



April 2, 2012

VIA ELECTRONIC DELIVERY

Marilyn Tavenner
Acting Administrator
Centers for Medicare & Medicaid Services
Department of Health and Human Services
Room 445-G
Hubert H. Humphrey Building
200 Independence Avenue SW
Washington, DC 20201

Re: CMS-2345-P (Proposed Rule, Medicaid Program; Covered Outpatient Drugs)

Dear Ms. Tavenner:

The Biotechnology Industry Organization ("BIO") is pleased to submit the following comments to the Centers for Medicare and Medicaid Services' ("CMS") Proposed Rule regarding covered outpatient drugs under the Medicaid Program, which was published in the Federal Register on February 2, 2012 (the "Proposed Rule").¹ The Proposed Rule represents rulemaking to implement changes enacted by the Patient Protection and Affordable Care Act of 2010 ("ACA").² BIO is the largest trade organization to serve and represent the biotechnology industry in the United States and around the globe. BIO represents more than 1,100 biotechnology companies, academic institutions, state biotechnology centers, and related organizations in the United States. BIO members are involved in the research and development of health care, agricultural, industrial, and environmental biotechnology products.

As the representative of an industry that is devoted to improving health care through the discovery of new therapies, BIO understands the importance of the Medicaid drug rebate program (the "Program"). The Program ensures that Medicaid is able to provide affordable drugs and therapies to low-income and other needy populations, and the ACA, with its wide-ranging revisions to the healthcare system, includes a number of provisions impacting the operation of the Program. BIO appreciates CMS' effort through the Proposed Rule not only to bring additional clarity to those ACA provisions, but also to address through regulation a number of additional

¹ Medicaid Program; Covered Outpatient Drugs, 77 Fed. Reg. 5318 (Feb. 2, 2012) (42 C.F.R. pt. 447)

² As used in these comments, the abbreviation "ACA" shall refer collectively to the Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010, the Medicare and Medicaid Extenders Act of 2010, the Education, Jobs, and Medicaid Funding Act of 2010, and other subsequent legislation.

topics not previously included in regulation but nevertheless of significance to Program operation and integrity. The resulting Proposed Rule represents a comprehensive overhaul of the existing regulation that governs the Program, and includes wholesale revisions to the calculation of Average Manufacturer Price ("AMP"), conforming revisions to and clarifications of the calculation of Best Price ("BP"), revisions to the rebate formulas, and extensive requirements governing reimbursement rates for drugs. Final implementation will significantly impact patient access to drugs and biologicals, and BIO urges CMS to provide the additional guidance and clarity described below to ensure continued beneficiary access to important drug and biological therapies.

The comprehensive nature of the Proposed Rule means that BIO's comments are correspondingly extensive as well. The Proposed Rule goes well beyond the provisions of the ACA to address multiple aspects of the Program. We support CMS' efforts to ensure that clear and comprehensive regulatory standards exist for this Program and appreciate the efforts CMS has made in the Proposed Rule to support that result. Certain aspects of the Proposed Rule, however, would impose requirements that are impractical and, coming 20 years into the Program, nearly impossible to implement.

The purpose of the rulemaking process is to ensure CMS is made aware of the legal, policy, and operational implications of its proposals. We provide that feedback below from the perspective of the manufacturers that generate the pricing data and pay the rebates upon which the entire Program relies. CMS' proposals to abandon the "presumed inclusion" approach to the AMP calculation and to expand the Program to the Territories are two issues that BIO strongly opposes, in part based on the immense operational burdens those changes would create. BIO also opposes CMS' effort to expand the line extension alternative rebate formula well beyond the limited scope provided by statute. There are many aspects of the Proposed Rule that BIO does support as well, including CMS' retention of the substantive bona fide service definition and clarification of the Best Price definition and patient transactions. It is very clear that CMS expended enormous effort in generating what can only be called a complete overhaul of the Medicaid rebate regulations. While BIO does not support all of those changes, we commend CMS for the effort it has made to provide all stakeholders with clear standards for compliance.

I. ANY FINAL RULE MUST BE PROSPECTIVE ONLY AND PROVIDE MANUFACTURERS WITH NECESSARY LEAD TIME FOR IMPLEMENTATION.

The Proposed Rule does not discuss whether CMS intends to apply any resulting final rule on a prospective basis. Given the breadth of changes suggested in this Proposed Rule and the impact many of those changes would have on manufacturer systems and processes, BIO strongly believes that any final rule should be applied prospectively only, as of that rule's stated effective date. To the extent CMS intends for any provision of a final rule to apply retroactively, CMS should specifically enumerate those provisions and state the basis for retroactive application. BIO notes that

retroactivity is not favored in the law, and a “grant of legislative rulemaking authority will not . . . be understood to encompass the power to promulgate retroactive rules unless that power is conveyed by Congress in express terms.”³

Even with prospective application, manufacturers still may require significant lead time to implement certain aspects of the final rule, particularly where those requirements diverge from current manufacturer practice and require significant systems or process changes. Manufacturers also will require time to develop and assign new classifications to data and customers. We indicate where that is the case below on an issue-specific basis, and urge CMS to adopt reasonably delayed effective dates as to those issues in any final rule.

II. THE AMP CALCULATION METHODOLOGY: CMS SHOULD RETAIN THE PRESUMED INCLUSION APPROACH – 42 C.F.R. § 447.504

BIO supports many of CMS’ proposals for calculating AMP under the provisions of the ACA. The Proposed Rule’s adoption of the “wholesaler” definition that was expanded by the ACA and the opportunity for manufacturers to restate base date AMP are among those provisions of the Proposed Rule that BIO supports. BIO nevertheless has significant concerns with regard to other AMP methodology proposals, and in particular the Proposed Rule’s rejection of the long-standing presumed inclusion approach to calculating AMP. Manufacturers have used the presumed inclusion approach since the Program’s inception and it should not be abandoned now, particularly given CMS’ desire to expand the use of AMP data to the determination of pharmacy reimbursement rates.

CMS relies on the stability of historical AMP data, as well as CMS’ own view that those data are an accurate measurement of pharmacy acquisition costs, to support its proposals to use AMPs to calculate Federal Upper Limits (“FULs”) and actual acquisition costs (“AACs”). That reliance cannot justify prospective use of AMP for these reimbursement metrics if the very framework for calculating AMP is completely overhauled prospectively as well, as would be the case with the elimination of the presumed inclusion approach. Abandonment of presumed inclusion in favor of the “build-up” methodology included in the Proposed Rule eliminates CMS’ ability to assume that the AMP trends of the past will continue going forward. As detailed below, use of a build-up approach will almost certainly lower reported AMP values for most products, possibly to \$0, and increase the volatility of all AMP data. Even the methodology requirements included in the Proposed Rule – such as the use of a 12-month rolling average estimation methodology for lagged price concessions – assume continued use of the presumed inclusion approach, which is the methodology used to calculate Average Sales Price (“ASP”) from which the Proposed Rule borrows the rolling average estimation approach.

³ See, e.g., *Bowen v. Georgetown Univ. Hosp.*, 488 U.S. 204, 208 (1988).

Simply put, the presumed inclusion approach provides the framework for the historical AMP trends and methodological assumptions on which all other aspects of the Proposed Rule rely, and the rejection of the presumed inclusion approach therefore undermines the reasonableness and feasibility of the Proposed Rule as a whole. For these same reasons, rejection of presumed inclusion also is contrary to all of the regulatory simplification mandates included in Executive Orders 12866 and 13563. We detail below the specific bases for this conclusion but wish to emphasize as strongly as possible at the outset the uniform opposition of the BIO membership to CMS' proposal to prohibit use of the presumed inclusion approach going forward.

A. Presumed Inclusion Must Be Retained to Ensure Accurate AMP Figures and Pharmacy Reimbursement.

CMS has proposed a major revision to the way that manufacturers calculate AMP. The Proposed Rule rejects the long-established and time-tested "presumed inclusion" methodology for calculating AMP,⁴ which directs manufacturers to assume that product sold to wholesalers is re-sold to AMP-eligible customers, absent "adequate documentation" to the contrary.⁵ The Proposed Rule instead directs manufacturers to calculate AMP "based upon their *actual sales* to retail community pharmacies or wholesalers for drugs distributed to retail community pharmacies."⁶ In other words, a manufacturer must be able to document that the product it sells to a wholesaler or distributor ultimately is re-sold to an AMP-eligible customer (a retail community pharmacy ("RCP") or an entity conducting business as an RCP in the case of non-5i AMP) before the manufacturer can include that original direct sale and any associated discounts in the AMP calculation.⁷

The Proposed Rule acknowledges that presumed inclusion is a "reasonable alternative approach" under the ACA. CMS nevertheless opts for the build-up approach on the assumption that it will result in more accurate AMPs by ensuring that only those sales to entities contemplated by the statutory definition are included in the AMP calculation.⁸ CMS' primary concern, given that AMPs will be used both for FULs as well as potentially for AACs, appears to be that the reported AMP figures not be inappropriately low.⁹ As detailed below, the opposite is the case. The build-up approach virtually ensures that many if not most (in the case of some drugs) AMP-

⁴ In the Deficit Reduction Act of 2005 Final Rule ("DRA Final Rule"), effective for the fourth quarter of 2007 and forward, CMS defined "retail pharmacy class of trade" as "*any entity that purchases prescription drugs from a manufacturer or wholesaler for dispensing to the general public . . . except as otherwise specified by the statute or regulation.*" Medicaid Program; Prescription Drugs, 72 Fed. Reg. 39,142, 39,147 (July 17, 2007) (42 C.F.R. pt. 447) (emphasis added).

⁵ Medicaid Drug Rebate Program Manufacturer Release No. 29 (June 5, 1997) (prices to wholesalers are included in AMP "except for sales to wholesalers which can be identified with adequate documentation as being subsequently sold to any of the excluded sales categories"); 72 Fed. Reg. at 39,241 (42 C.F.R. § 447.504(g)(1)).

⁶ 77 Fed. Reg. at 5330 (emphasis added).

⁷ The Proposed Rule's discussion of the "build-up" approach is not limited specifically to the "traditional" AMP calculation, defined in § 447.504(b), and therefore BIO requests that CMS clarify whether the "build-up" approach is applicable to the "5i" AMP calculation, defined in § 447.504(d), as well.

⁸ 77 Fed. Reg. at 5330.

⁹ *Id.* at 5329.

eligible sales are not captured in the AMP calculation, and that the resulting AMPs are both lower and more volatile. CMS cannot proceed with a build-up approach and achieve the statutory objective or policy goals of accurate reimbursement and rebate amounts.

1. The Build-Up Approach Will Result in AMPs That Are Lower, Lagged, and Subject to Volatility.

The build-up approach would permit manufacturers to include wholesaler sales and associated discounts in the AMP calculation only where the manufacturer can document that the wholesaler resold the product to an AMP-eligible end customer. The Proposed Rule itself recognizes that “there may be instances where the wholesaler actually re-sells the drug to the retail community pharmacies but the manufacturer does not have documentation regarding that actual sale to the retail community pharmacy.”¹⁰ The use of the term “may” suggests that CMS believes this may be only an infrequent occurrence. That is not the case. Manufacturers will encounter this for any non-contracted sale of an RCP product. Where a manufacturer does not sell directly to RCPs or otherwise offer discounts to RCP end-customers, as is often the case with single source products, older drugs that no longer are contracted, or products that do not have therapeutic class competition, manufacturers will have no such documentation and the calculated AMP will be \$0. Put simply, many products are only sold to wholesalers with no direct sales to or contracts with end-customers. Unless presumed inclusion is allowed, these products will have no AMP-eligible sales and so no AMP. BIO believes this is an unreasonable result.

The only sources of end-customer data that manufacturers currently use on a widespread basis in the AMP calculation are rebate and chargeback claims. Wholesalers submit chargeback claims to a manufacturer when the manufacturer has contracted with an end-customer for a discounted price, the wholesaler extends that discounted price to the end-customer, and then “charges back” the difference between that discount price and the current Wholesaler Acquisition Cost (“WAC”) to the manufacturer. With that chargeback claim, the wholesaler identifies the end-customer to which it sold the unit and the manufacturer can identify whether that end-customer is or is not eligible for the AMP calculation. Rebate claims can be submitted by the end-customer itself, where it has entered into a rebate arrangement with the manufacturer, or by an insurer, pharmaceutical benefit manager (“PBM”), or other third party payer to which the manufacturer has agreed to pay rebates on utilization paid for by that entity. In some cases, rebate claims data may provide the detail necessary to identify the end-customer that dispensed the drug to the patient, but that is not always or consistently the case.¹¹ Many if not most manufacturers rely on chargeback and rebate data under the presumed inclusion approach to identify indirect ineligible sales, i.e., sales to a

¹⁰ *Id.* at 5330.

¹¹ Certain insurer, PBM, and third party payer data may not provide data sufficient to determine whether the dispensing entity was an RCP or mail entity. Reliance on such data also may lead to the double-counting of RCP sales where such end-customer sales are otherwise subject to a chargeback.

wholesaler or distributor that were resold to AMP-ineligible entities, and then remove those sales from the AMP calculation.

- Lower AMPs: By their nature, chargeback and rebate claims can identify only discounted end-customer sales. Manufacturers do not enter into such contracted discounts with all of their end-customers or for all of their products. In fact, many manufacturers of single source or innovator multiple source drugs do not enter into such contracts with end-customers at all. Non-discounted sales, therefore, never could be identified by these types of data so as to be included in the AMP calculation under a build-up approach. These non-discounted, WAC sales to RCPs would not be captured in the AMP calculation. As a result, the build-up approach, using the only end-customer identifying data that manufacturers currently use in their AMP calculation on a widespread basis, necessarily will produce an average of a manufacturer's discounted prices to the retail channel rather than an average of the manufacturer's total sales to the retail channel, as the statute requires.¹² A build-up based AMP, therefore, always will be lower than a presumed inclusion based AMP because the former, where based on chargeback and rebate data, will never include non-discounted WAC sales. Presumed inclusion, in contrast, starts with a manufacturer's total sales to wholesalers, and only applies discounts that can be documented as related to RCP channel units, and therefore always will capture undiscounted sales to end-customers. It is important to note that the AMPs calculated using a presumed inclusion methodology, which in general are expected to be both more accurate but also higher, will generate higher rebates for manufacturers as well. Our members nevertheless support this approach and the higher rebate liability because of their serious concerns with the build-up methodology.
- Zero Dollar AMPs: The Regulatory Impact Analysis in the Proposed Rule specifies that the Proposed Rule's provisions and its corresponding burden analysis assume a manufacturer will only use "existing sales" data.¹³ These data will generate not just artificially-low AMPs, which is precisely what CMS sought to avoid by favoring the build-up approach, but zero-dollar AMPs as well. To the extent that a manufacturer has no end-customer contracted sales, then that manufacturer will have no end customer sales to support the AMP calculation at all, and the reported AMP will be zero. Congress specifically amended the ACA's AMP definition to

¹² Social Security Act ("SSA") § 1927(k)(1)(a), 42 U.S.C. § 1396r-8(k)(1)(a) (definition of AMP requires inclusion of sales to wholesalers for drugs distributed to RCPs as a whole).

¹³ 77 Fed. Reg. at 5355.

include the alternative “5i” AMP definition, discussed in more detail below, to eliminate the possibility of zero dollar AMPs. CMS should not adopt a methodology that almost certainly guarantees this result for non-5i products.

- Lagged and More Volatile AMPs: Finally, where rebate and chargeback data do exist to identify AMP-eligible end-customer sales, those data by definition will be lagged, and therefore any AMP values they do generate will be lagged as well and not reflective of the manufacturer’s net price for the reporting month. These lagged AMPs also have the potential to fluctuate significantly month-to-month based entirely on the timetable by which third parties submit their chargeback and rebate data to the manufacturer. These results are completely inconsistent with the statutory requirement (and policy goal) that AMP reflect the manufacturer’s actual average net price in the reporting period.

There may be other data sources available, for purchase, that could potentially facilitate manufacturer identification of end-customer sales for the AMP calculation. While manufacturers typically have not looked to such information to support their AMP calculations to date, these data include wholesaler outbound sales data, commonly known as “867” or “trace” data, as well as channel distribution data available from third party vendors. These data sources generally are used for forecasting purposes and are not certified or guaranteed in any manner. In fact, end-customers must permit wholesalers to identify their purchases in these reports, and a growing number of end-customers (including entities that would qualify as RCPs) are blinding their data. For these reasons, manufacturers, as a general matter, do not use any of these data to generate AMP values today, for reasons including that these data often are incomplete and cannot be sufficiently validated by manufacturers to ensure the generation of compliant, certifiable AMP values.

Even if such significant barriers to compliant use of these data could be overcome, CMS certainly cannot mandate their use as a basis for justifying the adoption of a build-up approach. As discussed above, the Proposed Rule’s manufacturer burden analysis assumes manufacturers would use only “existing sales” information to comply with the Proposed Rule’s requirements, and so does not address such added data costs at all. If CMS were inclined to explore the possibility of requiring manufacturers to use purchased data to support the build-up approach more fully, CMS would need to re-issue that analysis and address the costs associated with these data prior to finalizing the proposal.¹⁴ Such a mandate would be unlikely to pass muster under Executive Order 12866 in any event, as that order requires CMS “to design its regulations in the most cost-effective manner” such that the regulation imposes “the least burden on

¹⁴ Such data purchases themselves could drive AMP lower to the extent the purchase prices for the data do not qualify as fair market value and therefore as bona fide service fees.

society.”¹⁵ ***Where CMS already has concluded that a presumed inclusion approach is permissible, and that approach yields qualitatively and quantitatively superior results at a lower cost and burden to manufacturers, CMS simply cannot move forward with a build-up approach, with or without a mandate to purchase end-customer identifying data.***

Finally, the build-up approach is not a viable option because it cannot be implemented without significant lead time for manufacturers to prepare their calculation systems for the transition from a presumed inclusion approach. The government pricing systems currently sold and supported by Revitas (formerly known as i-Many) and Model N, the two software vendors utilized by a significant number of manufacturers, do not currently have the capability to calculate AMP using a build-up approach. In fact, BIO's members have confirmed that Revitas would require significant lead time to prepare software capable of handling a build-up calculation. If CMS were to issue a final rule that mandates the build-up approach, manufacturers would need a minimum of twelve months – and perhaps a number of years – to prepare to go live with a build-up methodology. The programming, implementation, and validation steps needed to ensure compliant implementation and results that can be certified absolutely require that a build-up approach not be required until at least 12 months from the final rule's publication.

2. A Build-Up Methodology Will Undermine Key Manufacturer Compliance Safeguards and Require Revisions to the AMP Certification.

The DRA Final Rule imposed a certification requirement on manufacturer AMP submissions for the first time.¹⁶ That certification requires manufacturers to certify that the submitted AMP data are both accurate and complete.¹⁷ That certification has made the validation of submitted pricing data a key compliance priority to BIO's members, as well as industry-wide, and has led to the development of a multitude of data and calculation validation measures.

One of the primary mechanisms manufacturers have developed to validate their AMP calculation under the presumed inclusion approach is to reconcile the direct sales figures used in that calculation to the direct sales amounts reflected in the manufacturer's own financial accounting records, such as the general ledger. The

¹⁵ Exec. Order No. 12,866, 58 Fed. Reg. 51,735, 51,736 (Oct. 4, 1993).

¹⁶ 72 Fed. Reg. at 39,243 (42 C.F.R. § 447.510(e)).

¹⁷ The manufacturer certification in DDR provides, in relevant part: “I hereby certify, to the best of my knowledge, the data being sent to CMS with this submission is complete and accurate at the time of submission, and was prepared in accordance with the manufacturer's good faith, reasonable efforts based on existing guidance from CMS... I understand that the information contained in the submission may be used for Medicaid Rebate and payment purposes and that civil monetary penalties and/or termination from the Medicaid Rebate Program may be enforced if the information provided is found to be misrepresented. ...” (emphasis added).

presumed inclusion approach allows manufacturers to begin their AMP calculations with all sales and then subtract excluded transactions. This approach enables manufacturers to ensure all AMP data points are matched to data on the company's general ledger and, most importantly, that no data are missing. General ledger reconciliation is one of the most effective means of assuring that all relevant data are captured for the calculation. Data on the general ledger are verified and reported in a number of other contexts and subject to additional legal regimes and industry standards such as Sarbanes-Oxley and Generally Accepted Accounting Principles. The general ledger reconciliation therefore is a critical component of data validation. Our members' experience is that the Department of Health and Human Services Office of Inspector General ("OIG") requires general ledger reconciliation when conducting manufacturer financial audits. We strongly recommend that CMS consult with the OIG regarding the audit implications of CMS' build-up methodology proposal, as we believe the OIG would need to revise its audit processes if the presumed inclusion approach is not retained in a final rule.

As discussed above, the build-up methodology does not rely on the manufacturer's own direct sales data to identify end-customers, but rather on lagged data that are supplied by third parties. Third party lagged sales data are very difficult (if not impossible) to validate through reconciliation to the manufacturer's own sales data. In fact, it is quite common for those data to be revised and corrected, often more than once, by the submitting party. CMS simply cannot retain the existing certification standard if it mandates an AMP methodology that necessarily relies on data that may not be subject to complete validation by the manufacturer. If CMS proceeds with the build-up approach, therefore, it must revise the current certification requirement so that it is limited to the manufacturer's own data.

B. A Build-Up Methodology Undermines the Use of AMP As A Reimbursement Metric.

CMS specifically opted for the build-up approach based on its assumption that "build-up" was the better option for avoiding artificially-low AMPs that would result in FULs that are inadequate to cover pharmacy acquisition costs.¹⁸ The same rationale supports CMS' proposal that states use AMP data as a basis for AAC-based reimbursement. In both cases, BIO respectfully submits that CMS is just plain wrong. The detailed discussion above should amply demonstrate that "build-up" undermines rather than supports use of AMP as a basis for FULs and AAC-based reimbursement.

It is the build-up methodology – not the presumed inclusion approach – that will result in artificially low and even zero-dollar AMPs, because that methodology, due to the data available to manufacturers, will include few if any WAC-based sales. For independent and community pharmacies, which often do not receive manufacturer discounts, the build-up methodology will almost certainly result in reimbursement rates

¹⁸ 77 Fed. Reg. at 5329.

that are too low. The build-up methodology also will generate AMPs that are lagged, and so not reflective of current period pricing, as well as more volatile. Those two attributes disqualify rather than support AMPs for use in reimbursement.

The presumed inclusion approach, with its basis in manufacturer sales to wholesalers, ensures that undiscounted sales to the RCP channel remain and are accounted for in AMP. That larger sales base as the starting point for the AMP calculation also works to dampen volatility in reported AMPs over time. Presumed inclusion also virtually eliminates the possibility of zero-dollar AMPs, as CMS should be able to validate based on its own experience with reported AMP data since the implementation of the DRA Final Rule. It is presumed inclusion, therefore, not “build-up,” that supports CMS’ use of AMP in FULs and AAC-based reimbursement.

C. A Build-Up Methodology Is Inconsistent with Other Federal Pricing Methodologies and Will Lead to Inappropriate Substitution of AMPs for ASP-Based Part B Payment Limits.

Manufacturers must calculate and report average prices under their Federal Supply Schedule (“FSS”) Agreement and for their Medicare Part B drugs as well. These two average calculations – the Non-Federal Average Manufacturer Price (“Non-FAMP”) and ASP calculations – both utilize a presumed inclusion approach. Use of a radically different approach for calculating AMP will complicate a manufacturer’s calculation processes and increase the risk of error.

Executive Order 12,866 specifically directs CMS to “avoid regulations that are inconsistent [and] incompatible” with those of other federal agencies, and President Obama’s 2011 Executive Order 13,563 adopts the principles of Executive Order 12,866 and exhorts CMS to adopt approaches that promote “coordination, simplification, and harmonization” across agencies.¹⁹ A mandate from CMS to use two vastly different approaches to calculate very similar price points is completely contrary to the President’s initiative for regulatory simplification. Coordination and harmonization instead require use of presumed inclusion methodologies across all three average price types.

Harmonized methodologies are not just good policy. In the case of ASP, it also is imperative to avoid inappropriate substitution of AMP for ASP as the basis for Part B reimbursement rates. Through the Physician Fee Schedule Rule for 2012, CMS moved forward with rules for the substitution of AMP for ASP as the basis for Medicare Part B payment limits.²⁰ Under those rules, CMS will substitute AMP for ASP when ASP exceeds AMP by 5 percent either in the two consecutive quarters immediately prior to the current quarter, or three of the previous four quarters immediately prior to the

¹⁹ Exec. Order, *supra* note 15; Exec. Order No. 13,563, 76 Fed. Reg. 3821, 3822 (Jan. 18, 2011).

²⁰ Medicare Program; Payment Policies Under the Physician Fee Schedule, 76 Fed. Reg. 73,026, 73,288 (Nov. 28, 2011) (42 C.F.R. pts. 410, 414, 415, and 495).

current quarter.²¹ BIO is very concerned that the use of a build-up methodology in AMP, and the resulting lower AMP figures, will trigger this substitution due solely to the difference in methodology used to calculate AMP (build-up) versus ASP (presumed inclusion).

CMS' implementation of AMP substitution under Part B necessarily is based on the assumption that any differences in the two pricing figures will be based on differences in actual discount rates provided rather than differences in calculation methodologies alone. In adopting these AMP substitution rules, CMS specifically rejected stakeholder requests to delay AMP substitution until the issuance of this Proposed Rule and its guidance on how to calculate an ACA-defined AMP. CMS stated that its "6-years' experience in monitoring AMP and ASP" provided CMS with the context needed to evaluate and move forward with its proposal.²² As discussed above, that historical experience is irrelevant if CMS abandons the presumed inclusion approach for AMP, because the AMPs reported on a prospective basis will be lower and more volatile, even where sales and discount rates do not change. The adoption of a build-up approach therefore threatens not only the adequacy of Medicaid reimbursement rates but Medicare Part B reimbursement rates as well.

D. A Build-Up Methodology Will Impose Significant Costs on Manufacturers.

BIO appreciates CMS' efforts in its burden analysis to evaluate and quantify the administrative and economic burdens that the Proposed Rule would impose on manufacturers. BIO is very concerned, however, that the analysis in no way contemplates the costs that the build-up approach would impose on manufacturers. The Proposed Rule ignores the enormous operational challenges that will be presented to manufacturers if a build-up AMP approach is finalized. Because presumed inclusion is the industry norm, manufacturers will need to invest significant funds and the time of numerous personnel to rebuild their government pricing systems to operate in a build-up framework. For many manufacturers, this effort will almost certainly involve the expense of hiring outside consultants and contractors in order to develop compliant government pricing systems. As noted above, these costs, at a minimum, support the need for an extended implementation period before any build-up methodology becomes mandatory. They also further undermine the reasonableness of this proposal in an age of regulatory simplification. BIO strongly urges CMS to take these costs into account and conclude that the build-up approach should be abandoned.

III. AMP CALCULATION METHODOLOGY – ADDITIONAL ISSUES – 42 C.F.R. § 447.504

The Proposed Rule includes many other provisions regarding the methodology for calculation of AMP. BIO addresses those additional topics below.

²¹ 76 Fed. Reg. at 73,288, 73,473 (42 C.F.R. § 414.904(d)(3)).

²² *Id.* at 73,295.

A. BIO Supports the Use of 12-month Rolling Average Ratios in the AMP Calculation But Believes They May Need to Be Reconsidered Under A Build-Up Approach – 42 C.F.R. § 447.510(d)(2)(iii)

Consistent with the ACA's amendment of the Medicaid rebate statute, the Proposed Rule directs manufacturers to use the ASP methodology for estimating lagged price concessions in the monthly AMP calculation.²³ CMS specifically proposes that "[i]n calculating monthly AMP, a manufacturer must estimate the impact of its lagged price concessions using a 12-month rolling average percentage to estimate the value of those discounts."²⁴ BIO supports the use of this approach in the ASP calculation and believes it would be appropriate in the AMP calculation under a presumed inclusion approach as well. BIO believes CMS should codify that methodology with the same specificity as is included in the ASP regulation, however, and in particular by specifying that (1) the numerator of the ratio should be 12 months of AMP eligible lagged price concessions, (2) the denominator of the ratio is 12 months of AMP eligible sales, and (3) the ratio should be applied to the current month's AMP eligible sales. These details are included in the ASP regulation, at 42 C.F.R. § 414.804(a)(3).

While BIO supports the use of the ASP lagged price concession ratio methodology under a presumed inclusion approach, BIO is concerned that use of an estimation methodology derived under a presumed inclusion approach and applying that methodology to a build-up calculation could result in even further distortions to the resulting AMP figures. As noted above, the ASP calculation methodology is based on a presumed inclusion approach, and its lagged price concession methodology therefore estimates such discounts by comparing lagged discounts over the most recent 12-month period to actual, non-lagged manufacturers sales in that same period. Under a build-up approach, AMP would no longer be calculated using actual, non-lagged manufacturer sales. Manufacturer sales instead would be quantified based on the same lagged data that would be used to quantify the lagged price concessions themselves. In that case, the 12-month ratio would compare lagged price concession data to lagged sales data, and it is difficult to predict whether the result would be an appropriate estimate for lagged price concessions. Indeed, if the underlying sales figures in the AMP calculation are based on lagged data themselves, it is possible that the lagged price concessions should be applied on an actual rather than estimated basis. In either case, BIO is concerned that this aspect of the AMP methodology requires greater analysis and input by stakeholders should CMS proceed with the build-up approach.

If CMS instead retains the presumed inclusion methodology, as BIO strongly urges CMS to do, BIO supports not only the use of the ASP methodology for estimating lagged price concessions but also urges CMS to permit manufacturers to use a similar methodology to estimate indirect ineligible sales that are identified by lagged price

²³ 77 Fed. Reg. at 5344. See 42 U.S.C. § 1396r-8(e)(5).

²⁴ 77 Fed. Reg. at 5365 (Proposed § 447.510(d)(2)(iii)).

concession data, such as FSS sales identified through chargebacks. CMS encourages manufacturers to use such an approach in the ASP calculation, but has refrained from imposing this as a requirement.²⁵ A common approach, and one identified by CMS as permissible but not required, is to develop a ratio of indirect ineligible units identified through chargeback and rebate data for the most recent 12-month period, in the numerator, to direct eligible sales units for the same period, in the denominator. The resulting ratio is then applied to the current period's direct eligible sales dollars and units to estimate the proportion of those sales dollars and units that are indirect ineligible sales. If CMS permits the continued use of the presumed inclusion approach, CMS should clarify that manufacturers may also estimate indirect ineligible sales using the methodology that the manufacturer uses for its ASP calculation. This is not only consistent with the ASP methodology but also will work to reduce unnecessary AMP volatility. If the manufacturer does not report ASP for its products, then manufacturers should be able to use any 12-month rolling average approach that is consistent with the lagged price concession ratio proposed by CMS.

B. Discounts and Financial Transactions "Passed Through" to RCPs and Entities Conducting Business as RCPs Should be Included in AMP Only Where Funded by the Manufacturer and Where There Is Evidence That Pass-Through Occurred – 42 C.F.R. § 447.504(b)(3)-(4)

BIO supports the CMS proposal to include discounts, rebates, payments, or other financial transactions that are "passed through to" RCPs only where a manufacturer has evidence to that effect.²⁶ The Proposed Rule recognizes that a manufacturer often may not have evidence that pass-through occurs, and CMS therefore would require a manufacturer to include such discounts only "where [the manufacturer] has evidence or documentation demonstrating that such discounts have been passed through to the pharmacy."²⁷ BIO supports the Proposed Rule's practical and realistic approach to this requirement. As AMP measures the manufacturer's net price, BIO requests that CMS also clarify that the requirement to include amounts passed through to RCPs necessarily relates only to those pass-through amounts that are funded by the reporting manufacturer itself.

C. CMS Should Clarify the Requirement to Include Transactions "Paid By" Wholesalers and RCPs in the AMP Calculation – 42 C.F.R. § 447.504(b)(4)

The same provision that requires manufacturers to include in the AMP calculation discounts that are passed-through to RCPs also directs manufacturers to include "other financial transactions . . . paid by" wholesalers and RCPs.²⁸ The Proposed Rule does

²⁵ Medicare Program; Revisions to Payment Policies, 71 Fed. Reg. 69,624, 69,670 (Dec. 1, 2006) (42 C.F.R. pts. 405, 410, 411, 414, 415, and 424).

²⁶ 77 Fed. Reg. at 5330, 5362 (Proposed § 447.504(b)(4)).

²⁷ *Id.* at 5330.

²⁸ *Id.* at 5330, 5362 (Proposed § 447.504(b)(4)).

not explain what types of transactions this language is intended to capture. At a minimum, BIO believes that such transactions should be included in AMP only where documentation exists that demonstrates the payment was made or passed through to the manufacturer itself. Wholesalers and RCPs may make purchase payments to manufacturers, but those amounts already would be accounted for in the requirement to include sales amounts in the AMP calculation. BIO requests that CMS clarify whether this language is intended to capture transactions other than purchase payments, and if so, that CMS include an explanation for why such transactions should be viewed as affecting the price realized by the manufacturer.

D. AMP Exclusions – 42 C.F.R. § 447.504(c)

Section 447.504(c) details the sales and other transactions that are excluded from the calculation of AMP. BIO requests further clarification regarding several of those exclusions below.

1. BIO Supports the Exclusion of All Patient Transactions From AMP.

The statutory definition of AMP under the ACA is limited to the prices paid to a manufacturer by “wholesalers for drugs distributed to retail community pharmacies” and “retail community pharmacies that purchase drugs directly from the manufacturer.” Sales and discounts to patients are not included in the statutory definitions of AMP, “wholesaler,” or “retail community pharmacy.” The alternative definition of AMP for 5i drugs, as discussed below, does include a laundry list of additional customer types, but patients likewise are not included in that AMP definition. Consistent with those terms, the Proposed Rule excludes direct sales to patients from the calculation of AMP.²⁹ BIO supports the exclusion of patient sales from the definition of AMP for both non-5i and 5i drugs because it is consistent with the ACA and the purpose of the Program.

Consistent with the view that patients simply are not a type of customer that is eligible for consideration in the AMP calculation, the Proposed Rule also excludes a wide variety of patient programs from AMP that do not involve direct sales to patients. The Proposed Rule exclusions apply to manufacturer coupons, voucher programs, drug discount cards, patient refund or rebate programs, and copayment and patient assistance programs. In all cases, the Proposed Rule explains that the exclusion is dependent on all program benefits flowing exclusively to the patient, such that no RCP (or in the case of a 5i drug, any other 5i-AMP-eligible entity) receives a price concession of any kind.³⁰ BIO fully supports this approach and believes it appropriately directs the exclusion from AMP of all patient benefits provided under these programs. BIO requests that CMS clarify, however, that if a program does generate funds for an AMP-eligible customer, such as an RCP, and those amounts are not otherwise excludable under section 447.504(c) or as a bona fide service fee for example, that the

²⁹ 77 Fed. Reg. at 5333.

³⁰ *Id.* at 5333–34.

manufacturer can continue to exclude the patient benefits from the AMP calculation and need only account for those non-excludable amounts generated for the AMP-eligible customer in the AMP calculation. BIO also requests that CMS confirm that the more detailed patient program criteria included in the DRA Final Rule, including the prohibition on purchase contingencies to patients, no longer are relevant provided the other provisions of the Proposed Rule are satisfied. CMS also should clarify that that copayment programs that provide financial assistance but not free goods to patients also are excluded from AMP.

2. BIO Supports The Retention of the DRA Final Rule Definition of “Bona Fide Service Fee” As Well As Continued Manufacturer Discretion To Determine Fair Market Value, And Believes Price Appreciation Credits, Like Service Fees, Should Be Evaluated On A Case-By-Case Basis.

The ACA provides that bona fide service fees (“BFSFs”) provided by manufacturers to retail community pharmacies and wholesalers “including (but not limited to) distribution service fees, inventory management fees, product stocking allowances, and fees associated with administrative services agreements and patient care programs (such as medication compliance programs and patient education programs)” are excluded from AMP.³¹ The Proposed Rule clarifies that such fees do not automatically qualify for exclusion from AMP and also do not constitute an exhaustive list of the fees that may qualify as BFSFs.³² The Proposed Rule instead requires that any fee paid to a wholesaler or RCP must satisfy the substantive requirements of the BFSF definition included in the DRA Final Rule for that fee to qualify as a BFSF and be excluded from the AMP calculation.³³ The DRA Final Rule “BFSF” definition requires that the fees be for legitimate services that a manufacturer would otherwise have to perform or have others perform for it, represent fair market value, and not be passed on in whole or in part to a client or customer.³⁴ As under the DRA Final Rule, the Proposed Rule does not define “fair market value.” The Proposed Rule continues to allow manufacturers to determine fair market value and “make reasonable assumptions consistent with adequate documentation that will support their payment for these services at fair market rates sufficient that an outside party can determine the basis for the fair market value determination.”³⁵

BIO supports the retention of the DRA Final Rule approach to identifying BFSFs and to determining fair market value. BIO members have a wide variety of legitimate service arrangements with wholesalers and other direct purchase customers, and those arrangements frequently change to address new patient needs and new challenges in

³¹ SSA § 1927(k)(1)(B)(i)(II).

³² 77 Fed. Reg. at 5332.

³³ *Id.* at 5332, 5359 (Proposed § 447.502). Where fees paid to other AMP eligible entities under the 5i AMP calculation satisfy the bona fide service fee definition, those fees should be excluded from the 5i AMP calculation as well.

³⁴ 77 Fed. Reg. at 5321, 5332; *see also* 72 Fed. Reg. at 39,182.

³⁵ 77 Fed. Reg. at 5332.

the drug distribution chain. Retention of the DRA Final Rule's substantive standard for BFSFs facilitates manufacturer compliance and allows manufacturers to develop new business models and contractual relationships to adapt to the changing prescription drug market. BIO also supports CMS' decision to provide manufacturers with flexibility to make reasonable determinations of fair market value based on the manufacturer's experience in the market. This approach appropriately balances the need for a clear standard with the need for flexibility to adapt to a changing market.

In contrast to this case-by-case approach for the evaluation of service and administrative fees as well as fair market value, the Proposed Rule categorically describes price appreciation credits as "retroactive price adjustments" and concludes that such figures categorically "do not meet the definition of bona fide service fee . . . or offset of a bona fide service performed on behalf of the manufacturer."³⁶ This position, articulated by CMS for the first time in the history of the Program, is improperly vague and by any reading is certainly not an accurate interpretation of any existing law. This statement also is completely inconsistent with CMS' approach to other fee arrangements, both in this Proposed Rule as well as the DRA Final Rule to date, and assumes that "price appreciation credit" is some sort of defined and standardized term across industry. It is not. Manufacturers and their direct purchasers enter into a multitude of diverse arrangements that may take into account changes in inventory valuation, and how that value is or is not treated in the AMP (or BP or ASP) calculation necessarily is dependent on the individual facts and circumstances of each arrangement. BIO strongly believes that price appreciation credits, like any financial transaction between a manufacturer and a customer, must be evaluated based on the facts and circumstances of the specific arrangement to determine the appropriate price reporting treatment. A one-size-fits-all approach is no more appropriate for service fees as for price appreciation credits, and BIO urges CMS to require manufacturers to evaluate both types of arrangements substantively to determine their appropriate treatment in the calculations.

3. CMS Should Provide Additional Guidance Regarding Exclusion of Reimbursement for Returned Goods.

The ACA states that reimbursement by manufacturers for "recalled, damaged, expired, or otherwise unsalable" returned goods is excluded from AMP, "including (but not limited to) reimbursement for the cost of the goods and any reimbursement of costs associated with return goods handling and processing, reverse logistics, and drug destruction."³⁷ The Proposed Rule largely adopts this broad exclusion, but specifies that such reimbursement may only be excluded from AMP "to the extent such payment covers the costs of returns and does not otherwise serve as payment to the pharmacy as a price concession."³⁸ BIO agrees that the proposed limit on what reimbursement may be excluded from AMP is a reasonable safeguard to prevent price concessions

³⁶ *Id.*

³⁷ SSA § 1927(k)(1)(B)(i)(III).

³⁸ 77 Fed. Reg. at 5332.

from being disguised as reimbursement for returns, and believes manufacturers should be able to conclude that this standard has been met where the manufacturer reimburses the returning party under a returns goods policy that the manufacturer has established in good faith. When evaluating the costs associated with returns, and in particular, the costs of “handling and processing” and “reverse logistics” services, BIO believes that manufacturers can and should rely on the bona fide service fee definition otherwise included in the Proposed Rule. CMS should confirm that would be an appropriate approach to this issue.

The Proposed Rule also adds that “the returned goods themselves” can be excluded from AMP “when returned in good faith.” CMS does not explain whether or how this is a distinct exclusion from the exclusion described in the above paragraph, or whether the good faith requirement applies to all returns transactions. CMS should clarify that manufacturers may use their own written and established company policies and procedures in order to define “good faith” returns. CMS also should explicitly incorporate this standard at section 447.504(c)(16) by included the following sentence: “Goods returned pursuant to manufacturer policies established in good faith.”

The Proposed Rule does not define “recalled, damaged, expired or otherwise unsalable” goods, and instead proposes to allow manufacturers to base their understanding of such terms on standard industry practice.³⁹ CMS expressly requests examples of what goods would qualify as “unsalable.” BIO does not believe that a specific definition of “unsalable” is required but that CMS should permit manufacturers to rely upon prevailing business standards and their own good faith returns policies to determine circumstances where products are unsalable.

4. CMS Should Clarify the Treatment of TRICARE Utilization.

CMS has proposed that AMP exclude prices to certain federal programs, including the TRICARE Retail Pharmacy Program.⁴⁰ CMS does not specify, however, whether the exclusion of prices to TRICARE requires that both the sales dollars and units associated with TRICARE utilization be excluded from AMP (as with a sale to the DoD under the Federal Supply Schedule), or if TRICARE instead should be treated as like all other third party payors, with the sales dollars and units associated with the utilization included in the calculation and the TRICARE rebates ignored. BIO requests that CMS provide specific guidance regarding this issue in any final rule.⁴¹

³⁹ *Id.* at 5332.

⁴⁰ *Id.* at 5331, 5361 (Proposed § 447.504(c)(1),(3)).

⁴¹ Removal of Tricare sales dollars and units from the AMP calculation (like an FSS sale) could result in negative AMPs under a build-up methodology. Tricare units typically are dispensed through RCPs, and therefore if treated like ineligible sales, would be used to reduce any RCP sales that the manufacturer otherwise could document. Where the manufacturer has few contracted commercial RCP sales, the reduction of those documented RCP units by the amount of Tricare utilization could result in a negative or false positive (negative numerator and denominator) AMP. This result is possible but much less likely to occur under the presumed inclusion approach because the Tricare sales dollars and units would be used to offset the manufacturer's total sales to wholesalers.

5. BIO Supports the Exclusion of Customary Prompt Pay Discounts To Wholesalers.

Section 1927(k)(1)(B) of the Social Security Act ("SSA") provides that customary prompt pay discounts extended to wholesalers are excluded from AMP.⁴² The Proposed Rule implements the same exclusion from the determination from AMP.⁴³ BIO supports the exclusion of customary prompt pay discounts to wholesalers and encourages CMS to finalize this proposal.

IV. CMS SHOULD CLARIFY THE DEFINITION OF "RETAIL COMMUNITY PHARMACY" AND BIO SUPPORTS THE DEFINITION OF "WHOLESALE" – 42 C.F.R. §§ 447.502 & 447.504(a)

RCPs and wholesalers play a central role in the AMP calculation. BIO appreciates CMS' efforts to provide substantive details and explanations regarding the definition of "RCP," including entities that conduct business as RCPs. BIO nevertheless believes that additional clarifications are needed on the "RCP" definition, as detailed below. BIO supports the revised statutory definition of "wholesaler."

A. CMS Must Provide Guidance Regarding the Identification of Specialty Pharmacies

The Proposed Rule specifies that "specialty pharmacies" are a type of entity that conducts business as an RCP but CMS provides no defining characteristics to support manufacturer identification of these entities. BIO urges CMS to provide additional guidance on this term given the significant role that specialty pharmacies can play in the AMP calculation for certain products.⁴⁴

The phrase "specialty pharmacy" commonly has become associated with pharmacies that perform value-added services for certain types of drugs or patient categories in return for a service fee. These types of services may be necessitated by complex patient counseling and ongoing monitoring requirements (e.g., in the case of REMS drugs), the cost of a drug (i.e., pharmacies may need special distribution arrangements or special volume guarantees to justify the expense of stocking the product and maintaining an inventory on its shelves), particular handling of a drug (e.g., the drug may need to remain refrigerated and so special packaging and shipping may be necessary), specific third party payor coverage requirements (e.g., payors may require prior authorization or other documentation from physicians in order to grant coverage), or other factors. These pharmacies adjust their services frequently based on the changing environment related to drugs, third party coverage, and patient

⁴² SSA § 1927(k)(1)(B)(i)(I).

⁴³ 77 Fed. Reg. at 5362 (Proposed § 447.504(c)(15)).

⁴⁴ CMS proposes to treat specialty pharmacies as RCPs to support the AMP calculations for certain oral drugs to ensure an AMP can be calculated for those products. 77 Fed. Reg. at 5329.

populations. It is worth noting that most state boards of pharmacy do not have a separate regulatory category for specialty pharmacies.

For manufacturers, this means there is no common definition of specialty pharmacy that can be used to normalize classifications across the industry. If manufacturers are to include specialty pharmacy sales in AMP, CMS first has to provide an appropriate definition to ensure consistent treatment across AMP calculations for all manufacturers and all products.⁴⁵

B. CMS Should Clarify the Meaning of “Primarily Through the Mail,” Particularly In Relation to Specialty Pharmacies.

CMS broadly interprets the ACA’s phrase “primarily through the mail,” in the context of the RCP definition, to mean “mail order pharmacies.”⁴⁶ CMS does not provide any guidance, however, regarding how to apply that definition to hybrid entities that may be or operate as RCPs but that also dispense product through the mail. CMS should provide explicit instruction or standards for determining when a pharmacy is distributing “primarily through the mail” in order to avoid potential inconsistencies across manufacturer AMP calculations.

The meaning of “primarily through the mail” is particularly important in the context of those entities that conduct business as RCPs, such as specialty pharmacies, but that also dispense product primarily through the mail. The Proposed Rule directs that entities that conduct business as RCPs are included in the AMP calculation and then specifies that such entities include “specialty pharmacies, home infusion pharmacies and home healthcare providers.”⁴⁷ Many if not most specialty pharmacies dispense product primarily through the mail, however, and CMS does not provide any guidance for how to reconcile the requirement to exclude mail order but include specialty pharmacy sales. BIO requests that CMS clarify its position on this issue and also make clear that manufacturers can and should make reasonable assumptions regarding the identification of specialty pharmacies as appropriate.

C. CMS Should Clarify The Treatment of PBM-Owned RCPs.

The Proposed Rule does not address whether discounts, rebates, or other price concessions provided to PBM-owned RCPs or PBM-owned entities conducting

⁴⁵ BIO understands that CMS may suggest use of National Provider Identifier (“NPI”) numbers, as maintained by the National Council for Prescription Drug Programs (“NCPDP”), to identify specialty pharmacies. BIO has concerns with such use of NPI numbers because our members understand that the pharmacies select their own pharmacy classification, and may select more than one classification at a time. This could result in pharmacies with similar business models being treated differently for purposes of the AMP calculation due solely to each pharmacy’s different selection of pharmacy category. In determining which sales to include or exclude from AMP, the use of NPI numbers to differentiate Mail Order versus Specialty Pharmacy or Retail Community Pharmacy transactions also would not work for pharmacies that operate using a primary distribution center because end-customer granularity will not be visible based on the distribution center and NPI number to which product is sold and shipped.

⁴⁶ 77 Fed. Reg. at 5331, 5361 (Proposed § 447.504(a)).

⁴⁷ 77 Fed. Reg. at 5361 (Proposed § 447.504(b)(4)).

business as wholesalers or RCPs should be included in the AMP calculation as discounts to RCPs, or whether such discounts should be excluded from AMP as discounts to PBMs. Where discounts attributable to PBM-owned RCPs, or PBM-owned specialty pharmacies, are separately quantifiable, manufacturers need guidance from CMS as to whether those discounts should be included in the AMP calculation defined at section 447.504(b). BIO requests that CMS include this direction in any final rule and also make clear, again, that manufacturers can and should make reasonable assumptions regarding the treatment of PBM-owned RCP and specialty pharmacy utilization as appropriate.⁴⁸

D. BIO Supports the Revised Statutory Definition of “Wholesaler.”

The ACA substantially revised the definition of “wholesaler.”⁴⁹ The Proposed Rule adopts that statutory definition, which is “a drug wholesaler that is *engaged in wholesale distribution* of prescription drugs to retail community pharmacies, including (but not limited to) manufacturers, repackers, distributors, own-label distributors, private-label distributors, jobbers, brokers, warehouses[,] independent wholesale drug traders, and retail community pharmacies that conduct wholesale distributions.”⁵⁰ CMS also proposes that a “wholesaler” need not be licensed by the state to satisfy the revised definition because the statute does not compel that requirement.⁵¹ BIO supports this revised definition of “wholesaler” which, consistent with the statutory definition, includes manufacturers that are engaged in wholesale distribution of prescription drugs.

V. AMP FOR INHALATION, INFUSION, INSTILLED, IMPLANTED, OR INJECTABLE (“5i”) DRUGS – 42 C.F.R. §§ 447.504(d) & 447.507

BIO has a number of concerns related to the Proposed Rule’s 5i AMP calculation and the associated “not generally dispensed through a retail community pharmacy” determination, as detailed below.

A. The Product Label Is Sufficient To Determine 5i Status.

CMS has proposed that manufacturers be required to use the FDA’s “Routes of Administration” to determine when a product qualifies as a 5i drug.⁵² BIO believes manufacturers should be able to make this determination based on the label of the product itself and that CMS should not mandate consultation with the FDA guidance. The FDA’s Routes of Administration are not published through any formal rulemaking, but instead are updated through sub-regulatory guidance, in the FDA’s *Orange Book*. For that reason, manufacturers should be able to make this determination on their own, based on each product’s label (which the FDA must approve), and should not be

⁴⁸ 72 Fed. Reg. at 39,174–75, 39,241 (42 C.F.R. § 447.504(g)(6)).

⁴⁹ ACA § 2503(a)(4), 42 U.S.C. § 1396r-8(k)(11).

⁵⁰ *Id.* § 2503(a); see also 77 Fed. Reg. at 5326, 5361 (Proposed § 447.502) (emphasis added).

⁵¹ 77 Fed. Reg. at 5326.

⁵² 77 Fed. Reg. at 5334, 5363 (Proposed § 447.507(a)).

obligated to consult the FDA's Routes of Administration to determine when a drug qualifies as 5i. If CMS finalizes its proposal to require that manufacturers consult the FDA's Routes of Administration to determine 5i status, and given the sub-regulatory nature of that guidance, CMS should assume responsibility for notifying manufacturers when the FDA's information has been updated or revised.

B. The DDR System Should Include a "5i" AMP Methodology Status Flag.

BIO urges CMS to add a field to the Drug Data Reporting ("DDR") system for identifying whether the 5i or non-5i/traditional AMP methodology was used in a given quarter for any 5i innovator product so that the appropriate base date AMP can be used to calculate the additional rebate applied. As discussed in more detail below, CMS should permit manufacturers to calculate a 5i and a non-5i base date AMP for those innovator products that the manufacturer expects could flip between the two AMP methodologies over time, so that the additional rebate for the drug is calculated using a quarterly and base date AMP calculated using the same methodology.

C. CMS Should Implement a 50 Percent Standard for Determining NGD Status and Define Parameters for the NGD Determination.

CMS proposes to define "not generally dispensed" ("NGD") through an RCP by reference to the 90 percent principle that is used for the Non-Federal Average Manufacturer Price ("non-FAMP") calculation for determining whether a buyer is a "wholesaler."⁵³ Based on this standard, a product is not generally dispensed through an RCP if 90 percent or more of its sales are to entities other than RCPs. CMS specifically requests comments on the 90 percent threshold. BIO believes that the 90 percent standard is too extreme, is likely to exclude products that are most appropriately viewed as not being RCP products, and may cause products to alternate in and out of the 5i AMP calculation based just on minor market fluctuations. This instability in the "not generally dispensed" determination also will cause fluctuations in AMP that will affect AMP-based pharmacy reimbursement.

BIO believes that it is most appropriate to adopt a 50 percent threshold for determining "not generally dispensed." A 50 percent standard will provide the stability that is needed for AMP values and will substantially minimize any fluctuations that might occur. BIO notes that CMS has defined terms similar to "generally" in other contexts, including by adopting a 50 percent standard for determining when a drug is "usually" self-administered in the Part B context.⁵⁴ In no circumstance, however, should CMS adopt a standard that is higher than 90 percent. Such a standard would only enhance the problems identified above for AMP fluctuations and reimbursement.

⁵³ *Id.* at 5335.

⁵⁴ 77 Fed. Reg. at 5335.

CMS has provided no specific guidelines or methodology for determining whether a particular drug satisfies the quantitative standard (whether 90/10 or a lower threshold) for being not generally dispensed through RCPs. Some level of specificity is needed to ensure that all manufacturers take a consistent approach to this determination, which is particularly important if the AMPs are combined to develop FULs. As a general matter, BIO recommends that manufacturers be permitted to review data within the last 12 months and that the analysis be based on sales units rather than sales dollars to avoid distortions due to price changes over time. BIO also recommends that CMS clarify that this determination should be made on an NDC-9 basis, as that is the level at which AMP is calculated.

Finally, BIO wishes to express its concern that the Proposed Rule appears to assume that manufacturers can conduct this determination using current period sales. It is both unrealistic and impractical to expect manufacturers to be able to identify current period end-customer dispensing data in the same period as it must generate the AMP values themselves. To date, BIO members primarily have relied on historical data to conduct this determination and BIO urges CMS to permit this approach going forward.

D. NGD Determinations Should Be Made On An Annual Basis, With More Frequent Determinations In the Discretion of the Manufacturer.

The Proposed Rule would require each manufacturer to determine a 5i drug's NGD status on both a monthly and quarterly basis.⁵⁵ This level of frequency is both unnecessary and unduly burdensome. As an initial matter, a monthly determination is unworkable as it would create the possibility that the same 5i drug could be subject to the two distinct AMP methodologies in single quarter. The resulting quarterly AMP would be distorted as a result. Such determinations also create the possibility of frequent fluctuations between AMP methodologies, which would lead to volatility in the reported AMPs and any associated AMP-based reimbursement rates.

BIO recommends that the "not generally dispensed" or NGD determination be required on an annual basis only, with more frequent determination in the manufacturer's discretion. The Department of Veterans Affairs, from which CMS borrowed the 90/10 standard, requires this determination on an annual basis only, and BIO recommends that CMS adopt the same standard here. If CMS adopts a quantitative standard that is devised to minimize switches between the two AMP methodologies, an annual determination should be adequate to confirm the appropriate AMP methodology is being applied. To address the possibility that changes in a drug's distribution might occur during the annual period, manufacturers should retain the capability to conduct the NGD analysis on a more frequent basis as appropriate.

⁵⁵ *Id.* at 5336.

E. CMS Should Clarify the Treatment of Entities That Conduct Business As RCPs in the “Not Generally Dispensed” Determination.

As discussed above, the Proposed Rule directs that traditional, non-5i AMP be calculated inclusive of sales to RCPs as well as sales to entities that conduct business as RCPs, such as specialty pharmacies. Section 447.507, which governs the NGD determination and therefore whether the AMP for a 5i drug is calculated under 447.504(b) or (d), does not address whether entities that conduct business as wholesalers or RCPs are to be treated as RCPs for purposes of the NGD determination. BIO believes that CMS should clarify whether such entities should or should not be treated as RCPs for purposes of the NGD determination to ensure a consistent approach across manufacturers and products.

F. Discounts Provided to SPAPs and Medicare Part D Plans Should Be Excluded From 5i AMP.

The Proposed Rule would include in 5i AMP all sales, rebates, discounts, or other financial transactions that are included in traditional AMP, as well as sales to a number of other entities, including insurers.⁵⁶ This inclusion does not distinguish between commercial insurers and those that are exempt from the Best Price calculation, such as State Pharmaceutical Assistance Programs (“SPAP”) and Medicare Part D Plans. Discounts to these entities are excluded from the determination of BP,⁵⁷ and CMS has proposed excluding other BP-ineligible transactions from the determination of 5i AMP, such as sales under the FSS.⁵⁸ BIO urges CMS to exclude all BP-exempt discounts from the 5i AMP calculation to ensure that the resulting AMP figure is not skewed lower by these BP-exempt transactions. This clarification would also be consistent with CMS’ stated policy of conforming the AMP and BP definitions.⁵⁹

G. CMS Should Permit the Restatement of Distinct Base Date AMPs for 5i Drugs That Reflect Both the 5i and Non-5i Calculations.

The Proposed Rule does not address the implications that the inflation penalty and base date AMP application will have in the context of the 5i AMP calculation. Whatever the threshold finalized by CMS to determine whether a drug is not generally dispensed through RCPs, it will always remain a possibility that a given 5i product will flip between the 5i and non-5i/traditional AMP calculation methodologies. A manufacturer, therefore, should have the ability to restate alternative base date AMPs using both the 5i and non-5i/traditional AMP methodologies so that an appropriate base date AMP (matching the current reporting period’s methodology) may be applied to

⁵⁶ 77 Fed. Reg. at 5336, 5362 (Proposed § 447.504(d)(4)).

⁵⁷ See *id.* at 5363 (Proposed §§ 447.505(c)(4), (6)).

⁵⁸ See *id.* at 5361, 5363 (Proposed §§ 447.504(c)(2) & 447.505(c)(3)).

⁵⁹ *Id.* at 5336.

determine the appropriate AMP for a given month or quarter. As noted above, BIO encourages CMS to permit manufacturers to do so for their 5i products and to add a field in the DDR for 5i drugs so that a manufacturer can indicate the AMP methodology used for a given quarter.

VI. NEW FORMULATIONS & LINE EXTENSION PRODUCTS – 42 C.F.R. § 447.509(a)(2)

BIO is concerned with numerous aspects of the Proposed Rule's broad interpretation of the ACA's provisions regarding the alternative rebate formula for line extensions of existing drugs.⁶⁰ BIO strongly opposes CMS' overbroad application of this formula to any drugs other than those identified as FDA Chemical Type 3. BIO does support, however, the requirement that both the old and new drugs both be solid oral dosage forms, as well as the inapplicability of the Alternative URA to products terminated from the Program. BIO also appreciates CMS' inclusion of a detailed example of the Alternative URA calculation example.

A. The ACA and its Legislative History Focus Exclusively on Minor Drug Revisions.

The ACA applies the Alternative URA solely to "line extensions." That phrase is defined in very limited terms, as "a new *formulation* of the drug, such as an extended release formulation."⁶¹ CMS proposes to rely on the FDA's Chemical Types to define what products qualify as a new formulation. The FDA does have a Chemical Type that is specific to new formulations – Type 3. CMS nevertheless proposes to treat as new formulations three additional Chemical Types – 2, 4, and 6 – despite the FDA's treatment of those Chemical Types as distinct from new formulations.⁶² This overly-broad interpretation defies FDA's own categorization standards, the plain language of the statute, and the clear and repeatedly documented intent of this provision.

The history of the alternative rebate formula begins in December 2008, when the Congressional Budget Office ("CBO") issued a Budget Options report on health care. This report contains the first proposal to impose an alternative rebate formula on certain drugs. The report targets only those products with "slight alterations" that appear designed to "avoid incurring an additional [inflation-adjusted] rebate."⁶³ The report specifies that its proposal would affect only a "certain type of new formulation—specifically, extended-release versions."⁶⁴ The CBO report goes on to discuss the

⁶⁰ ACA § 2501(d). CMS uses the term "Alternative URA" to describe the additional rebate imposed by ACA § 2501(d).

⁶¹ ACA § 2501(d) (emphasis added).

⁶² These comments necessarily assume that the FDA continues to support the assignment of Chemical Types and that the FDA will do so using the definitions included in the Proposed Rule. There currently is uncertainty, however, as to whether that is the case going forward. To the extent FDA no longer supports the assignment of Chemical Types to new drugs or revises their definition(s), CMS must give manufacturers another opportunity to comment on this aspect of the Proposed Rule in light of those revisions to FDA policy.

⁶³ Congressional Budget Office, *Budget Options, Volume I: Health Care*, at 143 (Dec. 2008).

⁶⁴ Budget Options, *supra* note 63.

proposed mechanics for applying such a rebate, and again specifies that the formula would treat a “new, extended-release version of an existing drug” more like the original drug for purposes of calculating the rebate.⁶⁵

A few months later, in February 2009, President Obama raised the issue of increasing rebates on line extensions in his Fiscal Year 2010 Budget. That budget proposed to impose an additional rebate on new drug formulations.⁶⁶ The President’s proposal also included a provision designed to prevent manufacturers from “reformulating existing products into new products to restart the exclusivity process, a process known as ‘ever-greening.’”⁶⁷ The budget proposal, therefore, emphasized a manufacturer’s reformulation of existing products for the purpose of restarting the exclusivity process, which speaks to targeting abusive life cycle management tactics.

With the CBO Report and the President’s Budget as support, Congress included an alternative rebate proposal in the various health reform proposals that culminated in the ACA. The legislative history for the ACA (and the prior related bills) demonstrates that Congress was concerned with minor drug revisions only. A precursor House bill to the ACA, America’s Affordable Health Choices Act of 2009, defined “line extension” exclusively as “an extended release formulation of the drug.”⁶⁸ A House of Representatives Energy and Commerce Committee Report related to this bill, dated October 14, 2009, also singles out the production of extended release products as the target of the new formulation additional rebate.⁶⁹ The Report discussed “line extension” exclusively as “an extended release formulation of the drug” and made no mention of new formulations generally or of combination products, new indications, or other types of innovations.⁷⁰

A Senate Finance Committee Chairman’s Mark related to another earlier bill, America’s Healthy Future Act of 2009 (“AHFA”), refers only to extended release products and indicates concern with the fact that “drug makers can avoid incurring additional rebate obligations by making *slight alterations* to existing products . . . while significantly increasing the price on these products.”⁷¹ The Chairman’s Mark, therefore, notes that extended release products would be treated as if they were original products for purposes of calculating rebates under the Program.⁷² The weight given to “slight alterations” in this Chairman’s Mark demonstrates a concern not with true scientific or technological advances, but with easy drug revisions that provide a manufacturer with the ability to avoid increased rebate liability.

⁶⁵ *Id.*

⁶⁶ Office of Management and Budget, Fiscal Year 2010 Budget Overview Document, *A New Era of Responsibility: Renewing America’s Promise*, at 28 (February 2009).

⁶⁷ *Id.* at 28.

⁶⁸ America’s Affordable Health Choices Act of 2009, H.R. 3200, 111th Cong. § 1742 (2009).

⁶⁹ H.R. Comm. on Energy and Commerce Rep. No. 111-299, at 635 (2009).

⁷⁰ H.R. Comm. on Energy and Commerce Rep. No. 111-299, at 216.

⁷¹ S. Comm. on Finance Chairman’s Mark, America’s Healthy Future Act of 2009, at 54 (Sept. 2009) (emphasis added).

⁷² *Id.* at 55.

An October 2009 Senate Finance Committee Report, again related to the AHFA, explicitly documents that Congress' focus was on ensuring that manufacturers no longer could avoid "incurring additional rebate obligations by making *slight alterations* to existing products."⁷³ A May 2009 Senate Finance Committee Financing Options Paper again shows that the target was "slight alterations to existing products."⁷⁴

Nowhere in this history is there any discussion of combination therapies or new indications. Instead, the history is consistent in its narrow focus on slight alterations designed to restart the exclusivity and additional rebate process. The FDA itself has a means of identifying such products, through a Chemical Type that matches the very language in the statute, and BIO believes CMS has no authority to extend the Alternative URA beyond those drugs.

B. The Proposed Rule's Definition of "Line Extension" Impermissibly Extends the ACA's Mandate to Products Other Than Chemical Type 3 Drugs.

The ACA is very clear as to the drugs subject to the Alternative URA: line extensions. The ACA does not leave that term undefined. Rather, the ACA specifically defines a line extension as "a new formulation of the drug, such as an extended release formulation."⁷⁵ Extended release formulations represent an easily-identifiable drug revision constituting a reduction in the frequency of administration of a drug in comparison with the conventional dosage form. The text of the statute – and the entirety of the legislative history surrounding the ACA – demonstrate that Congress was concerned only with new formulations that represent slight changes in the composition of the drug (like extended release formulations). That should be the end of this analysis.

The Supreme Court consistently has held that the interpretation of a defined term "must not stray" from the statutory definition.⁷⁶ More significantly, an agency may not read into a statutory definition a meaning that simply is not there. The Supreme Court has held that "[i]t is axiomatic that the statutory definition of [a defined] term *excludes unstated meanings of that term.*"⁷⁷ In applying this principle, for example, the U.S. Court of Appeals for the Federal Circuit has ruled that "[w]hen Congress makes such a clear statement as to how categories are to be defined and distinguished, neither the agency nor the courts are permitted to substitute their own definition for that of

⁷³ S. Comm. on Finance Rep. No. 111-89, at 92 (emphasis added).

⁷⁴ S. Comm. on Finance, *Financing Comprehensive Health Care Reform: Proposed Health System Savings and Revenue Options* at 12 (May 20, 2009).

⁷⁵ ACA § 2501(d). The statute itself also entitles the Alternative URA formula provision in the statute, at paragraph (c)(2)(C), as "Treatment of new formulations."

⁷⁶ See, e.g., *Stenberg v. Carhart*, 530 U.S. 914 (2000).

⁷⁷ *Mese v. Keene*, 481 U.S. 465, 484-85 (1987) (emphasis added).

Congress.”⁷⁸ It also is a well-settled principle of statutory construction that “every clause and word of a statute” must be given effect.⁷⁹

In the Proposed Rule, however, CMS acts as if “line extension” is not defined by statute. CMS even claims that “the statute did not provide further specificity as to how line extensions should be defined.” That is simply false. The statute does define line extension, explicitly, as a “new formulation of the drug, such as an extended release formulation.” In defiance of this explicit and limited definition, CMS spends many paragraphs explaining its approach to defining the term “line extension.” While BIO appreciates CMS’ efforts to implement this provision, those efforts cannot trump the plain language of the statutory definition itself: only those new formulations that are the type of slight alterations – like extended release products – that Congress believed were abusive. BIO respectfully submits that CMS’ definition of line extension is irrelevant because that term is already defined by statute, and agency rulemaking authority may not extend beyond the plain language of a statute where Congress has spoken clearly to an issue.⁸⁰

Despite this clarity in the statute, CMS has proposed that four FDA Chemical Types constitute new formulations: Type 2 (new ester, new salt, or other noncovalent derivative), Type 3 (new formulation), Type 4 (new combination), and Type 6 (new indication).⁸¹ As this list indicates, the FDA itself has defined new formulations, as Chemical Type 3, and only those products that fall under Chemical Type 3 and that also constitute slight alterations to drugs (like extended release formulations) should be subject to the Alternative URA. In its discussion of the other Chemical Types, CMS explains why it believes each of Types, 2, 4, and 6 qualify as “line extensions.” That would be relevant if “line extension” was not defined by the ACA, but it is, narrowly, as new formulations such as extended release formulations, and these other Chemical Types clearly are viewed by FDA as distinct.

1. Combination Therapies Specifically Should Be Excluded from the Alternative URA.

Combination therapies are not new formulations. The distinct Chemical Type for combination products proves this, but it is important to note that there are both scientific as well as policy-based reasons for FDA to distinguish the two. Combination products represent the development of new and completely distinct drug products through significant scientific and clinical research. The Proposed Rule acknowledges this fact,

⁷⁸ *AK Steel Corp. v. United States*, 226 F.3d 1361, 1372 (Fed. Cir. 2000).

⁷⁹ See, e.g., *Williams v. Taylor*, 529 U.S. 362, 404 (2000); *United States v. Menasche*, 348 U.S. 528, 539 (1995) citing *Inhabitants of Montclair Twp. v. Ramsdell*, 107 U.S. 147, 152 (1883).

⁸⁰ *Chevron U.S.A., Inc. v. Natural Res. Def. Council, Inc.*, 467 U.S. 837, 842 (1984) (courts are not called upon to defer to or consider an agency’s interpretation of a statute where Congress has directly spoken to the precise question at issue). See, e.g., *Usery v. Kennecott Copper Corp.*, 577 F.2d 1113 (10th Cir. 1977); see also *Barseback Kraft AB v. United States*, 121 F.3d 1475, 1480 (Fed. Cir. 1997) (“A regulation cannot override a clearly stated statutory requirement.”).

⁸¹ 77 Fed. Reg. at 5339.

noting that a Chemical Type 4 (new combination) product represents “a drug comprised of two or more components that are *physically, chemically, or otherwise combined or mixed to produce a single drug product*.”⁸² The outcome of this combining or mixing is not a “new formulation” of the active ingredients of already-existing drug as CMS suggests. Combination drugs instead represent a *new product* to treat patients in different and innovative ways.

The statutory language that defines the Alternative URA formula confirms that it is not and cannot be applicable to combination drugs. The statutory formula provides that in calculating the Alternative URA, the manufacturer is to compare the total URA for the new formulation product, as calculated under section 1927(c) to the “highest additional rebate . . . under this section for any strength of *the original single source drug or innovator multiple source drug*.”⁸³ ***This language refers to the original drug in the singular only, and does not even recognize the possibility of there being more than one original drug to consider, as must be the case with a combination therapy.*** The legislative history makes no mention of combination therapies, the FDA definition of new formulation is distinct from that for combination products, and now the statutory language makes clear that Congress could not have targeted combination therapies or it would have provided for the comparison to the additional rebate for more than one original drug.⁸⁴ There simply is no legal basis for CMS’ effort to extend the Alternative URA to combination products.

2. Expansive Application of the Alternative URA Conflicts with the Administration’s Efforts to Increase Patient Adherence and Compliance.

The ACA emphasizes the Obama Administration’s efforts toward the development and implementation of appropriate medication and treatment adherence programs. The ACA, for example, provides for grants or contracts to implement medication management services for the treatment of chronic diseases.⁸⁵ Such services under the ACA include “providing information, support services, and resources and strategies designed to enhance patient adherence with therapeutic regimens.”⁸⁶

CMS’ expansive interpretation of “new formulation” undermines those efforts by penalizing new therapies that promote patient adherence and compliance. Patient non-adherence with prescribed medication negatively impacts individual health outcomes

⁸² *Id.*

⁸³ ACA § 2501(d)(1).

⁸⁴ Courts have consistently held that the general rule that a statutory term incorporates the plural to the singular (and vice versa) shall not apply where the context of the statute indicates otherwise. *See, e.g., Prestop Holdings, LLC v. United States*, 96 Fed. Cl. 244, 249 (Fed. Cl. 2010). Common sense directs that combination products necessarily incorporate *two or more* separate and distinct drugs. Should Congress have intended for the Alternative URA to apply to these types of products, it would not have left the term “drug” in the singular in the statute.

⁸⁵ ACA § 3503.

⁸⁶ *Id.*

and may raise U.S. health system costs by as much as \$300 billion per year.⁸⁷ Non-adherence is a major inefficiency in our health system, and is associated with a higher risk of mortality, hospitalizations and emergency department admissions.⁸⁸ Poor adherence can lead to individuals with chronic illness failing to reach their treatment goals, despite the availability of effective therapies.⁸⁹ On average, 15 percent of individuals do not fill their first prescription after receiving it, and after six months an estimated 50 percent of individuals with chronic diseases do not take their medications as prescribed.⁹⁰ Optimal adherence improves the likelihood that patients will achieve desired treatment goals.⁹¹

CMS policies should promote rather than penalize innovations that hold promise for improving treatment adherence, but CMS' proposed application of the alternative rebate formula disincentivizes the development of the very therapies needed to encourage patient compliance. CMS, in accordance with the terms of the ACA, should encourage innovations that make individuals more likely to adhere to their prescribed treatment regimens, and should avoid implementing policies that discourage adherence. Research demonstrates that dosing frequency is strongly associated with medication adherence,⁹² and that this factor should be addressed with patients in order to support improved medication adherence, improved health outcomes and potentially lower overall U.S. health system costs. The Proposed Rule's application of the Alternative URA to combination products, extended release formulations, and other purported "line extensions" may have the effect of discouraging simpler dosing regimens that support adherence, and could inadvertently worsen this issue among those patients impacted by these policies. CMS should reconsider the proposed policies on rebates applied to "line extensions", and should not implement any policies that discourage reduced dosing frequency, due to its potential positive impact on medication adherence.

3. Application of the Alternative URA to Products Developed With Abuse-Deterrent Technologies Contradicts the Administration's Incentives to Develop These Products.

The Obama Administration has recently taken targeted steps to encourage the reduction in abuse of opiate products, including by specifically encouraging the development of new formulations that contain abuse deterrent technologies. As part of

⁸⁷ New England Health Institute, New England Health Institute (NEHI) Research Brief: *Thinking Outside the Pillbox: A System-Wide Approach to Improving Patient Medication Adherence for Chronic Disease*. Published Aug. 12, 2009.

⁸⁸ See, e.g., World Health Organization, *Adherence to Long-Term Therapies: Evidence for Action*, at 13 (2003), available at who.int/chp/knowledge/publications/adherence_report/en/index.html (accessed March 21, 2012); Nananda Col, James E. Fanale & Penelope Kronholm, *The Role of Medication Noncompliance and Adverse Drug Reactions in Hospitalizations of the Elderly*, Arch. Internal Med., April 1990, at 841-845; Dawn L. Hershman DL et al., *Early Discontinuation and Nonadherence to Adjuvant Hormonal Therapy are Associated with Increased Mortality in Women with Breast Cancer*, Breast Cancer Res. Treat., Apr. 1, 2011, at 529-537;.

⁸⁹ Michael P. Ho et al., *Adherence to Cardioprotective Medications and Mortality among Patients with Diabetes and Ischemic Heart Disease*, BMC Cardiovasc. Discord., Dec. 15, 2006, at 48-56.

⁹⁰ Abhijit S. Gadkari & Colleen A. McHorney, *Medication Nonfulfillment Rates and Reasons: Narrative Systematic Review*, Current Med. Res Opin., Mar. 2010, at 648-705; World Health Organization, *supra* note 88.

⁹¹ See, e.g., World Health Organization, *supra* note 88 at 69-70, 75.

⁹² See, e.g., *id.* at 13.

its "Response to the Prescription Drug Epidemic," the Administration included as an action item expediting research and development of pain medications with no abuse potential and abuse-deterrent formulations.⁹³ The Administration suggests expediting research through grants, partnerships with academic institutions, and priority New Drug Application review by FDA for drugs that have abuse-deterrent technologies, especially with regard to opioid medications.⁹⁴ The Administration has also indicated that the Department of Health and Human Services and the FDA should "provide guidance to the pharmaceutical industry on the development of abuse-deterrent drug formulations on post-market assessment of their performance."⁹⁵

In contravention of these very specific efforts to speed abuse-deterrent products to market, CMS has proposed specifically not to exclude from the Alternative URA "reformulations of existing products that incorporate abuse deterrent technologies from the definition of line extension drugs."⁹⁶ CMS cannot defend a policy that penalizes the very innovation that the Administration is seeking to encourage. Such innovations are not the "slight alterations" that Congress intended to target. CMS should therefore follow Congressional intent and revise this proposal by specifying that the term "line extension" excludes an abuse deterrent formulation of a controlled substance for which the FDA required one or more pre- or post-approval studies or clinical trials (other than for bioequivalence or bioavailability purposes) or meets FDA's anticipated (by the end of 2012) guidance on the development of abuse deterrent formulations.

C. BIO Agrees that New Product Strengths Should Not Constitute "Line Extensions" for Purposes of the Alternative URA.

CMS has proposed excluding from the definition of "line extension" any "new strength of the initial brand name drug."⁹⁷ CMS adopted this policy due to the fact that, if it were to consider new strengths as line extensions, "it would be difficult to identify the first strength of the initial brand name listed drug because multiple strengths are often launched simultaneously."⁹⁸ BIO supports the exclusion of new strengths from the definition of "line extension."

D. BIO Supports the Requirement That Both the Original and Line Extension Products Must Be Solid Oral Dosage Forms.

CMS proposes to define "oral solid dosage form" in accordance with FDA regulation as "capsules, tablets, or similar drug products intended for oral use."⁹⁹ CMS

⁹³ Obama Administration, *Response to the Prescription Drug Epidemic: Action Items* available at http://www.whitehouse.gov/sites/default/files/ondcp/issues-content/action_items_response_to_the_prescription_drug_epidemic.pdf

⁹⁴ *Id.*

⁹⁵ *Id.*

⁹⁶ 77 Fed. Reg. at 5338.

⁹⁷ 77 Fed. Reg. at 5388.

⁹⁸ *Id.* at 5340.

⁹⁹ *Id.* at 5324.

also notes that “an oral route of administration [is] any drug intended to be taken by mouth.”¹⁰⁰ CMS proposes that both the original and new formulations of the drug must be a solid oral dosage forms for the Alternative URA to apply. BIO supports that proposal, as consistent with the plain language of the statute.¹⁰¹ BIO also believes that this requirement appropriately retains the narrow focus of the legislation on products where both the new and old versions must be solid oral dosage forms.

E. BIO Supports the Exclusion of Terminated Drugs from the Alternative URA Formula But Strongly Opposes Manufacturer Data Sharing.

CMS has proposed that a drug will not qualify for inclusion in the Alternative URA calculation “when the initial brand name listed drug has been terminated.”¹⁰² BIO supports this proposal and agrees with CMS that new formulations for which the initial brand name listed drug, defined by the Proposed Rule as the drug identified by Chemical Type 1,¹⁰³ has been terminated from the Program cannot and should not be subjected to an additional rebate under the Alternative URA calculation because no additional rebate will be calculated for use in the Alternative URA formula. CMS should clarify, however, that this also will be the case where the manufacturer of the initial brand name listed drug does not participate in the Program.

The Proposed Rule also will require the line extension’s manufacturer to calculate the Alternative URA for that product, which will require that manufacturer to obtain to the “highest additional rebate . . . under this section for any strength of the original single source drug or innovator multiple source drug.”¹⁰⁴ The Proposed Rule notes that “manufacturers are responsible for ensuring that all necessary product and pricing data, whether such information is for the initial brand name listed drug or the line extension drug, are exchanged between the manufacturer of the initial brand name listed drug and the manufacturer of the line extension.”¹⁰⁵

BIO is concerned that a formula that relies on the additional rebate of the original drug enables the manufacturer of the original product to manipulate its price for the original product to generate higher rebate liability for the follow-on or combination product. This is particularly troubling where the original and new drugs compete with each other. Our members also are extremely concerned regarding their ability to obtain this data from the manufacturer of initial brand name listed drug on a timely basis to support the calculation of a drug’s URA for purposes of paying the states. As a result, BIO believes the alternative rebate formula should apply only where the same manufacturer markets both the original and new formulation of the drug. The alternative URA is intended to target manufacturers that engage in abusive strategies to avoid

¹⁰⁰ *Id.* at 5324.

¹⁰¹ *Id.* at 5338, 5364 (Proposed § 447.509(a)(4)).

¹⁰² *Id.* at 5340.

¹⁰³ *Id.* at 5339.

¹⁰⁴ *Id.* at 5340–41; *see also* ACA § 2501(d)(1).

¹⁰⁵ 77 Fed. Reg. at 5341.

rebates by making only slight alterations to a product. Those circumstances are not present when distinct manufacturers market the old and new versions of the product.

If CMS retains its proposal to require the line extension manufacturer to obtain these data from the manufacturer of original brand name listed drug, CMS should make explicit that this type of data sharing is a condition of the manufacturer's participation in the Program and impose a deadline for providing those data to the line extension's manufacturer. CMS also should require only the minimum possible level of data be shared between and among manufacturers in order to achieve the purposes of calculating the Alternative URA. BIO recommends that that deadline be 15 days after the quarterly submission deadline. This type of condition will ensure the efficient operation of this aspect of the rebate formula. CMS should also require the manufacturer of the initial brand name listed drug to certify these data to the same extent as other data reported to CMS.

VII. BEST PRICE

The ACA did not revise the definition of Best Price but CMS has proposed to make various conforming revisions to the BP regulation to increase its clarity. BIO appreciates CMS' efforts to ensure clarity as to the calculation of BP and its willingness to address these issues in the Proposed Rule.

A. BIO Supports the Revised Definition of Best Price.

CMS proposes to revise the regulatory definition of BP so that it conforms to the statutory definition of that term as provided in section 1927 of the Social Security Act. The statute defines BP for single source or innovator multiple source drugs as "the lowest price available from the manufacturer during the rebate period to any wholesaler, retailer, provider, health maintenance organization, nonprofit entity or governmental entity within the United States," unless specifically excluded by statute.¹⁰⁶ The Proposed Rule conforms the definition of BP so that it now mirrors the list of specific BP-eligible entities provided in the statute.¹⁰⁷ The Proposed Rule also states that BP includes "all prices and associated rebates, discounts or other transactions that adjust prices either directly or indirectly" to those entities, unless specifically excluded from BP elsewhere in the regulation.¹⁰⁸

BIO supports the Proposed Rule's simplification of the definition of BP to conform to the statute. Given that the statute and regulation specifically identify BP-eligible entities, CMS should clarify that manufacturer sales and discounts to all other entities are not included in the determination of BP. That would be the case as to any patient transactions, for example, where the entirety of any benefit goes to the patient, or in the case of drugs sold to another manufacturer for use in a clinical trial, because in that

¹⁰⁶ SSA § 1927(c)(1)(C)(i).

¹⁰⁷ 77 Fed. Reg. at 5336, 5362 (Proposed § 447.505(a)).

¹⁰⁸ *Id.* at 5336, 5362 (Proposed § 447.505(b)).

case the other manufacturer would not be acting as a wholesaler or one of the other entity types included in the revised definition. BIO requests that CMS confirm that is the case for both examples, and if not, CMS should explain the basis for those transactions' eligibility for the BP calculation.

B. BIO Supports Consistency Between the AMP and BP Definitions and Recommends Additional Revisions for Conformity as to Service Fees and Returns.

BIO supports the Proposed Rule's efforts to better align the methodologies for determining AMP and BP.¹⁰⁹ Consistent with those objectives, BIO requests that CMS clarify that the BP exclusion for bona fide service fees ("BFSFs") applies to BFSFs paid to any BP-eligible entity, such as PBMs. As phrased, the Proposed Rule would exclude BFSFs from BP in the same manner as from AMP, which excludes only those BFSFs "paid by manufacturers to wholesalers, retail community pharmacies, or any other entity that conducts business as a wholesaler or a retail community pharmacy."¹¹⁰ But because BP includes sales to other types of commercial entities, such as retailers, providers, health maintenance organizations, and government entities, the BP BFSF exclusion must reflect this difference between AMP and BP. In order for the exclusion of BFSFs to be consistent between AMP and BP, as CMS apparently intends, BFSFs to any BP-eligible entity should be excluded from BP. Accordingly, BIO requests that CMS revise the regulatory text in Section 447.505(c)(16) to include BFSFs to any "wholesaler, retailer, provider, health maintenance organization, nonprofit entity or governmental entity in the United States."¹¹¹

BIO also supports CMS' conforming exclusion of returns from the BP definition. BIO believes returns do not impact the price realized by a customer, and that therefore this revision is appropriate. BIO notes, however, that CMS failed to delete the reference to returns in section 447.505(d)(1) and requests that CMS do so to reflect the addition of the new returns exclusion at section 447.505(c)(14).

C. CMS Should Clarify that Proposed Section 447.505(a) Modifies Section 447.505(b) Such That Best Price Includes Only Transactions to Those Entities Identified in 447.505(a) That Are Not Otherwise Excluded.

The Social Security Act defines "Best Price" for single source or innovator multiple source drugs as "the lowest price available from the manufacturer during the rebate period to any wholesaler, retailer, provider, health maintenance organization, nonprofit entity or governmental entity within the United States," unless otherwise specifically excluded by statute.¹¹² Only prices to those entities listed in the statute are

¹⁰⁹ 77 Fed. Reg. at 5336.

¹¹⁰ Compare 77 Fed. Reg. at 5362 (Proposed § 447.504(c)(14)) with *id.* at 5363 (Proposed § 447.505(c)(16)).

¹¹¹ See 77 Fed. Reg. at 5362 (Proposed § 447.505(a)).

¹¹² SSA § 1927(c)(1)(C)(i).

eligible for consideration in BP.¹¹³ The statute also specifically excludes from BP prices to certain entities that might otherwise be interpreted as eligible for BP, such as prices to covered entities in the 340B Drug Pricing Program (i.e. prices to providers).¹¹⁴

As noted above, the Proposed Rule revises the regulatory definition of BP to conform to the statute, such that paragraph (a) of section 447.505 identifies as the entity types that are eligible for the BP calculation the exact same list of BP-eligible entities that are included in the statute.¹¹⁵ The BP regulation also states in paragraph (b) of section 447.505 that BP includes “all prices and associated rebates, discounts or other transactions that adjust prices either directly or indirectly,” unless specifically excluded from BP as provided in paragraph (c) of the regulation.¹¹⁶

BIO supports CMS’ efforts to conform the BP regulation to the statute. BIO nevertheless is concerned that the proposed language in the revised BP regulation is ambiguous and open to different interpretations that are not supported by the statute. Specifically, paragraph (b) of section 447.505 provides that BP includes “all prices and associated rebates, discounts or other transactions that adjust prices either directly or indirectly,” unless specifically excluded from BP,¹¹⁷ but does not expressly limit those prices to the entities listed in paragraph (a), which are the only entities that are eligible for consideration in the BP calculation by law. To ensure that the regulatory definition of BP accurately conforms to the statutory definition, BIO recommends that CMS revise the proposed language in section 447.505(b) to clarify that the prices described in paragraph (b) are eligible for consideration in BP only if they are prices to one of the entities listed in section 447.505(a). CMS should revise paragraph (b) to read as follows:

Best price for covered outpatient drugs includes all prices and associated rebates, discounts, or other transactions that adjust prices either directly or indirectly, provided to any entity included in paragraph (a), unless such prices are otherwise excluded as provided in paragraph (c) of this section.

D. CMS Should Clarify the Exclusion for Prices Under the 340B Drug Pricing Program and That Covered Entity Compliance Does Not Affect the BP Calculation.

The Medicaid statute excludes from the definition of BP “any prices” charged to 340B covered entities.¹¹⁸ The Proposed Rule nevertheless interprets this BP exclusion

¹¹³ For authorized generics, the statute also provides that prices to certain other entities—namely prices to other manufacturers—are eligible for consideration in BP. See SSA § 1927(c)(1)(C)(i); *id.* § 1927(c)(1)(C)(ii)(IV). BIO believes that this language is expressly limited to the circumstances of authorized generics and therefore prices to other manufacturers are not prices for authorized generics and are not eligible for consideration in BP.

¹¹⁴ SSA § 1927(c)(1)(C)(i)(I), (II).

¹¹⁵ 77 Fed. Reg. at 5336, 5362 (Proposed § 447.505(a)).

¹¹⁶ *Id.* at 5336, 5362 (Proposed § 447.505(b)).

¹¹⁷ *Id.* at 5336, 5362 (Proposed § 447.505(b)).

¹¹⁸ SSA § 1927(c)(1)(C); 42 U.S.C. § 1396r-8(c)(1)(C).

as applicable only to “[p]rices charged under the 340B drug pricing program.”¹¹⁹ If CMS’ proposal is permissible under the statute, and given the extremely low prices provided to 340B covered entities, it is imperative that CMS precisely define the scope of what it believes qualifies as prices charged under the 340B program. In particular, CMS should clarify that sub-ceiling prices provided to covered entities (including supplemental rebates to rebate-option AIDS Drug Assistance Programs), whether or not provided through the 340B prime vendor, do qualify as prices under the 340B Program and are exempt from the BP calculation as a result. Use of the 340B prime vendor for sub-ceiling prices should not impact the continued BP exemption of such prices, as exempting only prime vendor prices would provide an unfair market advantage to the prime vendor and also increase manufacturer costs given that the prime vendor requires manufacturers to pay fees under its sub-ceiling price contracts. CMS also should clarify with specificity whether the following additional transactions do or do not qualify as prices charged under the 340B program: voluntary ceiling prices on orphan drugs, when provided to the new covered entity types added by the ACA; non-340B prices provided to covered entities that elect to “carve-out” for Medicaid patients and purchase non-340B product for those patients, and inpatient prices to entities other than those described in section 340B(a)(4)(L) of the PHSA.

The Proposed Rule states that the BP exception for 340B prices applies only where covered entities “meet the conditions” of the 340B statute. BIO believes that manufacturers have no obligation to police covered entity compliance with the 340B program and that 340B entity noncompliance should in no way impact manufacturer BP exposure. BIO is concerned that the proposed language could be read to mean that the covered entity’s non-compliance with program requirements could somehow require a manufacturer to count an otherwise compliant 340B sale in the manufacturer’s BP calculation. 340B program guidance directs that manufacturers cannot question a covered entity’s compliance as a condition of selling product to that covered entity at the 340B price.¹²⁰ If the covered entity is listed as participating in the program on the 340B program website, then the manufacturer is required to treat that covered entity as entitled to the 340B price. If that covered entity otherwise fails to comply with program requirements, it should have no bearing on the manufacturer’s exclusion of the 340B price transaction from the BP calculation. BIO requests that CMS make this clarification in any final rule.

E. BIO Supports the Revisions to the Nominal Price Exclusion and Requests That CMS Develop A List of Qualifying Entities Under The New Exceptions.

The Proposed Rule revises the exclusion of nominal prices to certain entities from BP to add the two new types of entities that are eligible for the nominal price exclusion as provided by the Omnibus Appropriations Act of 2009: (1) public or non-

¹¹⁹ 77 Fed. Reg. at 5363 (Proposed § 447.505(c)(2)(i)).

¹²⁰ 340B Drug Pricing Program Notice, Release No. 2011-1, Clarification of Non-Discrimination Policy (Nov. 21, 2011).

profit entities or state-owned or operated facilities providing services to the same populations as 340B entities, and (2) public or non-profit entities or facilities at colleges or universities “whose primary purpose is to provide health care services to students” and that provide family planning services.¹²¹ CMS proposes to implement the two entities as required by the statute, but CMS declines to exercise any discretion to expand further the types of entities eligible for the nominal price exclusion.¹²²

BIO supports CMS’ revision to the nominal price exception so that it conforms to the updated statutory language. These new exceptions are intended to encourage manufacturers to provide nominal prices to the qualifying entities, however, BIO’s members have confirmed that it can be very difficult to identify with certainty which entities meets these standards and therefore are eligible for BP-exempt nominal prices. To facilitate access to nominal prices for these entities, BIO requests that CMS develop and maintain a list of eligible entities for these two categories, much as CMS currently does for SPAPs. BIO’s members routinely rely on the CMS SPAP list to confirm the BP-exempt status of SPAPs, and that certainty directly facilitates the provision of discounts to those state programs. If CMS could develop a similar list based on entity submission of information demonstrating compliance with these standards, as it does for SPAPs, that would support greater access to nominal prices for these entities, as Congress intended when it expanded the nominal price exception to include them.

F. BIO Supports The Exclusion of Patient Transactions From BP.

The Proposed Rule includes conforming exceptions to the BP calculation for the same patient transactions as discussed above in relation to AMP.¹²³ As discussed above, the revised regulatory definition also does not include prices to patients. BIO supports these revisions to the BP definition. BIO and its membership strongly believe that manufacturer-funded benefits to patients, in any form, and where the patient alone receives those benefits, are simply irrelevant to the BP calculation. BIO requests that CMS explicitly confirm this in any final rule. These clarifications will serve to support manufacturer funding of these very important programs, which provide patients with access to critical and life-saving therapies.

VIII. AUTHORIZED GENERIC DRUGS – 42 C.F.R. § 447.506

Section 1927(k)(1)(C) requires AMP to include any drug sales to wholesalers that the manufacturer “approves, allows, or otherwise permits . . . to be sold under a new drug application approved under section 505(c) of the Federal Food, Drug, and Cosmetic Act.”¹²⁴ CMS has proposed to carry out this statutory mandate, in part, by requiring the primary manufacturer of the branded product to “include in its calculation of AMP all sales of its authorized generic drug product sold or licensed to a secondary

¹²¹ Omnibus Appropriations Act of 2009 § 221, Pub. L. 111-8, 123 Stat. 524, 783, 42 U.S.C. § 1396r-8(c)(1)(D); 77 Fed. Reg. at 5337, 5364 (Proposed § 447.508(a)(4) & (a)(5)).

¹²² 77 Fed. Reg. at 5338.

¹²³ 77 Fed. Reg. at 5363 (Proposed § 447.505(c)(8)–(12)).

¹²⁴ SSA § 1927(k)(1)(C); 42 U.S.C. § 1396r-8(k)(1)(C).

manufacturer . . . when the secondary manufacturer is acting as a wholesaler.”¹²⁵ This is an appropriate revision to the DRA Final Rule standard, in which CMS directed that “primary manufacturers [are] not required to incorporate the sales of the authorized generic in the AMP of the brand drug,”¹²⁶ and is driven by the ACA’s expansion of the definition of the term “wholesaler” to include manufacturers “engaged in wholesale distribution to RCPs.”¹²⁷

BIO supports the requirement that the primary manufacturer include authorized generic sales to secondary manufacturers in its calculation of AMP for the original branded product where the secondary manufacturer engages in wholesale distribution of drugs to RCPs. If CMS reverts to the presumed inclusion approach, BIO believes that secondary manufacturer sales would qualify as wholesaler sales, and be included in AMP, so long as the secondary manufacturer, like any wholesaler, has as part of its business model the re-sale of drugs to retail community pharmacies. BIO asks CMS to confirm this point in any final rule.

IX. DEFINITIONS – 42 C.F.R. § 447.502

The Proposed Rule includes revised definitions of a number of key terms, a few of which BIO addresses below.

A. Bundled Sales.

CMS has proposed to add to the existing regulatory definition of “bundled sale” certain of the guidance included in a previously-issued in the form of a DRA Final Rule frequently asked question (“FAQ”). Specifically, CMS proposes to clarify that where discounts for different products in a single contract are each determined independently and with no contingencies across products, a bundle does not exist and no discount allocation across products is required.¹²⁸ CMS notes that it “continue[s] to agree with our response to this issue and thus have decided to include it in this discussion in order to further clarify the bundled sale definition.”¹²⁹ BIO supports this clarification and agrees with CMS that multi-product contracts with no cross-product contingencies do not constitute bundled sales requiring discount allocation across products.

While BIO supports CMS’ clarification, our members believe that the actual language CMS proposes to add to the bundled sale definition does not clearly convey the content of the DRA Final Rule FAQ. BIO suggests that CMS also add the following to the definition for purposes of clarification: “No bundled sale exists where multiple products are included in a single arrangement but the discount on each product is determined independently of the discount, pricing, and performance as to any other

¹²⁵ 77 Fed. Reg. at 5337.

¹²⁶ 72 Fed. Reg. at 39,200.

¹²⁷ SSA § 1927(k)(11).

¹²⁸ 77 Fed. Reg. at 5321.

¹²⁹ *Id.* at 5321.

product in the arrangement, and the discounts offered are not greater than would be the case if the products were purchased outside of the multi-product arrangement.”

BIO also requests that CMS clarify the new paragraph (1) that CMS proposes to add to the bundled sale definition. That language reads: “The discounts in a bundled sale, ***including but not limited to those discounts resulting from a contingent arrangement***, are allocated proportionally to the total dollar value of the units of all drugs sold under the bundled arrangement.”¹³⁰ This language, by its very terms, applies only where a bundled sale exists, and so BIO believes is not applicable in the context of a multi-product contract with no contingencies as discussed above. Where a bundled sale does exist, however, CMS should clarify whether this new paragraph (1) requires the allocation of both contingent as well as non-contingent discounts on a drug that is part of a bundled sale. For example, where a manufacturer offers a discount of 10 percent on Product A without condition (a “non-contingent” discount) and offers an additional 5 percent discount on Product A if the customer also purchases Product B (a “contingent discount”), CMS should clarify whether this new language is intended to require the allocation across Products A and B of both the 10 percent non-contingent discount on Product A as well as the 5 percent contingent discount on Product A.

If it is CMS’ intent to have the new paragraph (1) specifically require the allocation of non-contingent discounts on drugs that are part of a bundled sale along with any contingent discounts on those drugs, it is very important for CMS to recognize that the new paragraph (1) may require a change to the discount allocation methodologies that some manufacturers have implemented based on the current definition. If CMS finalizes the addition of paragraph (1) to the bundled sale definition, CMS should make clear that the new language applies as a requirement as of the effective date of the final rule on a prospective basis only.

B. Covered Outpatient Drug.

The Proposed Rule codifies the statutory definition of “covered outpatient drugs” and adds the requirement that a drug must be listed electronically with the FDA in order to qualify as a “covered outpatient drug” for purposes of the Program.¹³¹ CMS also proposes that a manufacturer will be required to submit the FDA application number for each drug to CMS, and where a drug does not have an application number, the manufacturer must provide evidence to CMS demonstrating that the drug meets the definition.¹³² CMS should clarify what application number is required to be listed if a drug has multiple application and/or supplement numbers.

The Proposed Rule indicates that a drug “would not be considered a covered outpatient drug when that drug or product is billed as a bundled service” and is provided

¹³⁰ 77 Fed. Reg. at 5359 (Proposed § 447.502) (emphasis added).

¹³¹ *Id.* at 5321–22 (Proposed § 447.502).

¹³² *Id.* at 5322–23.

in certain settings, including renal dialysis.¹³³ BIO understands this to mean that such drugs would not be subject to rebate, which is consistent with prior CMS guidance on this subject.¹³⁴ As you may know, the Medicare Part B program instituted a bundled payment rate for certain End-Stage Renal Disease ("ESRD") services effective January 1, 2011, and that payment rate includes a number of drugs.¹³⁵ BIO believes that where drugs are paid for under the ESRD bundled payment rate and a state Medicaid program pays for any portion of that bundled rate, the drugs included in that bundled payment rate do not qualify as covered outpatient drugs under the statutory and new regulatory definition of that term, and therefore are not subject to a rebate under the Program.¹³⁶ BIO requests that CMS specifically confirm this in any final rule.

C. Innovator Multiple Source Drug.

CMS is proposing to update the definition of "innovator multiple source drug" to include the FDA approval of an outpatient covered drug under a biologic license application (BLA), in addition to a product license application (PLA) or establishment license application (ELA).¹³⁷ The proposed rule does not make any other changes to the definition of a "multiple source drug," *i.e.*, "multiple source drug" continues to be defined as a drug for which there is at least one other drug product that is: 1) rated as therapeutically equivalent; 2) pharmaceutically equivalent and bioequivalent; and 3) sold or marketed in the U.S. during the rebate period.¹³⁸

BIO wants to take this opportunity to clarify that all biologicals should be recognized as single source drugs consistently across the Medicaid and Medicare programs. Although the definition of "multiple source drug" under Social Security Act § 1847A is nearly identical to the definition used in the current AMP rule,¹³⁹ under section 1847A, biologicals are "single source" therapies that can be treated as multiple source only if they were within the same billing and payment code as of October 1, 2003.¹⁴⁰ All other single source drugs and biologicals are excluded from the definition of "multiple source drug" under section 1847A. In contrast, the proposed change to the definition of "innovator multiple source drug" would include all biologicals. This would be inconsistent with the statutory definition of "multiple source drug" for Medicare payment purposes

¹³³ *Id.* at 5322.

¹³⁴ See, e.g., 72 Fed. Reg. at 39,219 (drugs that are billed as part of cost of service and bundled within cost of the service are not covered by the Program); State Release No. 33 ("all-inclusive claims are excluded from drug utilization data used to calculate rebates due from manufacturers").

¹³⁵ Medicare Improvements for Patients and Providers Act of 2008 § 153(b). There will be a 4-year transition period, with full implementation of the bundled rate beginning January 1, 2014.

¹³⁶ For example, a December 30, 2010 CMS Informational Bulletin indicated that although ESRD facilities will continue to be required to report to Medicare on the ESRD claim items and services they furnish, those items will not be separately paid. See CMS Informational Bulletin, *Recent Developments in State Medicaid and CHIP Policy*, at 5 (Dec. 30, 2010).

¹³⁷ 77 Fed. Reg. at 5360 (Proposed § 447.502).

¹³⁸ *Id.*

¹³⁹ SSA § 1847A(c)(6)(C)(i). This definition is a drug for which there are two or more drug products which (1) are rated as therapeutically equivalent, (2) are pharmaceutically equivalent and bioequivalent, and (3) are sold or marketed in the United States during the quarter.

¹⁴⁰ SSA § 1847A(c)(6)(C)(ii).

and could create confusion about the appropriate classification for biologicals. Thus, BIO requests that CMS revise the proposed rule's definitions to exclude biologicals from the definition of "innovator multiple source drug" in order to establish consistent policies across Medicare and Medicaid.

D. The Proposed Meaning of "Original NDA" Cannot Be Reconciled With the Statute and Represents a Change in Longstanding CMS Policy.

In defining "single source drug" and "innovator multiple source drug," the Proposed Rule interprets the term "original NDA" to mean any post-1962 NDA (*i.e.*, any NDA approved on the basis of safety and efficacy).¹⁴¹ This interpretation is inconsistent with the language and purpose of the statute, would reflect a significant change from CMS' long-held position, and would have a significant financial impact on our members. For the reasons discussed below, BIO respectfully suggests that CMS not adopt the proposed meaning of "original NDA." Rather, it would be appropriate to define "original NDA" (and we would suggest actually defining the term in the regulation itself, rather than just explaining the meaning in the preamble) as an NDA that, with approval, led to:

- An award of five- or three-year exclusivity;¹⁴²
- Patent term extension;¹⁴³ or
- *Orange Book* listed patents on the active ingredient.¹⁴⁴

CMS has long understood that the statute is intended to capture a higher rebate for products that, through the approval process, received a period of competitive advantage in terms of exclusivity or patent protection. The definition proposed by BIO reflects that Congressional intent, and has the added virtue of giving meaning to each of the words of the phrase, statutory "original new drug application."

1. CMS Has Long Recognized That an "Original NDA" Is One That Conferred Exclusivity or Patent Protection.

The Medicaid statute draws an essential distinction between "innovator" and "noninnovator" drugs for purposes of calculating a drug's rebate. An "innovator" drug is either a "single source drug," which the statute defines as "a covered outpatient drug which is produced or distributed under an original new drug application approved by" FDA,¹⁴⁵ or an "innovator multiple source drug," which is a "multiple source drug that was

¹⁴¹ 77 Fed. Reg. at 5360–61 (Proposed § 447.502).

¹⁴² See 21 U.S.C. § 355(c)(3)(E)(ii) & (iv).

¹⁴³ See 35 U.S.C. § 156.

¹⁴⁴ See 21 U.S.C. § 355(b)(1) & (c)(2).

¹⁴⁵ SSA § 1927(k)(7)(A)(iv) (emphasis added).

originally marketed under an *original new drug application* approved by" FDA.¹⁴⁶ A "noninnovator multiple source drug" is "a multiple source drug that is not an innovator multiple source drug."¹⁴⁷ In essence, therefore, the distinction is between drugs that were first approved under an "original new drug application" and those that were not, with products that fall within the former category subject to larger rebates.¹⁴⁸

The predecessor agency to CMS, the Healthcare Financing Administration ("HCFA"), explained that the larger rebates due from drugs approved under an "original NDA" reflect the fact that those products received with their approvals "some sort of patent or marketing protection for a specific period of time."¹⁴⁹ As a result, the sponsors of those approved applications "benefitted from a lack of competition and increased profits for a specific period of time."¹⁵⁰ Recognizing that the statute is intended to capture higher rebates for those products that obtained higher profits by virtue of approval-related exclusivity or patent protection, CMS previously proposed a regulatory definition of "original NDA" as "an FDA-approved drug or biological application that received one or more forms of patent protection, patent extension under [the Hatch-Waxman Amendments], or marketing exclusivity rights granted by the FDA."¹⁵¹

The protections that a sponsor may receive in conjunction with approval of an NDA include the following:

- Five-year exclusivity: Awarded if the product is a "new chemical entity," this delays the submission and approval of ANDAs and 505(b)(2) NDAs.
- Three-year exclusivity: This is available if the product is an improvement on previously-approved products, and the application required clinical data in order to be approved. It delays the approval of ANDAs and 505(b)(2) NDAs for the conditions of approval that were supported by the clinical data.
- Patent certification: An applicant is required to identify for listing in the *Orange Book* those patents that claim the drug or a method or using the drug. An ANDA or 505(b)(2) NDA that relies on an approved product as the reference listed drug must certify to those patents, and if the sponsor of the approved product sues within a

¹⁴⁶ *Id.* § 1927(k)(7)(A)(ii) (emphasis added). A "multiple source drug" is, with exceptions not relevant here, a covered outpatient drug for which there is at least one other drug that is (1) rated as therapeutically equivalent in the *Orange Book*, (2) pharmaceutically equivalent and bioequivalent, and (3) sold or marketed in the United States. *Id.* § 1927(k)(7)(A)(i).

¹⁴⁷ *Id.* § 1927(k)(7)(A)(iii); see also *id.* §§ 1927(c)(1)–(3).

¹⁴⁸ See SSA § 1927(c).

¹⁴⁹ Medicaid Program; Payment for Covered Outpatient Drugs Under Drug Rebate Agreements With Manufacturers, Proposed Rule, 60 Fed. Reg. 48,442, 48,453 (Sept. 19, 1995) (42 C.F.R. pts. 441 and 447).

¹⁵⁰ *Id.* at 48,453.

¹⁵¹ *Id.* at 48,453, 48,483 (Proposed § 447.504).

statutory timeframe to defend the patents, approval of the ANDA or 505(b)(2) NDA is stayed for 30 months.

- Patent term restoration: If approval of an NDA represents the first permitted commercial distribution of that product's active ingredient, the sponsor is entitled to have some of the term of a patent claiming the product restored, to make up for time spent in the development and approval process.

The final rule did not include a regulatory definition of "original NDA," instead incorporating "original NDA" into the definitions of "single source drug" and "innovator multiple source drug," reflecting the statutory construction. This nonetheless reflected CMS' understanding that a drug that "was originally marketed" or "is produced or distributed" under an original NDA is a drug that "receive[d] a certain amount of patent protection and/or market exclusivity,"¹⁵² which is the basis for justifying a higher rebate.

2. The Proposed Meaning of "Original NDA" Would Fail to Give Meaning to the Language of the Statute and Would Contravene Statutory Intent.

In the Proposed Rule, CMS interprets the term, "original NDA," to mean "an NDA filed by the manufacturer for approval under section 505 of the [Federal Food, Drug, and Cosmetic Act] for purposes of approval by the FDA for safety and effectiveness."¹⁵³ This would include all NDAs that have been submitted since the Food, Drug, and Cosmetic Act was amended in 1962 to require NDAs to demonstrate both safety and effectiveness.¹⁵⁴ Such a meaning would read the word "original" out of the term "original NDA," thus failing to give effect to every word of the statute. Congress should be presumed to have intended the term "original NDA" to mean something other than "NDA," but the Proposed Rule would erase any distinction, however, thus rendering the word "original" superfluous.¹⁵⁵ This is not a permitted interpretation or application of the statute.¹⁵⁶

Further, under the proposed interpretation, a product would be deemed to have been approved under an "original NDA" even if the product received no period of regulatory exclusivity, no *Orange Book*-listed patents, no patent term restoration, and no 30-month stay for patent litigation. This would be flatly inconsistent with the purpose of the statute, which (as discussed above) CMS has recognized is to obtain higher rebates

¹⁵² 72 Fed. Reg. at 39,144.

¹⁵³ 77 Fed. Reg. at 5318, 5323, 5326, 5360–61 (Proposed § 447.502) (defining "single source drug" and "innovator multiple source drug").

¹⁵⁴ Previously, an NDA was required to demonstrate only the product's safety.

¹⁵⁵ In fact, CMS says the terms would be "equivalent." 77 Fed. Reg. at 5323, 5326, 5360–61 (Proposed § 447.502).

¹⁵⁶ See, e.g., *Astoria Fed. Savings & Loan Ass'n v. Solimino*, 501 US 104, 112 (1991) (statute should be construed "so as to avoid rendering superfluous" any statutory language); *Ramsdell*, 107 U.S. at 152 (court should "give effect, if possible to every clause and word of a statute").

from those sponsors that had received an approval that carried with it some form of market protection.

3. The Proposed Meaning of “Original NDA” Would Lead to Problematic Outcomes.

In addition, the proposed interpretation of “original NDA” would lead to undesirable results in any number of situations. By way of example:

- Repackaged Parenteral Products: Before 1996, a new NDA was required for a parenteral product that had been sold in a glass container but that the sponsor wanted to distribute in a plastic container. This was the case even for drug products that had been marketed prior to 1938. There was no exclusivity or patent term extension associated with these NDAs; in fact, typically there were no patents associated with the product listed in the *Orange Book*. Recognizing that these NDAs did not convey any market protection, CMS previously concluded that they were not “original NDAs.”¹⁵⁷ Such NDAs would be “original NDAs” under the Proposed Rule, however; the mere change in the material of the container would lead CMS to impose a larger rebate. This makes even less sense in light of the fact that products changed after 1996, when FDA no longer required an NDA, would not be subject to the higher rebate.
- 505(b)(2) Generics: In most instances, differences in inactive ingredients between a putative generic product and the reference listed drug are immaterial. For some products, however, a generic must (with exceptions not relevant here) have the same active and inactive ingredients as the reference drug; parenteral solutions, ophthalmic or otic drugs, and topical products are examples.¹⁵⁸ Proposed generics that don’t meet that requirement can still obtain approval, but they are submitted to FDA in a 505(b)(2) NDA, not through an ANDA. These NDAs typically are approved on the basis of bioequivalence to the reference product, and they provide no exclusivity or other market protection for the active ingredient. In the marketplace, the products are generic versions of the reference products, even though there were approved by means of an NDA. The Proposed Rule would have these products categorized as innovator multiple source drugs and subject to a larger rebate, however, just because they were approved under an NDA.

¹⁵⁷ 60 Fed. Reg. at 48,453. The historical CMS approach is consistent with how FDA handles many of these NDAs, which are the responsibility of the Office of Generic Drugs.

¹⁵⁸ See, e.g., 21 C.F.R. § 314.94(a)(9)(iii)-(v).

Because of its importance, the term “original NDA” should be defined in regulation, not by implication in a preamble. And because of the purpose of the relevant statutory provision, the term should be defined to include those NDAs that have associated with them some form of market protection for the active ingredient, *e.g.*, five- or three-year regulatory exclusivity, patent listings, or patent term restoration.

X. EXPANSION OF THE PROGRAM TO THE TERRITORIES – 42 C.F.R. § 447.502

The Proposed Rule announces that CMS intends to expand the Program beyond the 50 states and D.C. to include the Commonwealth of Puerto Rico, the U.S. Virgin Islands, Guam, Northern Mariana Islands, and American Samoa (collectively, the “Territories”).¹⁵⁹ BIO opposes this expansion to a Program that for more than 20 years has been operated exclusive of the Territories. At most, CMS should limit the expansion to impacting manufacturer rebate liability and should not require manufacturers to include the Territories in their AMP and BP calculations because of the enormous burden and compliance concerns that such an expansion would pose.

A. CMS Should Not Expand Rebate Liability To the Territories.

The Medicaid drug rebate program has operated for over 20 years without including the Territories and CMS offers no substantive basis for this radical expansion of the program. It is not clear that CMS has the legal authority to extend the Program to the Territories given that the agency consistently has applied the Program only to the 50 states and D.C. since the inception of the program. In its first proposed rule on the Program, CMS declined to extend the Program to the Territories.¹⁶⁰ The DRA Final Rule also defined “States” as “the 50 States and the District of Columbia.”¹⁶¹ CMS has therefore established that it was Congress’ intent to apply the Program only to the 50 states and D.C., and Congress has never taken action to change this course. In fact, Congress has amended the Social Security Act provisions governing the Program seven times since the original CMS proposed rule, including substantial revisions in 2003, 2006, and under the ACA in 2010. This type of inaction on the part of Congress can be viewed as *de facto* endorsing the longstanding CMS position that the Program does not apply to the Territories.¹⁶²

BIO believes CMS must first more substantively demonstrate the need for this expansion beyond a generalized belief that doing so will benefit the Territories. Manufacturers already offer voluntary rebates to the Territories through a number of mechanisms and CMS has offered no basis for concluding the any additional rebate

¹⁵⁹ 77 Fed. Reg. at 5326.

¹⁶⁰ 60 Fed. Reg. at 48,444–43.

¹⁶¹ 72 Fed. Reg. at 39,241 (42 C.F.R. § 447.502).

¹⁶² See, *e.g.*, *Bob Jones Univ. v. United States*, 461 U.S. 574, 600–01 (1983) (IRS appropriately interpreted the tax code in part because there had been thirteen bills introduced in Congress to overturn that interpretation and not one of them had made it out of committee).

revenue through a Medicaid expansion will justify the burden on states of manufacturers that will result from this expansion.

B. Expansion of the AMP and BP Calculations to Include the Territories Presents Prohibitive Data and Compliance Concerns for Manufacturers.

While BIO strongly opposes the expansion of the Program to the Territories and believes CMS does not have the legal authority to do so, if CMS nevertheless proceeds with this expansion it is important to note that any revision to the terms "States" and "United States" also would require that prices to AMP-eligible and BP-eligible entities in the Territories be included in a manufacturer's AMP and BP calculations. This is a prohibitively complicated process for those manufacturers who sell into the Territories through related but distinct corporate entities, possibly under different labeler codes. These foreign entities do not participate in the Program and are not signatories to any rebate agreements. Manufacturers are not able to effect, and CMS should not require, the incorporation of sales and discount data from these distinct corporate entities. Those of our members with this corporate set-up have uniformly and vehemently emphasized the barriers that exist to sharing this type of information. Where those separate corporate entities operate under distinct labeler codes, for example, a single product may be sold under one NDC-9 in the continental United States and a distinct NDC-9 with distinct labeling in the Territories.¹⁶³

Manufacturers have not contemplated these issues to date when setting up operations in the Territories precisely because the Program has operated for 20 years without this requirement. If sales and associated discounts to AMP and BP-eligible entities in the Territories are to be included in the calculation of AMP and BP, manufacturers will need time to operationalize that requirement. Manufacturers are unfamiliar with the dispensaries and other providers in the Territories, making class of trade assignment a significant obstacle to implementation. Deeply discounted commercial prices into the Territories may need to be terminated to avoid best price impact. Finally, our members will need time to review and revise existing contractual arrangements with Territory Medicaid programs.

Expansion of the calculations to include prices in the Territories also is inappropriate because those prices, in some cases, are be subject to regulation and therefore would distort the AMP and BP calculations. The Secretary of Puerto Rico's Department of Consumer Affairs, through Price Regulation No. 37, retains the power to set the maximum sale price for medicinal products at the distributor and pharmacy level.¹⁶⁴ Products that are subject to price controls include those with the highest

¹⁶³ For this very reason, the Department of Veterans Affairs only requires manufacturers to include the Territories in their Non-FAMP calculations if the manufacturer treats those Territories as part of the United States for financial accounting purposes. See VA Amended Master Agreement § 1.Q (inclusion or exclusion of U.S. island territories dictated by the manufacturer's customary accounting practice, i.e., if sales to Puerto Rico are reported as domestic sales then those sales must be included in the non-FAMP"); See also Dear Manufacturer Letter (Oct. 19, 1993).

¹⁶⁴ Commonwealth of Puerto Rico, Department of Consumer Affairs, Price Regulation No. 37, Amend. 1.

volume of sales in Puerto Rico, those used for the treatment of chronic diseases, and those used by the aged or infants.¹⁶⁵ These price controls have the clear capacity to distort manufacturers' calculations of AMP and BP, and further counsel against expanding the calculations to the Territories. If CMS finalizes its proposal to expand the Program to the Territories, BIO strongly urges CMS to limit manufacturer responsibility to rebate liability only, thereby allowing manufacturers to continue to calculate AMP and BP based on the geographic sales that the Program has always included – the 50 states and the District of Columbia.

C. CMS Should Consider Impact of the Program Expansion on ASP.

An additional reason for limiting expansion of the Program to rebate liability only is the impact that expansion to the AMP and BP calculation could have on the ASP calculation. The Social Security Act defines the prices eligible for the ASP calculations by reference to the prices eligible for consideration in the calculation of BP.¹⁶⁶ Manufacturers have historically excluded prices to the Territories from the ASP calculation because such prices were excluded from BP as well. If CMS expands the BP calculation to entities in the Territories, then CMS must clarify whether those prices must be included in ASP as well.

If CMS does not require prices to entities in the Territories to be included in ASP but does require those prices be included in AMP, the discrepancy between the prices included in the determination of AMP and the prices included in the determination of ASP may have unpredictable and unintended consequences for reimbursement for drugs under Medicare Part B. As noted above, CMS has moved forward with a policy to substitute AMP for ASP for purposes of Part B reimbursement where ASP exceeds AMP by five percent during the period specified in the regulations.¹⁶⁷ BIO is concerned that differential treatment of Territory sales between the AMP and ASP calculation could lead to the inappropriate substitution of AMP for ASP as the basis for the Part B payment limit. AMP substitution for ASP that is triggered solely because of differences in methodology for the two calculations is inappropriate and yet another example of the types of concerns related to the reliability of comparisons between AMP and ASP that CMS and commenters expressed in connection with the AMP substitution policy.¹⁶⁸

D. Manufacturers Need Sufficient Lead Time Prior to Implementation.

Any expansion of the Program into the Territories would require great time and expense for implementation by both the Territories and manufacturers. The Proposed Rule recognizes that the Territories would need additional time in order to come into compliance with Program requirements and would allow for a phased-in implementation by setting the effective date for those requirements at one year after the first day of the

¹⁶⁵ *Id.* at 1, § 1.

¹⁶⁶ SSA § 1847A(c)(2)(A).

¹⁶⁷ 76 Fed. Reg. at 73,086, 73,289, 73,294–95.

¹⁶⁸ *See id.* at 73,292–93.

first full quarter after the publication of the final rule.¹⁶⁹ Manufacturers similarly would need sufficient lead time in order to prepare for the expansion of the Program. For example, manufacturers would need to revise or wind down any existing commercial sales contracts with entities if those prices otherwise must be included in AMP or BP. In addition, manufacturers will need to set up their price reporting policies and systems to include sales in the territories and to collect and validate pricing data from those sales before manufacturers can begin to pay rebates for covered outpatient drugs utilized in the Territories.

While the Proposed Rule provides that the expansion will not be mandatory on the Territories until one year after the first day of the first full quarter after the publication of the final rule, the Proposed Rule does not address the potential for Territories to implement rebate liability on manufacturers on a voluntary basis and on an earlier timetable than the Proposed Rule's timeline. Manufacturers, therefore, face the very real possibility that Territories will submit rebate claims to them faster than they are able to accomplish systems upgrades. CMS therefore should clarify that manufacturers likewise will only be required to comply with the expansion of the MDRP to the Territories effective one year after the first day of the first full quarter after the publication of the final rule.¹⁷⁰ CMS also should clarify when rebate liability will begin for those Territories that take advantage of a "phase-in" approach. Manufacturers should not be subject to numerous and inconsistent implementation timeframes. BIO therefore requests that each Territory be required to announce its "go-live" date no less than six months prior to implementation.

E. Expanded Rebate Liability Must Be Imposed On A Prospective Basis Only.

Finally, given the potential significant financial impact that expansion of rebate liability to the Territories would represent, such rebate liability must be prospective only and effective at the end of the Territories' phase-in period. As a matter of law, rebate liability must be prospective only given that existing regulation specifically limits the "States" and "United States" to the 50 states and the District of Columbia, but BIO requests that CMS specify this effective date in any final rule for avoidance of doubt.

XI. MEDICAID MCO UTILIZATION – 42 C.F.R. § 447.509(b)

The ACA expands the Program to require manufacturers to pay rebates to states for the utilization of covered outpatient drugs by patients enrolled in Medicaid Managed Care Organizations ("MCOs").¹⁷¹ The Proposed Rule implements this requirement and specifies that manufacturers must pay rebates for drugs dispensed to such patients "if the MCO is contractually required to provide such drugs."¹⁷² The Proposed Rule also

¹⁶⁹ 77 Fed. Reg. at 5345.

¹⁷⁰ See 77 Fed. Reg. at 5345 (implementation timeline for mandatory Territory participation in the MDRP).

¹⁷¹ ACA § 2501(c), SSA § 1927(b)(1)(A).

¹⁷² 77 Fed. Reg. at 5364 (Proposed § 447.509(b)(1)).

states that manufacturers are exempt from paying rebates for covered outpatient drugs that are dispensed by HMOs and for covered outpatient drugs that are discounted under the 340B Drug Pricing Program.¹⁷³ Although BIO appreciates the additional details regarding this aspect of the ACA that are included in the Proposed Rule, there are several important issues related to the implementation of the expansion of the Program to Medicaid MCOs that the Proposed Rule does not address.

A. CMS Should Confirm The Effective Date and Conditions For Rebate Eligibility.

The Proposed Rule does not expressly address the effective date on which manufacturers' rebate obligations for Medicaid MCO utilization began to accrue. This provision of the ACA was effective upon enactment, March 23, 2010, and therefore manufacturers should be obligated to pay rebates for drugs only where those drugs were both dispensed and paid for by Medicaid MCOs on or after that date. CMS adopted this approach in State Release 158, where it stated "manufacturers are responsible for paying rebates on such covered outpatient drugs effective with respect to drugs dispensed by the MCO on or after March 23, 2010".¹⁷⁴ In addition, the Proposed Rule requires manufacturers to pay rebates for drugs dispensed to Medicaid MCO enrollees only "if the MCO is contractually required to provide such drugs."¹⁷⁵ CMS should restate that manufacturers are responsible for rebates only for those drugs dispensed and paid by Medicaid MCOs on or after March 23, 2010 and only where such MCOs have contracts requiring them to cover drugs for which the rebates are being claimed.

B. CMS Should Require Medicaid MCOs to Cover Participating Manufacturer Drugs to the Same Extent As Required for Fee-For-Service Medicaid.

As a condition of having its products covered under fee-for-service Medicaid, each manufacturer enters into a Medicaid drug rebate program agreement with the Secretary.¹⁷⁶ States cannot decline to cover any covered outpatient drug of any manufacturer that participates in the Program, although States do have the authority to subject a manufacturer's drugs to prior authorization. CMS has long stated this as a governing principle of the Program as to fee-for-service utilization,¹⁷⁷ and nothing in the ACA's expansion of rebate liability to MCO utilization exempts that utilization from this coverage mandate. The Proposed Rule does not address whether MCOs are obligated to cover a participating manufacturer's covered outpatient drugs to the same extent as

¹⁷³ *Id.* (Proposed § 447.509(b)(2)).

¹⁷⁴ State Release No. 158 (July 13, 2011).

¹⁷⁵ 77 Fed. Reg. at 5364 (Proposed § 447.509(b)(1)).

¹⁷⁶ SSA § 1927.

¹⁷⁷ See, e.g., State Release No. 19, at 4 (noting that the Omnibus Budget Reconciliation Act of 1990 requires coverage of all non-excludable or non-restricted drugs of a participating manufacturer; states may not impose restrictions on participating manufacturer drugs where the result would be the "manufacturer's drug not being covered at all under the Medicaid program").

is required under fee-for-service Medicaid, and CMS should clarify this point as a result. To the extent CMS believes that coverage mandate does not apply, BIO requests that CMS articulate the legal basis for that conclusion.

C. BIO Supports the Proposed Rule's Express Prohibition of Duplicate Discounts on 340B Units.

The Medicaid and the 340B Program statutes prohibit 340B "covered entities" from seeking Medicaid payment for a drug that is subject to discounts under the 340B Drug Pricing Program.¹⁷⁸ This prohibition protects manufacturers from paying "duplicative discounts" by paying a Medicaid rebate on drugs that are already subject to a discount under the 340B program. The Proposed Rule appropriately expressly codifies this prohibition by stating that manufacturers are not required to pay rebates for covered outpatient drugs dispensed to Medicaid MCO enrollees if such drugs are "discounted under section 340B of the PHSA."¹⁷⁹ To help ensure compliance with the prohibition on duplicative discounts, CMS should require Medicaid MCOs to collect individual prescription numbers and pharmacy IDs (in NCDCP format) for the drugs dispensed to Medicaid enrollees. Medicaid MCOs also should be required to make that information available to manufacturers so that manufacturers can verify that the prohibition on duplicative discounts is being correctly applied.

D. MCO Utilization Rebate Invoices.

Based on our members' experience with rebate claims submitted to date for MCO utilization, BIO requests that states be required to submit FFS utilization on a distinct invoice from MCO utilization. Our members believe separate invoices will greatly further their ability to confirm the integrity of the data, which in turn will facilitate claims processing and payment. The MCO invoice should specify the actual MCOs included on the invoice as well, again to assist in the validation of the data. As discussed in more detail below, CMS should also mandate that states provide prescription-level detail and the dispensing pharmacy's identifying information when submitting invoices. CMS further should require that the states require 340B entities billing Medicaid MCOs to use the NCPDP 340B pharmacy claim flag. This identifier will permit manufacturers to see through to the script-level on the invoice in order to ensure that manufacturers are calculating and paying rebates appropriately in conformance with all Program requirements.

Many states have yet to submit any MCO utilization to our members for payment. In addition to the quarterly deadline for timely submission of data, discussed below, BIO requests that CMS impose a fixed deadline for the submission of MCO claims. BIO is concerned that without such a deadline there is nothing to prevent states and MCOs from waiting months if not years to begin the submission of their rebate claims, which would put manufacturers in an untenable financial position. It is certainly reasonable to

¹⁷⁸ See SSA § 1927(a)(5)(C); Public Health Service Act ("PHSA") § 340B(a)(5), 42 U.S.C. § 256B(a)(5).

¹⁷⁹ 77 Fed. Reg. at 5364 (Proposed § 447.509(b)(2)).

impose a deadline for the initial submission of those claims, and BIO requests that CMS impose a deadline of no more than 180 days after publication of any final rule. Utilization submitted after that deadline should not be eligible for rebates.

XII. MANUFACTURER OBLIGATIONS – 42 C.F.R. § 447.510

A. BIO Supports CMS' Proposal to Permit Manufacturers to Restate Base Date AMPs But Manufacturers May Lack the Data Necessary to Restate Under a Build-Up AMP Methodology.

The Proposed Rule allows but does not require manufacturers to restate revised base date AMPs to reflect the revised ACA definition of AMP.¹⁸⁰ Specifically, CMS proposes to give manufacturers “the option to report a recalculated base date AMP based on the [ACA] . . . for a period of four full calendar quarters beginning with the first full quarter after the publication of the final rule.”¹⁸¹ The Proposed Rule recognizes that some manufacturers may not wish to restate base date AMPs due to the associated administrative burden or for other reasons. BIO supports this approach, as we did when CMS took this same approach to restatement of base date AMPs for the following the publication of the DRA Final Rule.¹⁸² BIO requests, however, that CMS explicitly state the deadline date for submission of revised base date AMPs when it publishes a final rule to ensure that manufacturers are on clear notice as to the applicable deadline. As noted above, BIO also requests that CMS permit manufacturers of 5i drugs to restate a base date AMP for each 5i drug under both AMP calculations. Finally, as many manufacturers chose not to restate their base date AMPs under the DRA Final Rule, CMS should clarify that the restatement option under the ACA is available whether or not a manufacturer previously restated base date AMP for a drug under the DRA Final Rule.

In addition to the concerns articulated above regarding the build-up methodology, BIO also is concerned that the adoption of that approach almost certainly will make the restatement of any base date AMPs prohibitive. The vast majority of manufacturers do not currently have the data needed to restate base date AMP under a build-up AMP methodology because those data were not required at the time the original base date AMP was calculated. This provides an additional reason to reject the build-up approach.

B. Exceptions to the 12-quarter Restatement Period.

CMS reports in the Proposed Rule that it regularly receives requests from manufacturers to revise reported pricing data outside of the 12-quarter period.¹⁸³ CMS proposes, therefore, to create exceptions to the current 12-quarter restatement limit for

¹⁸⁰ *Id.* at 5344, 5365 (Proposed § 447.510(c)(3)).

¹⁸¹ *Id.*

¹⁸² See 72 Fed. Reg. at 39, 211.

¹⁸³ 77 Fed. Reg. at 5343.

five specific reasons: (1) "a drug category change or a market date change"; (2) initial product submissions; (3) the termination of a manufacturer from the Program; (4) technical corrections (such as a keying error); and (5) "specific underpayments to States, or potential liability regarding those underpayments, as required by CMS, applicable law or regulations, or an OIG or DOJ investigation."¹⁸⁴ The Proposed Rule states that CMS will consider a request for revision outside of the 12-quarter period only if it falls within one of these categories.¹⁸⁵ CMS also proposes that a manufacturer may submit a "recalculation request" outside the 12-quarter time period for "good cause."¹⁸⁶ CMS suggests that this good cause exception will allow a manufacturer to resubmit its pricing data "due to a recalculation of the methodology for calculating AMP and best price" as required by a subsequent review of the manufacturer's pricing data by CMS, the OIG, or another authorized government agency that determines that such adjustments or revisions are necessary.¹⁸⁷

It is unclear from the Proposed Rule how this good cause exception differs from the fifth exception and requests that CMS clarify that point. BIO otherwise commends CMS for recognizing the potential need for manufacturer to revise of pricing data outside of the 12-quarter period, including restatements for good cause, and supports this aspect of the Proposed Rule. If CMS finalizes any of the proposed exceptions, BIO also requests that CMS explain how manufacturers should submit requests to CMS for a filing under one of these exceptions.

The language of the Proposed Rule states that that requests for revisions outside the 12-quarter period "will not be considered" except for the reasons provided in the regulation.¹⁸⁸ BIO interprets this language, therefore, solely as a grant of discretion to the agency to waive the 12-quarter limit in certain circumstances. BIO does not view this language as the creation of a new affirmative obligation on manufacturers to report revisions to pricing data outside the 12-quarter period. That would be an inappropriate and complete revision to the long-standing 12-quarter limit on such true-up obligations. BIO requests that CMS explicitly clarify that the exceptions do not create new reporting true-up obligations on manufacturers beyond the 12-quarter period.

Finally, as revisions outside of the 12-quarter period often can result in revisions to pricing data that can both increase as well as decrease rebate liability, CMS should clarify in any final rule that these exceptions provide CMS with discretion to accept only the totality of revisions proposed by a manufacturer, inclusive of revisions that decrease liability, assuming that CMS does not otherwise have a legal basis for declining the revisions as impermissible based on the AMP and BP calculation regulations. Simply put, CMS should not be able to cherry-pick among revisions outside of the 12-quarter period and accept only those that increase rebate liability. If a manufacturer requests

¹⁸⁴ *Id.* at 5343, 5365 (Proposed § 447.510(b)(1)).

¹⁸⁵ *Id.* at 5365 (Proposed § 447.510(b)(1)).

¹⁸⁶ *Id.* (Proposed § 447.510(b)(2)).

¹⁸⁷ 77 Fed. Reg. at 5343.

¹⁸⁸ *Id.* at 5365 (Proposed Rule § 447.510(b)(1)).

revisions, then those revisions should be accepted or rejected as a whole if they are supported by the applicable legal standards.

C. Civil Monetary Penalties.

CMS has proposed language regarding the imposition of civil monetary penalties (“CMP”) for late reporting of AMP data.¹⁸⁹ The Proposed Rule notes that, in accordance with statutory requirements, any manufacturer that “fails to submit and certify a quarterly AMP to CMS for a product by the 30th day after the end of each quarter . . . will be subject to a civil monetary penalty for each product not reported on the thirty-first day.”¹⁹⁰ CMS extends the same discussion to the context of monthly AMP reporting, and writes that failure to submit monthly AMP information timely “will” subject the manufacturer to a civil monetary penalty.¹⁹¹

The language proposed by CMS appears to indicate that CMPs will be imposed automatically in the event that a manufacturer is late in reporting monthly or quarterly data. BIO understands the importance of timely submission of price reporting data, and therefore also appreciates the potential need for penalties in association with late reporting. Nevertheless, BIO strongly believes that CMPs should not be imposed automatically, as the Proposed Rule implies will be the case.

Each manufacturer’s price reporting systems work somewhat differently, and there are numerous complexities within each. A significant amount of time and effort goes into each pricing calculation, certification, and submission, and there is much room for error in the process. Manufacturers are generally reliant upon different technologies and systems that can fail or produce unintended and unexpected errors. There are times, as well, when the DDR system is not functioning correctly or is inaccessible to a manufacturer, and these types of circumstances certainly should not cause CMPs to be imposed on a manufacturer. For all of these reasons, the imposition of CMPs should never be automatic, and CMS instead should retain the right to exercise its discretion in determining whether CMPs are warranted based on the specific facts and circumstances of each particular situation. CMS can accomplish this result by substituting the term “may” for the term “will” in the appropriate provisions of section 447.510.

D. Reporting of AMP Units.

CMS has instructed manufacturers to report AMP units on a monthly basis for each covered outpatient drug, along with the drug’s AMP figure itself.¹⁹² CMS specifically proposes to have manufacturers “report the monthly AMP units as the number of units that are used to calculate the monthly AMP to be reported to CMS.”¹⁹³

¹⁸⁹ *Id.* at 5342, 5344–45, 5365–56 (Proposed § 447.510(a)(5) & (d)(7)).

¹⁹⁰ 77 Fed. Reg. at 5343 (emphasis added).

¹⁹¹ *Id.* at 5344.

¹⁹² *Id.* at 5344, 5365–66 (Proposed § 447.510(d)(6)).

¹⁹³ *Id.*

In this discussion, however, CMS does not address the potential for double reporting of authorized generic units by both the primary and secondary manufacturer when the primary manufacturer includes in its calculation of AMP sales of its authorized generic drug product sold or licensed to a secondary manufacturer.¹⁹⁴ Where the primary manufacturer is including authorized generic sales in the branded product's AMP and the secondary manufacturer also is reporting AMP units for the same authorized generic, the authorized generic's units will be double-counted – once in the branded product's AMP units reported by the primary manufacturer and a second time in the authorized generic units reported by the secondary manufacturer. This could be viewed as over-weighting the branded product's AMP in the weighted average used to generate the applicable FUL. To avoid this result, BIO recommends that the primary manufacturer report only those AMP units related to the branded prescription drug itself, and not inclusive of any authorized generic units. BIO requests that CMS address this issue in any final rule.

XIII. STATE OBLIGATIONS – 42 C.F.R. § 447.511

A. CMS Should Impose the Statutory Deadline for States to Submit Invoices to Manufacturers.

The Medicaid statute requires States to report to manufacturers on covered outpatient drugs utilized “not later than 60 days after the end of each rebate period.”¹⁹⁵ The ACA extended this reporting requirement to include “such information reported by each Medicaid managed care organization,”¹⁹⁶ and without altering the statutory 60-day time limit. There is no exception to this requirement and the statute does not authorize the Secretary of Health and Human Services to grant extensions. The 60-day period is a firm deadline for the submission of invoice data to manufacturers for both fee-for-service and MCO utilization.

Despite the mandatory time limit for States to report their utilization of covered outpatient drugs set forth in the statute, CMS previously declined to impose any consequences for States that fail to timely submit drug utilization to manufacturers.¹⁹⁷ CMS did not provide any statutory support or other explanation for that policy. The Proposed Rule, in contrast, now expressly requires that “[w]ithin 60 days of the end of each quarter, the State must bill participating drug manufacturers an invoice, which includes, at a minimum” certain drug utilization data as specified in the regulation.¹⁹⁸ CMS should clarify that, consistent with the statute, the Proposed Rule implements the statutory deadline as a mandatory obligation for States and that States must submit their prior quarter drug utilization data, including any revisions to those data, within 60

¹⁹⁴ See *id.* at 5337, 5363 (Proposed § 447.506(b)).

¹⁹⁵ SSA § 1927(b)(2)(A).

¹⁹⁶ ACA § 2501(c)(2)(A)(ii).

¹⁹⁷ 60 Fed. Reg. at 48,460.

¹⁹⁸ 77 Fed. Reg. at 5366.

days of the end of that quarter. CMS should also expressly state that manufacturers are not obliged to pay Medicaid rebates for claims that are not timely submitted.

Not only would a policy establishing a maximum time frame during which a manufacturer is obliged to pay rebates to the States be consistent with the statute, but a firm deadline also would shorten the time between the date the utilization occurs and the date the manufacturer initiates any dispute with the state regarding that utilization. The passage of time between those events necessarily increases the complexity of the dispute and makes it more difficult for the parties to reach a resolution. It is inefficient and burdensome for both manufacturers and States to attempt to substantiate rebate claims to resolve disputes months or even years after the drug is utilized. Such delays in reporting also make it difficult for manufacturers to maintain accurate sales records and to finalize their books regarding past utilization. Manufacturers also frequently use information about past utilization to project their future rebate obligations, and these projections are rendered less-accurate where there are delays in reconciling sales data.

CMS should also clarify that even though states that have participating Medicaid MCOs are required to report the drug utilization data for Medicaid MCOs separately, the same statutory deadline of “within 60 days of the end of each quarter” applies to those reports as well.¹⁹⁹

B. CMS Should Clarify that Data Submissions To CMS Must Be Timely Submitted and Revised.

The Medicaid statute requires a state to “promptly transmit a copy” of the drug utilization data reported to manufacturers to CMS as well.²⁰⁰ The Proposed Rule also implements this requirement by requiring the State to submit, on a quarterly basis, “the same information as submitted to the manufacturers.”²⁰¹ The Proposed Rule does not clearly specify a timeframe for that submission. The Proposed Rule also does not address whether, to the extent that the data initially submitted to the manufacturer and CMS subsequently are revised, the State is obligated to revise the data previously submitted to CMS and in a timely matter. Revisions may occur, for example, when a manufacturer disputes a rebate invoice and the state and the manufacturer later resolve that dispute. CMS should require States to provide prompt updates to correct the utilization data previously submitted to CMS. The calculation of the annual branded prescription drug fee under the ACA depends on the manufacturer’s share of total sales to Medicaid and other government programs.²⁰² To ensure the accuracy of the IRS Annual Fee Medicaid sales calculation, CMS should require States to appropriately correct the sales data submitted to CMS within 30 days of resolution with the manufacturer.

¹⁹⁹ *Id.* at 5366 (Proposed Rule § 447.511(c)).

²⁰⁰ See SSA § 1927(b)(2)(A).

²⁰¹ 77 Fed. Reg. at 5366 (Proposed § 447.511(b)).

²⁰² ACA § 9008, as amended by HCERA § 1404; I.R.B. 2011-40, T.D. 9544 (Oct. 3, 2011), available at http://www.irs.gov/irb/2011-40_IRB/ar09.html

As discussed above in relation to MCO utilization, CMS should require the states to submit prescription-level information, including pharmacy identifiers and the NCPDP 340B flag, for all fee-for-service utilization. To the extent this requires the providers themselves to use the NCPDP 340B flag, then CMS should require the states to impose this requirement as a condition of those providers' participation in the Medicaid program. Due to the expanding scope of the Program, manufacturers are encountering greater challenges to auditing and verifying state rebate claims. The requested claims detail information will aid manufacturers in their ability to validate state rebate claims and in particular any utilization sourced through the 340B Program. The OIG just last year pointed to significant concerns with regard to rebate claims associated with drugs purchased under the 340B Program. The OIG's 2011 report noted that it has significant concerns about states' "ability to conduct oversight activities related to 340B-purchased drugs."²⁰³ The OIG found that "[n]early half of States (25 of 51) do not have 340B policies" to govern the prohibition on duplicate discounts. BIO shares the OIG's concerns and urges CMS to require states to submit prescription-level information for both fee-for-service and MCO utilization.

C. CMS Should Implement State Plan Assurances Regarding the Payment Methodology for Covered Outpatient Drugs.

CMS proposes that each State's Medicaid State Plan must describe the State agency's reimbursement methodology for covered outpatient drugs, including drugs dispensed by a 340B covered entity or its contract pharmacy, as well as by an Indian Health Service ("IHS") tribal or urban Indian pharmacy.²⁰⁴ CMS proposes that a State's payment methodology must be consistent with the proposed shift from EAC to AAC, and that a state proposing changes to the ingredient cost reimbursement or professional dispensing fee must provide adequate data to support any proposed change and submit the proposal to CMS through a State Plan Amendment ("SPA") and formal review process.²⁰⁵

Implementing the State plan requirement and the formal review process required for SPAs is an appropriate mechanism for CMS to exercise oversight to ensure that states are capturing the savings that result from the federal discounts available to 340B covered entities and IHS pharmacies.²⁰⁶ BIO requests that CMS extend these requirements to the documentation of the state's mechanism for ensuring compliance with the statutory prohibition on "duplicative discounts," which protects manufacturers from paying a Medicaid rebate on fee-for-service or MCO utilization that is sourced through a 340B-priced unit.²⁰⁷ As an additional mechanism to ensure compliance with the statutory prohibition on duplicative discounts, BIO requests that CMS encourage

²⁰³ OIG Report, *State Medicaid Policies and Oversight Activities Related to 340B-Purchased Drugs*, at 16 (June 2011), available at <http://oig.hhs.gov/oei/reports/oei-05-09-00321.pdf>.

²⁰⁴ 77 Fed. Reg. at 5350, 5367 (Proposed § 447.518(a)).

²⁰⁵ *Id.* (Proposed § 447.518(d)).

²⁰⁶ See OIG Report, *supra* note 203.

²⁰⁷ See SSA § 1927(a)(5)(C), PHSA § 340B(a)(5).

state Medicaid agencies to cooperate with manufacturer requests for data as needed to evaluate 340B covered entity compliance with this prohibition.

D. BIO Supports Flexibility for State Coverage of Investigational Drugs.

Section 1905(a)(12) of the SSA grants states the option to cover investigational drugs.²⁰⁸ Federal matching funds are available to states that elect to provide coverage for investigational drugs to the extent consistent with Section 1903(i) of the Social Security Act and federal Medicaid regulations. CMS proposes a new regulation to clarify that states are permitted to provide coverage for investigational drugs when such drugs have been indicated by the FDA for human trials.²⁰⁹ Federal matching funds are available if a state includes a description of its coverage and payment for investigational drugs in its Medicaid State Plan and the State Plan provides that reimbursement for such drugs will be in accordance with FDA regulations codified at 21 C.F.R. Parts 312 and 316.²¹⁰

The Proposed Rule's approach to allow flexibility for states to provide coverage for investigational drugs for Medicaid patients is vital to innovation. Clinical trials to develop new products and treatment indications depend on the participation of patients with different backgrounds and co-morbidities and should include Medicaid patients. Participating in clinical trials may also provide crucial access to potentially beneficial experimental treatments for Medicaid patients whose conditions have not responded to existing therapies or who have conditions for which there are no existing therapies. BIO strongly urges CMS to finalize this aspect of the Proposed Rule.

E. CMS Should Postpone Any Shift to AAC-Based Reimbursement Until Stakeholders Have An Opportunity To Review NADACs and AMPs Calculated Under A Build-Up Methodology.

CMS has proposed replacing EAC with AAC as the metric for state Medicaid pharmacy reimbursement to ensure that reimbursement amounts are based on a "more accurate reference price."²¹¹ CMS proposes to require states to provide data to support any proposed changes in reimbursement using AAC, and CMS suggests that such data could include the results of a national survey or that states could perform their own state-specific surveys.²¹² CMS also suggests that states could use AMP, which CMS describes as "based on actual sales data," to support AAC-based reimbursement.²¹³

BIO recognizes the need for alternative sources of pharmacy acquisition cost data in response the decision by First DataBank to cease publishing AWP in September 2010, and appreciates CMS' own efforts to generate such data through the National

²⁰⁸ SSA § 1905(a)(12).

²⁰⁹ 77 Fed. Reg. at 5351, 5367 (Proposed § 447.522(a)-(c)).

²¹⁰ *Id.*

²¹¹ *Id.* at 5320 (Proposed § 447.512(b)(1)).

²¹² *Id.* at 5350 (Proposed § 447.518(c)).

²¹³ *Id.* at 5350.

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Average Drug Acquisition Cost ("NADAC") survey. CMS should nevertheless postpone the use of either AMP or NADAC for this purpose until more data are available and stakeholders have a chance to study what might be the most appropriate benchmarks for AAC.

In the case of AMP, transition to a build-up methodology has the potential to cause future AMP figures to depart radically from their historical trends. In the case of NADAC, CMS has initiated a national survey of pharmacy prices, utilizing Myers & Stauffer LC as its contractor, and the results of that national survey have not been published for any quarter. Nor has CMS responded to stakeholder comments on this initiative. The results of this National Average Drug Acquisition Cost ("NADAC") survey will be of particular interest to manufacturers and states alike, and stakeholders will require some time in order to assess the validity of the NADAC survey. Given the uncertainty surrounding AAC-based reimbursement at this time, CMS should stay the shift from EAC to AAC until industry stakeholders have a clearer picture of the AMP and NADAC figures upon which CMS proposed to base this reimbursement.

* * *

BIO thanks CMS for this opportunity to comment on the Medicaid covered outpatient drugs Proposed Rule. We look forward to continuing to work with the agency to ensure that Medicaid drug rebates are calculated in a way that ensures adequate access to affordable medicines while appreciating manufacturers' business and government price reporting operational concerns.

Please contact Alyson Pusey at 202-449-6384 if you have any questions regarding our comments. Thank you for your attention to this very important matter and for your consideration of BIO's views.

Respectfully submitted,

/s/

Alyson A. Pusey
Director, Reimbursement and Health Policy

CC: (via electronic mail)

Amy Bassano
Director
Hospital & Ambulatory Policy Group
Centers for Medicare and Medicaid Services
Department of Health and Human Services
7500 Security Boulevard
Baltimore, Maryland 21244

