a generic available have not been shown to impact prices. In both cases, however, copay card availability

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<sup>145</sup> Alan M. Lotvin et al., Specialty Medicines: Traditional and Novel Tools can Address Rising Spending on these Costly Drugs, 33 *Health Affairs* 1736 (October 2014), available at <https://www.healthaffairs.org/doi/10.1377/hlthaff.2014.0511>.

<sup>146</sup> Karen Van Nuys et al., A Perspective on Prescription Drug Copayment Coupons, USC Schaeffer, (February 20, 2018), available at [http://healthpolicy.usc.edu/documents/2018.02\\_Prescription%20Copay%20Coupons%20White%20Paper\\_Final.pdf](http://healthpolicy.usc.edu/documents/2018.02_Prescription%20Copay%20Coupons%20White%20Paper_Final.pdf)

<sup>147</sup> Commercially-Insured Patients Pay Undiscounted List Prices for One in Five Brand Prescriptions, Accounting for Half of Out-of-Pocket Spending on Brand Medicines, PhRMA (2017), available at <http://www.google.com/url?sa=t&rct=j&q=&esrc=s&source=web&cd=1&ved=0ahUKEwjmi6P6r47cAhUJMd8KHQ9jBvEQFggqMAA&url=http%3A%2F%2Fphrma-docs.phrma.org%2Fdownload.cfm%3Fobjectid%3DC6A51770-0FCD-11E7-ACCC0050569A4B6C&usq=AOvVaw3KlosmpJm4taP5yrtcCGtA>.

<sup>148</sup> Id.

improved patient access and adherence.<sup>149</sup> Lack of adherence to medication regimens results in increased hospitalizations, irreversible disease progressions, overall poorer health, and costs the U.S. between \$100 to \$290 billion annually.<sup>150</sup> As HHS looks for ways to reduce out-of-pocket costs, it should preserve the structure of copay cards, including the current exclusion for such cards from the determination of Best Price and AMP.

We are concerned about a recent trend in benefit design that again shifts costs to the patient. Specifically, some PBMs and plans will not recognize copay discount cards when determining whether the patient has reached their deductible or out-of-pocket maximum. These programs can lead to patients incurring significant unexpected costs if they continue taking their prescribed medication. As HHS seeks to reduce costs to patients, we encourage the Department to support programs that positively impact patient costs, like copay cards, and deter activity that is intended to shift more costs to patients.

## 2. Price Reporting

The exclusion of copay discount cards from the calculation of Best Price and AMP is critical to ensuring consistency with the statute, and avoiding both costly and significant operational difficulties, as well as an increase in Medicaid prices in some instances. We strongly recommend HHS maintain the current exclusion for copay cards from both Best Price and AMP and not seek any change, legislative or otherwise, that might impact the current system.

The Best Price policy is intended to ensure that Medicaid receives the lowest price for drugs, taking into account all negotiated discounts. Best Price refers to the lowest price provided by manufacturers during the rebate period to any wholesaler, retailer, provider, health maintenance organization, nonprofit entity, or governmental entity.<sup>151</sup> Because copay cards are provided to patients and not to any of the entities identified in the statute (e.g., wholesalers, retailers), they do not fall within the statutory definition of Best Price, and it would not be appropriate to include them in the calculation of Best Price.<sup>152</sup>

Likewise, copay discounts should continue to be excluded from AMP. Under the statute relating to AMP, discounts provided to certain entities including “any other entity that does not conduct business as a wholesaler or a retail community pharmacy” is excluded from the calculation of AMP.<sup>153</sup> As a result, by statute, price concessions (e.g., copay

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<sup>149</sup> Karen Van Nuys et al., A Perspective on Prescription Drug Copayment Coupons, USC Schaeffer, (February 20, 2018), *available at* [http://healthpolicy.usc.edu/documents/2018.02\\_Prescription%20Copay%20Coupons%20White%20Paper\\_Final.pdf](http://healthpolicy.usc.edu/documents/2018.02_Prescription%20Copay%20Coupons%20White%20Paper_Final.pdf)

<sup>150</sup> Rachelle Louise Cutler et. al., Economic impact of medication non-adherence by disease groups: a systematic review, 8 *BMJ Open* (January 21, 2018), *available at* <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5780689/#R6>.

<sup>151</sup> 42 U.S.C. § 1396r-8(c)(1)(C)(i).

<sup>152</sup> *Id.*

<sup>153</sup> 42 U.S.C. § 1396r-8(k)(1)(B)(i)(IV).

cards) to other parties, such as patients, are excluded from AMP calculations. From a policy perspective, it does not appear there is any benefit from amending the statute to include patient discounts in AMP. Such a change would lower AMP, which would lower Medicaid rebates provided to states and, thus, increase costs to states.

For these reasons, we strongly urge HHS not to seek a legislative change to these policies and, instead, to maintain the current exclusion of copay cards from the calculation of Best Price and AMP.

### 3. Third-Party Payments and Annual Out-of-Pocket Maximums

HHS, in conjunction with the Departments of Labor and Treasury, (the “tri-agencies”) should issue clarifying guidance that, under federal law, third-party contributions, including manufacturer coupons, toward copayments and other cost-sharing obligations, must be counted toward enrollees’ annual out-of-pocket (OOP) maximums for essential health benefits (EHBs) under non-grandfathered group health plans and non-grandfathered individual and small group market health insurance coverage. Consistent with the public policy priorities set forth in the RFI, such guidance would benefit patients by lowering their OOP costs for drugs and other healthcare items and services, as patients would reach their annual OOP maximums faster where third-party cost-sharing payment amounts are counted toward their annual OOP thresholds.

Non-grandfathered group health plans are required by statute to adhere to federal limits on the annual “cost-sharing” they charge enrollees for EHBs.<sup>154</sup> By regulation, CMS has interpreted the statutory term “cost-sharing”<sup>155</sup> to include “any expenditure required by *or on behalf of* an enrollee with respect to essential health benefits; such term includes *deductibles*, coinsurance, copayments, or similar charges, but excludes premiums, balancing billing amounts for non-network providers, and spending for non-covered services.”<sup>156</sup> A plain reading of the phrase “or on behalf of” indicates that a cost-sharing payment made by a third party on behalf of an enrollee should be treated no differently than a cost-sharing payment made by the enrollee himself or herself. Therefore, for EHBs under non-grandfathered health plans, third-party cost-sharing payments must count toward the annual OOP maximum no less than any other cost-sharing payments.

Federal law also supports the issuance of guidance clarifying that non-grandfathered individual and small group market health insurance coverage must count third-party cost-sharing payments toward enrollees’ deductibles (in addition to their annual OOP maximums) for EHBs. The statute requires that such plans offer coverage that “includes the essential health benefits package.”<sup>157</sup> That requirement necessarily sweeps in the definition of “cost-sharing” set forth above—a component of the “essential health benefits package”—which includes deductibles and, more specifically under CMS’s regulation, third-party deductible payments.

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<sup>154</sup> Public Health Service Act (PHSA) § 2707.

<sup>155</sup> S Affordable Care Act (ACA) § 1302(c)(3).

<sup>156</sup> 45 C.F.R. § 155.20 (emphasis added).

<sup>157</sup> PHSA § 2707(a).

Per our comments above, CMS should issue guidance to the effect that manufacturer coupons remain exempt from the Medicaid Best Price calculation regardless of whether or how the patient's health plan applies those coupon dollars to the patient's annual OOP or deductible obligation. Medicaid regulations provide that manufacturer coupons are excluded from Best Price consideration when the coupon benefits the patient alone and no Best Price-eligible customer receives a price concession.<sup>158</sup> Some PBMs offer their member plans a program that accepts a manufacturer coupon as payment of the patient's OOP obligation at the point-of-sale but does not apply those funds to reduce the patient's annual OOP/deductible obligation. As the Best Price regulatory exceptions are not dependent on a coupon's application to the patient's OOP or deductible obligation, these programs should have no bearing on the excludability of a manufacturer coupon from Best Price.

### **I. Improving Price Transparency in Medicare & Medicaid**

HHS seeks comment on proposals the Department can pursue to improve price transparency in Medicare, Medicaid, and other forms of health coverage in a way that will allow consumers to seek value when choosing and using their benefits.

Novartis continues to support increasing price transparency for Medicare and Medicaid patients, particularly within the context of value-based pricing models for appropriate products. We believe it is important to provide greater transparency where the availability of the information serves a meaningful purpose, as opposed to transparency simply for transparency's sake. When executed correctly, greater transparency can empower consumers to make more informed choices, including understanding the relative value of the therapy and, ultimately, the financial impact of their decisions.

We commend CMS on its recent release of the Scorecard on Medicaid and CHIP. We believe that the Scorecard and similar efforts, including projects designed to increase transparency and understanding within the patient, caregiver, and provider populations, will not only improve the efficiency of program operations but also improve patient outcomes.

It is important to recognize that there are instances when additional transparency is useful and instances when it is not. Providing greater information is helpful when better, more cost effective decisions can be made based on such information. However, providing additional information that is meaningless or lacks context can be confusing and only adds burden to beneficiaries and the system as a whole. To help make this point, below we discuss a few examples of where greater transparency can be helpful and where it can be harmful:<sup>159</sup>

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<sup>158</sup> 42 C.F.R. § 447.505(c)(8)-(11).

<sup>159</sup> Some of these issues are discussed elsewhere in the letter but since transparency is at the core of each, we wanted to include them here as well.

- **Transparency designed to bring down costs.** We are supportive of transparency that is intended to lower costs, without compromising access. For instance, we support transparency that enables government programs to choose the most cost effective product. To this end, CMS should encourage state Medicaid programs and their Managed Medicaid affiliates to maximize the savings available to the state when mandated brand price discounts make the price of a branded drug significantly cheaper than available generic equivalents. More specifically, as we have previously discussed, the agreement between manufacturers, CMS and state Medicaid agencies ensures that state Medicaid programs receive the best commercially available price on brand drugs, in addition to an inflation penalty tied to the consumer price index. When an innovator drug loses patent protection, the first generic to market is competing only with the innovator product in price, and thus the innovator product is frequently less expensive to Medicaid programs during the initial period post loss of patent exclusivity. Typically there is only a modest price differential between the WAC of the branded product and the initial generic. Medicaid brand drug rebates can more than offset the difference in WAC prices of brand and the initial generic products. The time it takes to have sufficient generic products on the market to lower the generic price varies, and depends on a variety of factors, including level of manufacturing complexity and patient population. For example, drugs with approved orphan indications or specialty medications may not see as many generic competitors within the first several months as other drugs. This could result in a delay in the drop of the price of generics to plans and patients. For Medicaid programs, the price of the branded product is typically significantly lower than the price of generic product(s) for an extended duration beyond the 180-day exclusivity period due to mandated discounts. Greater transparency around this issue would help Medicaid programs select the most cost effective product.
- **Transparency to provide more accurate pricing information.** Novartis supports the disclosure of rebates to reveal the differential between gross and net prescription drug prices. As mentioned above, Novartis publishes key financial information annually in its Form 20-F, Annual Report and Transparency and Patient Access Report, including information on total rebates and discounts and total gross and net sales. Many pharmaceutical companies provide substantial rebates for their products. However, the reported price of a product often does not account for these rebates. Accounting for rebates in pricing data is critical in providing patients with a true understanding of a product's price. We support sharing information pertaining to the overall net cost of a particular drug with patients, providers and CMS. In addition, CMS should require increased transparency around rebates received by plans/PBMs and other direct and indirect remuneration, as well as the impact the rebates have on formulary placement. As with any disclosure, we urge HHS to protect the confidentiality of proprietary information.
- **Transparency that only provides confusing or irrelevant information could have a negative impact.** As discussed above in the section relating to Medicare Part D, HHS asks whether additional information should be added to the Part D End of Year Statement, including about the rate of change in the prices over the course

of the benefit year. While we support transparency that drives better decisions, we do not believe the proposed changes to the current explanation of benefits would have that result. To the contrary, we believe adding such information would be confusing, at a minimum, and, ultimately, would not be useful to beneficiaries. In evaluating these sorts of transparency proposals, we urge HHS to consider whether the information would be useful to the end user or whether it would only create unnecessary confusion.

To realize the full benefits of transparency, we support greater transparency throughout the healthcare system. The cost of the same healthcare service varies across providers and settings. However, this variation is often not reflective of value. As a result of gaps in information, consumers make uninformed choices that can lead to unnecessary spending and lower quality care.<sup>160</sup> Policies that ensure transparency for all healthcare services would allow patients to make informed, cost-effective choices that produce greater value for both the patient and the healthcare system.<sup>161</sup>

Importantly, as HHS pursues various transparency policies and laws, we urge the federal government to preempt state policies, where appropriate, to prevent a patchwork of differing, and possibly contradictory, policies throughout the country. In addition, in developing transparency policies, we urge HHS to preserve the confidentiality of proprietary information.

## **J. 340B Drug Pricing Program**

The 340B Program was established in 1992 and, since that time, it has experienced exponential growth. HHS seeks comment on a variety of questions related to many aspects of the 340B program including program eligibility requirements, duplicate discounts, and unintended consequences of the program. HHS also questions whether explicit general regulatory authority over all elements of the 340B program would materially impact the elements of the program affecting drug pricing.

Novartis has commented on the 340B program extensively in the past and our previous comments, which are incorporated herein by reference,<sup>162</sup> provide further details

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<sup>160</sup> Transparency in Health Care: A Priority Roadmap for Consumer Engagement, Network for Excellence in Health Innovation (July 2017), *available at* [https://www.nehi.net/writable/publication\\_files/file/nehi\\_transparency\\_report.pdf](https://www.nehi.net/writable/publication_files/file/nehi_transparency_report.pdf)

<sup>161</sup> Jim Stergios and Gregory Sullivan, Are Drug Prices Driving Healthcare Cost Growth? Pioneer Institute, 12 (April 2016), *available at* <https://pioneerinstitute.org/healthcare/are-drug-prices-driving-healthcare-cost-growth/>.

<sup>162</sup> Novartis comment letters on 340B include, but are not limited to: comment letter submitted on May 18, 2018 in response to 340B Drug Pricing Program Ceiling Price and Manufacturer Civil Monetary Penalties Regulation Notice of Proposed Rulemaking. See 82 Fed. Reg. 20, 0008 (May 7, 2018); comment letter submitted on September 18, 2017 in response to a 340B Drug Pricing Program Ceiling Price and Manufacturer Civil Monetary Penalties Regulation Notice of Proposed Rulemaking See 82 Fed. Reg. 39,553 (Aug. 21, 2017); comment letter submitted on April 19, 2017 in response to 340B Drug Pricing Program Ceiling Price and Manufacturer Civil Monetary Penalties Regulation Interim Final Rule. See 82 Fed. Reg. 14,332, 14,332 (Mar. 20, 2017); and comment letter submitted on August 14, 2015 in response

regarding our recommendations for improving the 340B program. While we support the 340B program, it has grown beyond its original intent and should be refocused to better meet the needs of vulnerable patients.<sup>163</sup> There are several policies relating to 340B that are of particular concern to us and we highlight those below:

- **Penny Pricing:** The penny pricing policy is not supported by the 340B statute and imposes significant burdens on 340B stakeholders. The Health Resources and Services Administration (HRSA) should permit manufacturers to adopt an alternative, reasonable approach, such as charging the Federal Ceiling Price (FCP), if a manufacturer has an FCP, instead of mandating penny pricing. In the event that a manufacturer does not have an FCP for a particular product (e.g., a generic product approved under an abbreviated new drug application), the manufacturer should have discretion to calculate an FCP proxy or to apply any other reasonable method by which to calculate an alternative 340B ceiling price.
- **Netting of Over and Under Charges:** HRSA should permit manufacturers to follow established commercial practices when issuing refunds, including offsetting undercharges and overcharges and applying de minimis thresholds. HRSA's current refund requirement is, as a practical matter, unduly burdensome.
- **Definition of Eligible Patient:** We believe an eligible 340B patient should be defined as one that has: (1) an established relationship with the covered entity and provider (e.g., hospital's employee or independent contractor); (2) received outpatient care at a covered entity's facility resulting in a prescription drug being ordered or administered as part of that care, including refills; and (3) care provided within the scope of the contract or powers that bestow that covered entity 340B eligibility.
- **Contract Pharmacies:** The number of contract pharmacies has grown significantly in recent years from 1,300 in 2010 to about 18,700 in 2017.<sup>164</sup> We urge HRSA to revisit its policies related to contract pharmacies and take steps to prevent the occurrence of challenges often associated with the use of contract pharmacies, such as diversion and duplicate discounts. A recent report from the U.S. Government Accountability Office identified several oversight weaknesses that impede HRSA's ability to ensure compliance with the program.<sup>165</sup>

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to a 340B Drug Pricing Program Ceiling Price and Manufacturer Civil Monetary Penalties Regulation Proposed Rule. See 80 Fed. Reg. 34, 583 (June 17, 2015).

<sup>163</sup> Aaron Vandervelde, 340B Growth and the Impact on the Oncology Marketplace: Update, Berkley Research Group, 4 (December 15, 2015), available at <https://www.thinkbrg.com/pp/publication-417.pdf?39862> (report finds that regardless of the specific metric of growth one evaluates, research into the 340B program and the oncology marketplace in particular suggests that 340B program growth is a function of both newly enrolled 340B hospitals and the expansion of hospital outpatient facilities at existing 340B hospitals).

<sup>164</sup> Status of Agency Efforts to Improve 340B Program Oversight. Government Accountability Office, 7 (May 15, 2018), available at <https://www.gao.gov/assets/700/691742.pdf>.

<sup>165</sup> Federal Oversight of Compliance at 340B Contract Pharmacies Needs Improvement, Government Accountability Office (June 21, 2018), available at <https://www.gao.gov/assets/700/692697.pdf>

- **HRSA Rulemaking Authority:** With respect to HRSA’s authority, we support providing HRSA with targeted rulemaking authority relating to 340B, where such authority would be helpful in aligning the program with the statutory text and original purpose of 340B. For instance, we support legislation providing HRSA with rulemaking authority for defining “patients” for purposes of the program. Although legislation may be necessary for certain reforms, we strongly encourage HRSA to begin implementing needed changes to the 340B program where the agency has interpretive authority.
- **Child Sites:** A covered entity’s on- and off-campus facilities may be eligible for participation in the 340B Program if they are an integral part of a hospital that participates in the 340B Program. These on- and off- campus facilities, often referred to as child sites, must be an outpatient location and appear on the most recently filed hospital cost report. However, we believe using the cost report alone to determine child site eligibility is insufficient and HRSA should revise these standards to better align with the intent of the 340B statute. We recommend that in order to be considered an integral part of a 340B covered entity, the child site should be required to: meet regulatory provider-based status requirements; be wholly owned by the hospital; provide the same level of charity care as the parent hospital; provide care to the same level of low-income or uninsured patients as the parent hospital if it is a disproportionate share hospital (DSH); be listed as reimbursable on the covered entity’s Medicare cost report or in the case of children’s hospitals, be listed on the reimbursable line of the parent hospital’s cost report if it were to provide a Medicare cost report; and provide outpatient services beyond providing drugs or drug administrative services.

Finally, as mentioned above, in an effort to incentivize the use of biosimilars, we encourage CMS to adjust payments in the 340B program post pass through status to ensure biosimilars that have been on the market beyond pass through status are not disadvantaged relative to their reference product.

#### **K. Proposals for Reducing Out-of-Pocket Costs**

In the RFI, HHS seeks comments on any additional regulations or policies that may contribute to increasing list prices, net prices, and out-of-pocket drug spending. As this Administration has recognized, reducing out-of-pocket costs for patients is critical to increasing access to needed therapies. For instance, a recent article concluded that higher out-of-pocket costs were associated with higher rates of oral prescription abandonment and delayed treatment initiation.<sup>166</sup> This article, from the Journal of Clinical Oncology, determined that “fiscally sustainable strategies are needed to improve patient access to cancer medications.”<sup>167</sup>

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<sup>166</sup> Jalpa A. Doshi et al., Association of Patient Out-of-Pocket Costs with Prescription Abandonment and Delay in Fills of Novel Oral Anticancer Agents, 36 J Clin Oncol 476 (February 10, 2018), *available at* <https://www.ncbi.nlm.nih.gov/pubmed/29261440>.

<sup>167</sup> Id. at 1.

## 1. Aligning Benefit Design

The prescription drug benefit should be improved to create more meaningful alignment between value and access. As part of this, we recommend aligning out-of-pocket costs with a product based on its relative value for the beneficiary. Under such a design, Part D cost-sharing amounts would be changed such that beneficiary out-of-pocket costs would be lower for highly valuable products and higher for products of lesser value.

As mentioned above, we also encourage CMS to establish a Part D MOOP spending limit, consistent with the steps the agency took to require MA plans to apply a MOOP limit on annual patient cost-sharing for services covered under Parts A and B. We believe parity in benefit design as it relates to out-of-pocket spending is critical in removing perverse incentives and important in reducing the financial burden and uncertainties for beneficiaries.

In addition, there is a need to better align patient costs for drugs versus other services. Currently, for prescription drugs, patient cost-sharing is typically based on the product's list price, even though manufacturers have provided rebates to plans that significantly reduce that price.<sup>168</sup> Those rebates, however, are rarely, if ever, passed on to the patient.<sup>169</sup> The rebate system for prescription drugs is in contrast to plan negotiations with providers for medical services. Generally, plans negotiate discounted rates for services delivered by providers such as hospitals or physicians. The benefit of those negotiated rates are typically passed on to the patient. We recommend HHS do more to ensure that discounts provided by manufacturers are passed on to the patient. This would be more in line with benefit design for healthcare services.

Finally, for purposes of Medigap and benefit design, we are concerned that beneficiary out-of-pocket spending will significantly increase beginning in 2020 with the prohibition on new beneficiaries' purchase of Medigap plans that provide first dollar coverage. Current Medigap plans have 11 different standard benefit packages. Of the 11 standard packages, two (Plan C and Plan F) cover virtually all Medicare cost sharing (i.e., first-dollar coverage). In addition, a discontinued plan (Plan J) covers all Medicare cost sharing. In 2015, 72 percent of Medigap beneficiaries had one of these policies.<sup>170</sup>

In 2017, Medicare covered 58.4 million people: 49.5 million aged 65 and older, and 8.9 million disabled. The 2018 Medicare Trustees Report estimates the number of Medicare

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<sup>168</sup> Estimate of Medicare Part D Costs After Accounting for Manufacturer Rebates A Study of Original Branded Products in the U.S., QuintilesIMS Institute (October 2016), *available at* <https://www.iqvia.com/-/media/iqvia/pdfs/institute-reports/estimate-of-medicare-part-d-costs-after-accounting-for-manufacturer-rebates.pdf?la=en&hash=C2AE92B591D0E059BDC9D90FE526E23E73493F84>.

<sup>169</sup> Medicare Program; Contract Year 2019 Policy and Technical Changes to the Medicare Advantage, Medicare Cost Plan, Medicare Fee-for-Service, the Medicare Prescription Drug Benefit Programs, and the PACE Program, 82 Fed. Reg. 56336, 56419 (November 28, 2017).

<sup>170</sup> Trends in Medigap Enrollment, 2010 to 2015, The MedPAC Blog (February 13, 2017), *available at* <http://www.medpac.gov/-blog/-trends-in-medigap-enrollment-2010-to-2015/2017/02/13/trends-in-medigap-enrollment-2010-to-2015>.

beneficiaries is currently increasing by about 3 percent per year.<sup>171</sup> This translates into more than 10,000 people joining the program each day as the Baby Boom generation retires.<sup>172</sup> While approximately 35 percent of beneficiaries are enrolled in Medicare Advantage, the change in Medigap will still result in millions of beneficiaries paying increased out-of-pocket costs.

## 2. Specialty Tiers

Patients with certain health conditions that require medication on a specialty tier are often particularly vulnerable. Prescription therapies, in these cases, can become cost prohibitive for individuals who rely on a specific therapy to sustain or improve their quality of life. As we have noted above and in previous comment letters, studies have found a link between cost sharing and medication adherence.<sup>173</sup> Nonadherence decreases health outcomes and increases cost to the healthcare system as a whole.<sup>174</sup> High cost-sharing in situations where a beneficiary must take a specific medicine and has no appropriate alternative could be considered discriminatory based on a particular patient's clinical needs or health status. We encourage CMS to eliminate the tiering exemption for the Medicare Part D specialty tier in future rulemaking, as this exemption effectively discriminates against beneficiaries needing drugs on the specialty tier and can lead to significant financial hardship or barriers to access.

### L. Access to Reference Product Samples

HHS is interested in additional steps that can be taken to review existing REMS to determine whether distribution restrictions are appropriate. HHS requests comment on whether there are terms that could be included in REMS, or provided in addition to REMS, that could expand access to products necessary for generic development.

Novartis understands the complexity of these issues given that our product portfolio consists of branded medicines, generic drugs and biosimilar biopharmaceuticals. Set forth below is our perspective on how the current REMS misuses have hampered our

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<sup>171</sup> 2018 Annual Report of the Boards of Trustees of the Federal Hospital Insurance and Federal Supplementary Medical Insurance Trust Funds.

<sup>172</sup> Dan Diamond, 10,000 People are Now Enrolling in Medicare - Every Day, Forbes (July 13, 2015), available at <https://www.forbes.com/sites/dandiamond/2015/07/13/aging-in-america-10000-people-enroll-in-medicare-every-day/#12efdedb3657>.

<sup>173</sup> Stacie Dusetzina et al., Cost sharing and adherence to tyrosine kinase inhibitors for patients with chronic myeloid leukemia, 32 J Clin Oncol. 306 (February 1, 2014), available at [https://www.ncbi.nlm.nih.gov/pubmed/?term=J+Clin+Oncol.+2014+Feb+1%3B32\(4\)%3A306-118](https://www.ncbi.nlm.nih.gov/pubmed/?term=J+Clin+Oncol.+2014+Feb+1%3B32(4)%3A306-118); and Jalpa Doshi et al., Impact of cost sharing on specialty drug utilization and outcomes: a review of the evidence and future directions. 22 Am J Manag Care. 188 (March 2016), available at [https://www.ncbi.nlm.nih.gov/pubmed/?term=Am+J+Manag+Care.+2016+Mar%3B22\(3\)%3A188-97](https://www.ncbi.nlm.nih.gov/pubmed/?term=Am+J+Manag+Care.+2016+Mar%3B22(3)%3A188-97).

<sup>174</sup> Leonard Egede et al., Longitudinal effects of medication nonadherence on glycemic control, 48 Ann Pharmacother 562 (May 2014), available at <https://www.ncbi.nlm.nih.gov/pubmed/24586059>; and Aurel O Luga and Maura J McGuira, Adherence and health care costs. 7 Risk Manag Healthc Policy 35 (2014), available at <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3934668/>.

generics and biosimilar development, while also noting how FDA's current RLD<sup>175</sup> website has been misconstrued.

## 1. REMS Misuse and Biosimilar Sampling

In the RFI, HHS seeks comments in response to concerns that certain manufacturers are gaming REMS-related distribution limitations to prevent generic developers from accessing drugs samples that are legally required for bioequivalence testing and, thereby, limiting the development and access to generics.

Generic drugs are an important part of the full spectrum of healthcare solutions, as they improve patient access to cost-efficient medicines following loss of patent protection. As a leading manufacturer of generics, via our Sandoz unit, Novartis supports the development of generic products to ensure access to affordable medicines for patients. Our mission is to provide access to life-improving and life-saving therapies to all patients. Therefore, as a company, we do not impose restrictions preventing other generic manufacturers from accessing Novartis branded products and we support policies that facilitate generic drug development, including policies that prevent the use of REMS to block generics coming to market.

With respect to biosimilars, Novartis strongly endorses the concept that biosimilar developers should have adequate and timely access to samples of reference products so that development of biosimilars is not impeded. The analytical comparisons that form the foundation of biosimilarity require multiple samples of reference product from multiple batches. We appreciate that the actual amounts needed will vary based on the nature of the biological drug and the assays to be conducted. Additional samples will also be needed to support the clinical program as biosimilar product development proceeds. It is critical that an uninterrupted clinical study supply be secured so that patients are not forced to drop out of comparative clinical studies due to lack of reference product supply.

## 2. FDA's Reference Listed Drug Site

Novartis notes and emphasizes that the FDA's RLD site<sup>176</sup> states that "...FDA has not independently investigated or confirmed the access limitations described in the inquiries received." Novartis is concerned that the structure and content of FDA's RLD website leads the public, including patients and providers, to believe that all manufacturers listed on the site have participated in "gaming" tactics to delay generic competition. While we cannot speculate as to the reasons for any particular inquiry or complaint by generic manufacturers, in each case involving a Novartis product, generic manufacturers were

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<sup>175</sup> RLD Access Inquiries, FDA, *available at* <https://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/AbbreviatedNewDrugApplicationANDAGenerics/ucm607738.htm> (last updated May 17, 2018).

<sup>176</sup> *Id.*

able to obtain the necessary samples of Novartis medicines to file their applications in a timely manner.

We believe the lack of FDA investigation into each inquiry, or at least the lack of providing more context for readers of the site, has created an impression that all sponsors listed on the site have abused the system to delay generic products when that is not the case. Additionally, we believe that FDA should better articulate the appropriate context surrounding individual circumstances to ensure a more informed understanding by the public of the challenges involved in generic drug development. By lumping all inquiries together, regardless of individual circumstances, the FDA has created the impression that all manufacturers listed on the site are “gaming” the system when the facts of individual cases may reveal the opposite to be true. Therefore, we recommend that FDA provide additional context and update the list as closely as possible in real-time with investigative confirmation of actual access limitations leading to generics development delays. Ideally, we recommend FDA alert the RLD manufacturer once a complaint has been received. The RLD manufacturer could then conduct an internal review of the reason for and potential resolution to the issue, thereby ensuring the product is accessible. At a minimum, FDA should provide the RLD manufacturers with notification at least 48 hours prior to any updates of the RLD site. This would enable the conduct of an internal review to better prepare for a public response and allow for potential resolution with the complainant.

#### **M. Direct to Consumer Advertising**

The FDA is currently evaluating the inclusion of list prices in direct to consumer (DTC) advertising. Novartis supports policies that would better inform patients. However, it is important to provide beneficiaries with information that is useful and improves their understanding in some relevant way. We are concerned that including the WAC in advertisements would be confusing and meaningless as beneficiaries do not pay list price for the drug. Publishing only the list price without context to patient out-of-pocket costs would create more confusion and result in beneficiaries questioning whether they can afford a given product, even if that is not the ultimate price they would pay for that product.

#### **N. Site Neutrality**

Novartis urges CMS to create a site neutrality policy that encourages access to innovative products, while reducing costs and improving quality, specifically for newly launched drugs/technologies that utilize miscellaneous codes for a temporary period. Current coding system limitations do not allow for use of an unlisted code in the Ambulatory Surgery Center (ASC): 42 CFR 416.2 and 416.166 General Exclusions in the ASC and covered surgical procedures do not include those that can only be reported using a CPT unlisted surgical procedure code”. This exclusion forces services to be performed in higher cost settings of care, like the hospital outpatient department (HOPD). Novartis recommends CMS modify coding exclusions and create pathways is to support new technology/innovative drug commercialization.

## **O. International Drug Pricing**

In the RFI, HHS states that U.S. consumers and taxpayers generally pay more for brand drugs than do consumers and taxpayers in other Organisation for Economic Co-operation and Development (OECD) countries, which often have reimbursements set by their central government. HHS seeks comment on a series of questions related to ensuring other countries are contributing equitably to the cost of new drug development.

HHS indicates that the Administration will update historical studies that analyze drug prices paid in countries that are a part of the Organisation for Economic Co-operation and Development (OECD). As they undertake this work, we encourage any new analysis to provide a deeper understanding of the underlying economic drivers that differentiate total healthcare costs, not only prescription drug costs, across the member countries. Factors that can drive different cost bases include salary differences between all types and levels of healthcare providers, how governments may subsidize medical school and other training of healthcare professionals, speed and breadth of patient access to healthcare services due to limited availability of providers, etc. Additionally, any multi-country comparison must look at true net costs between countries, given the deep level of discounting that occurs across the U.S. healthcare system.

In order to bring new treatments and cures to patients, innovative pharmaceutical companies must be able to:

- Secure and effectively enforce patents and protect regulatory test data;
- Obtain timely marketing approval for new medicines; and
- Make those therapies available to patients according to pricing and reimbursement rules and procedures that are fair, transparent, reasonable and non-discriminatory, and that appropriately value and reward patented pharmaceuticals.

In recent years, however, select governments have weakened intellectual property rights and sought compulsory licenses for innovative medicines and proposed or implemented pricing and reimbursement policies that discriminate against medicines made in America, do not appropriately value innovation and lack predictable, transparent, and consultative processes. These practices include international reference pricing, therapeutic reference pricing, and health technology assessment based largely on cost. These practices can impede market access for innovative products and can result in significant negative impacts on patients.

Global, regional, and bilateral trade and investment negotiations provide important opportunities to build on the existing foundation of international rules and to secure commitments needed to drive and sustain innovation. In addition to strengthening intellectual property rights protections, Congress has identified unreasonable foreign pricing and reimbursement policies as major concerns to be addressed in trade negotiations. Specifically, the Trade Promotion Authority (TPA) legislation identifies as a

principal negotiating objective for free trade agreements “to ensure that government regulatory reimbursement regimes are transparent, provide procedural fairness, are nondiscriminatory, and provide full market access for United States products.”

We believe U.S. trade and intellectual property (IP) policy can serve as effective tools to confront other governments’ actions on drug pricing. In doing so, the Administration should coordinate efforts among the Department of Commerce, the U.S. Trade Representative, and the White House IP Enforcement Coordinator (IPEC) to pursue the following:

- **Utilize Available Tools:** We urge the Administration to utilize the tools at its disposal including the annual “Special 301” report, Generalized System of Preferences country reviews, free trade agreements (FTAs), and bilateral and plurilateral consultation mechanisms.
- **Systematically Review Foreign Pricing Practices:** It is critical to conduct more systematic reviews of foreign pricing practices, eliminate distortions, and seek enforceable commitments to honor the value of innovation.
- **Update Price Control Analysis:** In 2004, the Department of Commerce released an analysis of pharmaceutical price controls in OECD countries.<sup>177</sup> We encourage the Administration to update this analysis to identify and assess current price control policies.

For purposes of bilateral and regional FTAs used to address government pricing and reimbursement practices in other OECD countries, we suggest the agreement be comprehensive and enforceable and contain the following elements:

- Commitments to recognize the value of innovation through premium pricing, reduce distortions caused by price controls, reference pricing, and health technology assessments (HTAs);
- Provide transparency in pricing and reimbursement decisions and consult with stakeholders;
- Provide opportunity for appeal to an independent review body; and
- Ensure compulsory licenses are not used to force technology transfer or to deprive patent owners of the full value of their innovations.

#### **P. Promoting Interoperability**

Novartis applauds CMS for its efforts to promote greater interoperability. As a drug development company that both produces and relies on external data, we recognize its importance in providing higher quality, less costly, care to patients. Interoperability is crucial to harnessing the value of data and advancing the healthcare system

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<sup>177</sup> Pharmaceutical Price Controls in OECD Countries: Implications for U.S. Consumers, Pricing, Research and Development, and Innovation, Department of Commerce International Trade Administration (January 2004), available at <https://2016.trade.gov/td/health/DrugPricingStudy.pdf>.

forward. Patients often seek care from multiple providers across a variety of care settings and, for purposes of both quality and cost, it is critical that each is able to easily access a patient's medical history, including laboratory data and the patient's prescription therapies. Recognizing that interoperability is a collective action problem, we also applaud CMS's efforts to seek feedback and incentivize CMS to actively engage with other stakeholders in the healthcare system in order to co-create pragmatic solutions to enhance interoperability at scale.

**Q. Conclusion**

Novartis appreciates the opportunity to comment on this RFI. We understand the need to examine drug reimbursement in Medicare and Medicaid, despite the significant complexities involved. As the Administration continues its work in this area, we urge HHS to maintain a deliberate and thoughtful approach, testing policies on a smaller scale before launching them more broadly and seeking stakeholder feedback regularly. We look forward to working with the Administration on these initiatives as they move forward.

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Novartis greatly appreciates HHS' consideration of these comments. We would be happy to discuss them at greater length. If you have any questions, please do not hesitate to contact me at (862) 778-3284.

Sincerely,

Leigh Anne Leas  
Vice President and U.S. Country Head, Public Policy  
Novartis Services, Inc.

## APPENDIX A

### *Additional Comments on Interchangeability*

There are three critical areas where the draft interchangeability guidance has established criteria that we believe are scientifically unnecessary and, as such, are a barrier towards development of interchangeable biologics in the United States. These regulatory recommendations stipulate that:

- (1) clinical switching studies should be designed with PK or PD endpoints
- (2) reference product material should be purchased only in the US, unless explicitly justified otherwise
- (3) the statistical analysis specified by the human factor studies of the administration device exceed that required of any other class of drugs, including originators and are requiring far more than is necessary.

#### A. Use of PK/PD endpoints

##### i. Underlying premise supporting use of PK endpoints is flawed

The underlying premise for specifying a PK/PD endpoint in an interchangeability study is that there may be underlying safety concerns due to product differences that are triggered by repeated switching between reference product and biosimilar. However, this concern is purely hypothetical and as such is speculative. There is no data cited in the draft interchangeability guidance or published in scientific literature that supports this hypothesis. However, a large body of studies reveals that a one-time switch has not led to concerns. A recent review identified 90 switching studies that cumulatively enrolled 14,225 individual patients, which concluded that “the risk of immunogenicity-related safety concerns or diminished efficacy is unchanged after switching from a reference biologic to a biosimilar medicine.”<sup>178</sup> These conclusions are corroborated by other reviews of studies of one-time switches from a reference biologic to a biosimilar.<sup>179,180,181</sup>

It is hard to understand how one can speculate that there may be a safety concern after multiple switches even though >100 single switch studies did not detect a safety concern.

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<sup>178</sup> Hillel P. Cohen et al., Switching Reference Medicines to Biosimilars: A Systematic Literature Review of Clinical Outcomes, 78 *Drugs* 463 (2018), available at <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5854749/>.

<sup>179</sup> Hans C. Ebbers et al., The safety of switching between therapeutic proteins. 12 *Expert Opin Biol Ther* 1474 (July 31, 2012), available at <https://www.tandfonline.com/doi/full/10.1517/14712598.2012.711308>.

<sup>180</sup> Javier P. Gisbert and Maria Chaparro, Switching from an originator anti-TNF to a biosimilar in patients with inflammatory bowel disease: Can it be recommended? A systematic review. 41 *Gastroenterol Hepatol*. 389 (May 9, 2018), available at <https://reader.elsevier.com/reader/sd/8305E4EB134CE39398D408B482EABD3C4FF84264384586966F232FB7075C429E906E6C8F6A44179959271F4D25FFE726>.

<sup>181</sup> Robert J. Moots et al., Efficacy and Safety Outcomes for Originator TNF Inhibitors and Biosimilars in Rheumatoid Arthritis and Psoriasis Trials: A Systematic Literature Review. 32 *BioDrugs* 193 (May 22, 2018), available at <https://link.springer.com/article/10.1007%2Fs40259-018-0283-4>.

Surely, if there is a systemic concern, one would expect that at least a few of the single-switch studies would also have revealed safety concerns.

Additionally, Sandoz has conducted three studies that evaluated multiple switches between reference biologics and biosimilars: one study with a biosimilar filgrastim, the second study with a biosimilar etanercept, and the third study with a biosimilar adalimumab.

In support of Zarxio® (filgrastim-sndz) registration, Sandoz conducted a clinical safety and efficacy study that incorporated five switchover events, comparing 109 breast cancer patients that had been switched with 52 patients that had been treated continuously with either the reference medicine or the biosimilar. The results showed no differences in efficacy or overall safety over the course of the study. No neutralizing antibodies were detected in either arms of the study.<sup>182</sup>

A cross-over study design incorporating three switchover events was incorporated into the clinical safety and efficacy study that supported licensure of Erelzi® (etanercept-szszs). This was a phase III clinical confirmation study in patients with moderate-to-severe chronic plaque psoriasis. In the initial phase of this study, 264 patients received Erelzi® and 267 received the reference medicine. After 12 weeks, each of the two arms was further randomized 2:1 to continue the same treatment or to receive the other medicine. The switched arms were then switched several more times so that after 52 weeks of follow-up, data were available from 178 patients who were switched three times and from 274 patients who remained on the same therapy throughout the study. The safety, efficacy, and immunogenicity profiles of the switched and non-switched arms were similar.<sup>183</sup>

A third multiple switching study was conducted and published by Sandoz that compared in 231 adalimumab biosimilar patients versus 234 reference medicine patients in moderate-to-severe chronic plaque psoriasis patients, using a four-switchover study design similar to that used to evaluate Erelzi® (etanercept-szszs). Efficacy, adverse events and immunogenicity were similar for both drugs after 51 weeks.<sup>184</sup>

These three studies provide the very first data of the impact of multiple switches between a reference biologic and a biosimilar, and as such, the results should be examined

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<sup>182</sup> Kimberly Blackwell et al., Safety and efficacy of alternating treatment with EP2006, a filgrastim biosimilar, and reference filgrastim: a phase III, randomised, double-blind clinical study in the prevention of severe neutropenia in patients with breast cancer receiving myelosuppressive chemotherapy, 29 Ann. Oncol. 244-249 (Oct. 28, 2017), available at <https://academic.oup.com/annonc/article-abstract/29/1/244/4575094?redirectedFrom=fulltext>.

<sup>183</sup> Christopher Griffiths et al., The EGALITY study: a confirmatory, randomized, double-blind study comparing the efficacy, safety and immunogenicity of GP2015, a proposed etanercept biosimilar, vs. the originator product in patients with moderate-to-severe chronic plaque-type psoriasis. 176 Br J Dermatol 928-938 (Apr. 2017), available at <https://onlinelibrary.wiley.com/action/showCitFormats?doi=10.1111%2Fbjd.15152>.

<sup>184</sup> Andrew Blauvelt et al., Phase 3 randomised study of the proposed biosimilar adalimumab GP2017 in psoriasis – impact of multiple switches, Br J Dermatology (June 19, 2018), available at <https://onlinelibrary.wiley.com/doi/abs/10.1111/bjd.16890>.

carefully to ascertain what learnings may be applied to future interchangeability requirements. The results of the multiple switching studies did not show any hint of the hypothetical concerns postulated in the draft interchangeability guidance.

Given the body of evidence from single and multiple switch studies, it is difficult to understand how one can speculate that there may be a safety concern about single and multiple switches, especially given the switch studies did not detect a safety concern. If there were a systemic concern, one would have expected that a few of the single-switch studies would have revealed safety concerns.

ii. PK/PD endpoints are not appropriate in many situations

It is possible that changes may be detected in PK or PD that are not caused by immunogenicity but to changes in the underlying disease or concomitant medication. For example, in individual patients with active disease the PK response to given antigen may vary with time, with drug clearance rates either increasing or decreasing. It would be misguided to assume that changes in PK or PD rates in patients who are suffering from active disease correlates with changes in immunogenicity as the PK or PD changes in these patients may be reflective of changes in underlying physiology. One way to avoid this confounding factor might be to conduct the switching studies in healthy subjects. This is in fact the recommendation from the Agency in the final guidance entitled “Clinical Pharmacology Data to Support a Demonstration of Biosimilarity to a Reference Product” (December 2016) that states:

*“A study in healthy subjects is considered to be more sensitive in evaluating the product similarity because it is likely to produce less PK and/or PD variability compared with a study in patients with potential confounding factors such as underlying and/or concomitant disease and concomitant medications.”*

In addition, immunogenic events with significant safety sequelae may occur without impacting PK or PD responses in patients. These include (but not be limited to) neutralizing antibodies that interact with endogenous proteins and neutralizing antibodies that bind to the active site of the biologic (thereby impacting efficacy) but that do not impact the clearance rate of the biologic. PK or PD studies would not detect these types of immunogenicity.

Given these reasons, the relationship of immunogenicity to changes in PK is not sufficiently strong to justify the use of PK parameters in **all** cases as primary endpoint(s) applying standard bioequivalence criteria.

iii. Immunogenicity assays are the best method for detection of immunogenicity-related safety concerns

From a scientific perspective, the most sensitive methods to detect antibodies are immunoassays that are designed explicitly to detect antibody molecules. There are many potential formats for such assays, and such assays can be validated. A validated

immunogenicity assay with a low limit of detection is a much more direct and scientifically relevant method to detect potential immunogenicity-related safety concerns than PK endpoints which are merely surrogates for detection of the impact of immunogenicity.

iv. Large-scale PK studies are exceptionally difficult to conduct from a logistical perspective

From a logistical perspective, the call for a long-term PK study that has extensive sampling requirements may be more logistically challenging than that required for other drugs, including novel drugs and biologics. The recommendation for extensive PK measurements at all time points as well as with intensive PK sampling at the latter stages of the study may require hospitalization of patients, potentially including overnight stays in order to control for variability in PK endpoints for which the study will be powered.

It is important to note that repeated, prolonged hospitalization/in-house periods are likely to increase patient burden and would be problematic from the patient's benefit-risk perspective, in particular in fragile, higher-risk patient populations, such as oncologic and/or profoundly immunosuppressed patients. Given this, repeated hospitalizations are unrealistic. Therefore, sponsors will need to conduct intensive PK sampling in an outpatient setting. There is no question that this will lead to sampling errors and high dropout rates. To account for these unavoidable logistical challenges, it will be necessary to increase sample size, which in turn will increase logistical complexity.

The call for a study design with intensive PK sampling is a major barrier to establishing interchangeability of a proposed interchangeable biologic, independent of whether or not there are any true safety concerns.

v. Proposal for a more appropriate and feasible study design

In the light of all considerations described above, instead of conducting a logistically challenging switching study with PK or PD primary endpoints that contains an assessment of PK bioequivalence necessitating intensive PK sampling, we recommend an alternative design for the switching study that contains the following elements:

- Utilization of an efficacy endpoint related to the indication being studied or validated alternative biomarker;
- Descriptive safety monitoring;
- "Sparse" PK sampling (limited sampling, but targeting important parameters; e.g. measure  $C_{\text{trough}}$  levels if applicable) following sequential switches;
- Immunoassays to detect circulating antibodies (and if present, neutralizing antibodies).

Sparse PK sampling is often used in clinical practice to guide the selection of appropriate dosing and the overall therapeutic strategy. Furthermore, the clinical utility of therapeutic drug monitoring (typically  $C_{\text{trough}}$ ) and anti-drug antibody assessments was demonstrated

in patients with inflammatory bowel diseases treated with the highly immunogenic anti-TNF- $\alpha$  mAbs.<sup>185</sup>

## B. Use of non-US Reference Product

We strongly urge that the final guidance on interchangeability be revised to provide greater openness and flexibility to accept use of non-US licensed reference product to seek approval of an interchangeable biologic in the U.S. if scientifically justified. The stated reason for requiring US-sourced reference biologic material is that the U.S.-sourced material may differ in some analytically undetected manner from ex-U.S. material, and while such a difference does not impact biosimilarity it has the potential to impact safety or efficacy after multiple switching. In our opinion, this is a far-fetched hypothetical concern that is not supported by data.

In the first instance, “the analytical tools designed to measure differences at the molecular level are far more sensitive and specific than tools available to physicians during clinical trials,” including PK endpoints.<sup>186</sup>

Secondly, there is only a single underlying safety and efficacy database supporting a reference biologic, irrespective of where it is licensed. If there is any divergence in critical quality attributes in a specific region from that in another region due to local factors, the sponsor of the reference biologic must provide the local health authority sufficient experimental data to establish that the proposed difference has no impact on the safety or efficacy that was established in the initial safety and efficacy studies.

As proposed by Webster and Woollett (2017)<sup>187</sup>, we recommend that ex-U.S. reference material be acceptable under the following conditions:

1. “The chosen reference has been approved in a jurisdiction that has formally adopted the guidelines of the ICH. This criterion ensures that any comparability studies that have been conducted to support manufacturing changes of the reference have been conducted according to an internationally accepted process and standard, and also that the reviewing authority is experienced in operating to this standard.
2. The formulation of the chosen reference has the same pharmaceutical form and route of administration as the reference biologic; the same content of active pharmaceutical ingredient as a presentation of the reference biologic; and the

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<sup>185</sup> Dario Sorrentino et al., Therapeutic Drug Monitoring and Clinical Outcomes in Immune Mediated Diseases: The Missing Link. 22 *Inflamm Bowel Dis.* 2527-37. (2016), available at <https://academic.oup.com/ibdjournal/article/22/10/2527/4561861>.

<sup>186</sup> Arnold Vulto and Orlando Jaquez, The process defines the product: what really matters in biosimilar design and production? 56 *Rheumatology* iv14–iv29 (Aug. 30, 2017), available at [https://academic.oup.com/rheumatology/article/56/suppl\\_4/iv14/4097922](https://academic.oup.com/rheumatology/article/56/suppl_4/iv14/4097922).

<sup>187</sup> Christopher Webster and Gillian Woollett, A ‘Global Reference’ Comparator for biosimilar development, 32 *BioDrugs* 279 (May 19, 2017), available at <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5541093/>.

same composition of excipients as the reference biologic; or, if the compositions of excipients in the products are different, there are data to show that the differences are without clinical effects.

3. There is substantial evidence in the public domain that the chosen reference and the reference biologic have been approved in their respective jurisdictions on the basis of essentially the same original data, including clinical safety and effectiveness data.”

C. Statistical criteria should not be imposed on comparative use human factors studies

We support the FDA’s recommendation to use a threshold analysis to understand if the presentation of the interchangeable biologics has minor, moderate or major difference from the originator’s presentation. However, the specific recommendation to use human factors study with a clinical non-inferiority statistical analysis in the guidance is a new concept and standard that has not previously been applied to pharmaceutical agents. This recommendation is not consistent with the agency’s previous human factor study guidance and has the potential to be a barrier to establishing interchangeability.

The imposition of non-inferiority statistical analyses increases the data burden while providing limited, if any, practical information. Novartis believes that a human factor validation study, as already described by the FDA in the 2016 guidance “Applying Human Factors and Usability Engineering to Medical Devices,”<sup>188</sup> would provide the greatest value in assessing any potential increased use-related risks associated with the use of the proposed interchangeable product. Elements from this draft guidance include:

- Multiple user groups;
- Participants experienced with use of the reference biologic or proposed interchangeable product as well as those naive to the use of the reference product;
- With a focus on observing use errors and difficulties; and
- Understanding the root cause of those use errors and difficulties.

Consistent with the final guidance “Applying Human Factors and Usability Engineering to Medical Devices”, these analyses should be descriptive, and the most important assessment should be whether the presentation of the interchangeable biologics has any negative impact on the use-related risks and not on whether or not the responses are “highly similar”. It then follows that the final guidance on Interchangeability should not require the demonstration of non-inferiority in terms of percentage use error with a statistical standard.

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<sup>188</sup> Applying Human Factors and Usability Engineering to Medical Devices: Guidance for Industry and FDA Staff, FDA (February 2016), *available at* <https://www.fda.gov/downloads/medicaldevices/.../ucm259760.pdf>.

This approach would then be consistent with other FDA guidances and FDA recognized standards related to the application of human factor and usability engineering. Novartis also believes that the agency should encourage the biosimilar sponsor to develop presentations/devices with improved user-device interface wherever possible, but not simply hold to “comparative” or “as similar as possible” criteria.