

BIO Policy White Paper: Models to Incentivize the Antimicrobial Pipeline

Background

In recent years, the global community has directed a high level of political attention to the crisis of antimicrobial resistance (AMR). In 2014 the United States (U.S.) released a national action plan on combating AMR¹ and formed the Presidential Advisory Committee on Combating Antibiotic Resistant Bacteria (PACCARB)² to oversee domestic AMR efforts. In 2016, the United Nations General Assembly released a political declaration on AMR³, and the G20 specifically addressed AMR in a communiqué⁴. The biopharmaceutical industry also has recognized that it too has a role to play in combating AMR. In 2016, the Davos Declaration on AMR⁵ was released, signed by over 100 companies, organizations, and trade groups; this was followed up by the Industry Roadmap for Combating AMR⁶, put forward by 13 leading Davos signatories. In early 2017, the AMR Industry Alliance⁷ was announced to oversee progress towards the commitments outlined in the Declaration and Roadmap.

One common message from many of these efforts is the need to add new tools to our arsenal to better identify, treat, and prevent AMR infections. The biopharmaceutical industry, encompassing both established and early-stage biotechnology companies, plays a key role in developing and bringing these innovative new medicines to patients. However, we have seen a recent decline in AMR product research investment from early venture capital investment and from established biopharmaceutical companies.⁸ This trend clearly illustrates the economic challenges to traditional market approaches in sustainably incentivizing AMR product development.

To best address the threat of AMR, the global community must identify ways to promote a diverse and robust pipeline, with both short-term and novel higher risk products, that is populated by sponsors that develop a wide range of products to address AMR. BIO acknowledges that the biopharmaceutical community is engaged with several international AMR efforts through the Davos Declaration. However, no trade organization is representing a unified industry voice in the U.S. Seeking to fill this void, BIO has developed the following set of key principles and incentives policies for consideration for U.S. policymakers.

A Range of Incentives Policies must be considered

BIO's member companies are developing a diverse array of AMR products, including small molecule antimicrobials, biologics, products with a prophylaxis indication, diagnostics, and

¹ https://obamawhitehouse.archives.gov/sites/default/files/docs/national_action_plan_for_combating_antibiotic-resistant_bacteria.pdf

² <https://www.hhs.gov/ash/advisory-committees/paccarb/>

³ https://www.un.org/pga/71/wp-content/uploads/sites/40/2016/09/DGACM_GAEAD_ESCAB-AMR-Draft-Political-Declaration-1616108E.pdf

⁴ http://europa.eu/rapid/press-release_STATEMENT-16-2967_en.htm

⁵ https://amr-review.org/sites/default/files/Declaration_of_Support_for_Combating_AMR_Jan_2016.pdf

⁶ http://www.ifpma.org/wp-content/uploads/2016/09/AMR-Roadmap-Press-Release_FINAL.pdf

⁷ <https://www.ifpma.org/resource-centre/new-alliance-to-drive-and-measure-industry-progress-to-curb-antimicrobial-resistance/>

⁸ <https://www.nature.com/nature/journal/v472/n7341/full/472032a.html>

new technologies that include microbiome-based and phage-based therapies, immune targeting therapies, and anti-biofilm agents. Any single incentive will likely be insufficient to support all types of AMR products, highlighting the need for a combination of incentives in concert to promote a healthy, diverse development pipeline. Moreover, each AMR product faces different challenges that need to be considered when developing a specific incentives policy.

In this document, we advance BIO's support for general incentives policies with the potential to help advance the entire range of AMR products supported by our member companies. BIO welcomes the opportunity to engage the AMR stakeholder community to identify how best to tailor a specific incentives policy to be advanced so that it is of the most benefit to the appropriate range of AMR products.

Key principles to incentivize antimicrobial discovery and development

BIO believes that stakeholders should consider these key principles when developing policies to incentivize AMR product discovery and development. These principles are adapted from and aligned with the International Federation of Pharmaceutical Manufacturers and Associations (IFPMA)'s recent public white paper on AMR incentives⁹.

- **The societal value of antimicrobial medicines should be reflected in the incentive model:** Antimicrobial medicines are undervalued in a payment model that bases compensation on utilization only. Value assessments for new AMR products need to account for the broader, long-term value that AMR medicines have to patients, the healthcare system, and society as whole, as well as address the challenges of demonstrating the value of innovative antimicrobials approved based on data from non-inferiority trials¹⁰.
- **Predictable and sustainable funding:** Given the time needed to develop new novel treatments to combat AMR, the mechanisms put in place to support R&D should be predictable, reliable and sustainable to effectively incentivize investments.
- **An early return that is sufficient to justify ongoing investment of limited R&D resources:** Attractive and predictable prospects of an early return on investments are needed to encourage further investments in R&D. The impact of these incentives will be determined by the specific type of R&D investment being considered, the value of other push-pull incentives that are available, as well as company-specific considerations.
- **Market-based models should be retained to allocate limited resources and reward successful innovation:** Competition and market forces remain an effective tool to incentivize the development of products that are best suited to meeting patients' needs (safety, efficacy, access). Existing market-based systems, while important, do not create a return on investment that is sufficient to support the development of AMR products. However, these systems can be refined to incentivize innovation and reinforce antimicrobial stewardship as well as take public health goals into account.
- **Clear definitions for products that would earn a pull reward are needed:** To further incentivize R&D, a list of the characteristics of new agents that would earn a pull reward should be developed. BIO supports an approach where a body of relevant scientific experts contributes to the development of a review process that identifies qualifying products for these incentives policies.

⁹ <http://www.ifpma.org/resource-centre/sustainable-models-to-overcome-the-challenging-economics-of-antimicrobial-rd/>

¹⁰ <https://aspe.hhs.gov/report/analytical-framework-examining-value-antibacterial-products>

- **Alignment with stewardship principles that support global access:** Efforts to incentivize sustainable investment in novel antimicrobials should be aligned with initiatives by public and private stakeholders to ensure antimicrobials are only used in patients who need them. The incentives should support mechanisms to facilitate affordable and appropriate access to both new and existing high quality antimicrobials, vaccines, and diagnostics for the patients who need them.
- **There is no “one size fits all” solution:** Although AMR is a global challenge, solutions should be tailored to different health systems and priorities. Global and regional coordination could help to identify priorities and facilitate regulatory processes.

BIO-supported Incentives Policies

This document organizes incentives policies under three categories: push incentives, pull incentives, and the promotion of value. These policies are not listed in order of priority.

Push incentives to sustain innovative R&D for AMR products

The biopharmaceutical industry and academic institutions play complementary roles in researching and developing AMR products as well as bringing them through the commercialization process to patients. Push incentives that provide direct support for R&D by sponsors, helping to de-risk their efforts to create an AMR product, are of particular value in sustaining these innovative efforts. BIO acknowledges the excellent progress to develop push incentives for AMR thus far, and believes we should continue to build on and expand these programs.

Grants and Contracts

BIO has a history of highlighting the critical importance of U.S. Government funding that includes basic research, small business grants, and clinical development support for novel AMR product development. We will continue to educate policymakers on the importance of the U.S. government’s role in combating AMR. BIO advocates for increased appropriations funding for the National Institutes of Health (NIH), Department of Defense (DOD), the Biomedical Advanced Research and Development Authority (BARDA), and other agencies to continue their support for both early and advanced stage R&D of AMR products.

Public Private Partnerships

BIO strongly supports Public Private Partnerships (PPP) that support R&D, such as BARDA’s innovative portfolio partnerships, its new CARB-X incubator, and the Innovative Medicine Initiative’s (IMI) efforts in Europe. As mentioned above, BIO will continue robust advocacy for appropriations that maintain strong funding support for these efforts. BIO believes that these promising programs could be expanded from small molecule antimicrobials to support the broader range of AMR products under development. BIO also acknowledges that these PPPs can help provide a foundation to support additional incentives policies, both push and pull.

Tax Credits

Clinical research and development (R&D) costs represent a major challenge for companies developing AMR products under current market challenges. BIO supports establishing tax credits to spur the development of qualifying AMR products and stimulate continued investment in this space. Our organization also believes that an AMR product tax credit should ideally be transferable to help encourage R&D investments in AMR products by companies with smaller tax liabilities.

Pull incentives to create a viable market for AMR products

Pull incentives are policies that aim to create a viable market demand and reward success for developing AMR products. Despite initial successes with push incentives mechanisms, if there are not attractive pull mechanisms to justify expensive Phase 2 and 3 studies, there is a risk that push incentives funding may not be sufficient to secure the full development and commercialization of new AMR products. BIO strongly supports the development of pull incentives to create a viable, sustainable market for AMR products. Pull incentives can also be paired with stewardship provisions to ensure that new AMR products are utilized in the most appropriate manner possible.

Transferable Market/Regulatory Exclusivity

BIO believes that Transferable Market/Regulatory Exclusivity—a mechanism where a developer with a qualifying AMR product would receive an exclusivity extension that could either be used for another marketed product or sold—would greatly improve the market viability for AMR products. This approach has a key advantage by not requiring upfront or sustained appropriations. BIO believes this mechanism, if crafted with an appropriate focus and guardrails, can balance the costs of developing new AMR products with their societal benefits in combating resistant infection.

Market Entry Rewards

BIO supports a market entry reward model that rewards innovation earlier in the product life cycle and serves to share risk with developers. In such a model, qualifying AMR products that reach the market would receive a monetary reward that partially de-links early sales volume from profits. This earlier return provides needed revenue that could be effectively reinvested into future AMR studies. This model is currently of great interest for AMR stakeholders, as it can be crafted to promote stewardship of therapeutic AMR products. BIO believes that any market entry reward should follow a model where milestone payments supplement—but do not replace—sales revenue. Our organization also believes that a developer should retain intellectual property rights and be responsible for approval, manufacturing, and sales of the qualifying AMR product.

Within the U.S. market, BIO believes that BARDA is best suited to oversee this program given its strong relationship with industry partners. Moreover, BARDA is a highly effective and efficient government organization with expertise in public health and procurement. BIO agrees that guardrails should be incorporated into this model to ensure that stewardship, access and other considerations are appropriately addressed. Our organization remains open to other market entry reward approaches, including fully de-linked models, and welcomes a dialogue with stakeholders to explore these further.

Extended Exclusivity

The Generating Antibiotic Incentives Now (GAIN) Act¹¹ of 2011 provides fast-track and priority review by the Food and Drug Administration (FDA) and extends the data exclusivity of any qualified infectious disease product (QIDP) by five years. BIO supports policies that expand the GAIN mechanism to include a broader range of AMR products as well as provide additional years of exclusivity where appropriate.

PDUFA Fee Waivers for small company AMR products

Prescription Drug User Fee Act (PDUFA) fees can represent a significant financial investment for small biotech companies when submitting their new drug application (NDA). BIO supports a mechanism that waives PDUFA fees for small biotech companies, below a defined market capitalization, when the said companies submit a NDA for an AMR product meeting a

¹¹ <https://www.congress.gov/bill/112th-congress/house-bill/2182>

set criteria. This can help drive continued innovation by biotechnology companies to develop AMR products.

Policies that more appropriately value AMR products and their societal benefits

BIO acknowledges that payment reform for hospital-administered AMR products can address challenges posed by bundled-payment mechanisms that may discourage the appropriate use of antimicrobials. BIO is actively exploring value-based arrangements between manufacturers and payers, and we appreciate the critical benefit of a market-based approach that complements and supports antimicrobial stewardship efforts.

Supplemental Payment

Our organization also understands that the move to value-based arrangements will take time, and recognizes that efforts can be undertaken to improve the current state of AMR product reimbursement in the interim. One effort that BIO supports is a mechanism that addresses challenges with Medicare reimbursement of AMR products. Traditional Medicare payments for inpatient antibiotics are based on a system where a fixed payment is derived from the average cost of services to treat a defined diagnosis or set of clinical characteristics. These Medicare severity-related groups (MS-DRGs) are designed to incentivize hospitals to operate efficiently, but can also present a barrier for the appropriate valuation and payment of all new therapies, including antimicrobial medicines.

BIO supports a mechanism that creates a supplemental payment for novel therapies, including qualifying AMR products used in the hospital setting, outside of the bundled DRG payment. This can help address the inadequate payment received for innovative products captured in these bundled payment models and support future efforts regarding value-based arrangements.

Conclusion

BIO, as a signatory to the Davos Declaration, has agreed to the clarion call to help develop a sustainable, predictable, and diverse market of AMR products. BIO can take a leading role within the U.S. to shape and advance the incentives necessary to achieve these goals. While the task is monumental, we believe sustained efforts by BIO and other stakeholders will lead to the rise of the novel tools we need to stem the tide of AMR.