

Options Paper: Incentives to Bring New Antibiotics to APEC Markets

APEC Health Working Group

March 2024



**Asia-Pacific
Economic Cooperation**



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APEC Project: HWG 05 2022A

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**APEC Health Working Group (HWG)
Project 05 2022A: “Incentives to Bring New
Antibiotics to APEC Markets”**

Antimicrobials are arguably the most important drug class in human history and have saved millions of lives worldwide. However, rising levels of resistance to antimicrobials is a serious risk to public health, a safe and sustainable food supply, and economic growth. There is an urgent need for the development of new antimicrobials to address growing resistance, however without substantial changes to the economic landscape, including policies that would enable a predictable and sustainable return on investment, pharmaceutical companies experience increasing difficulty in justifying the investment needed to develop new drugs and diagnostics. The APEC Health Working Group project “Incentives to Bring New Antibiotics to APEC Markets” ([HWG 05 2022A](#)) seeks to survey existing strategies and best practices for economic incentives relevant to APEC economies, including examining and addressing barriers to market entry for new drugs and diagnostics.

Gap Analysis¹

The purpose of the gap analysis was to identify current challenges and compile strategies to address antimicrobial market failure and incentivize the development of novel antimicrobials to meet public health needs. It also highlights steps all APEC economies can consider to improve access to antimicrobials. A voluntary survey distributed to APEC member economies informed the gap analysis. Based on the survey findings, several key gaps and opportunities in addressing antimicrobial resistance (AMR) and promoting access to novel antimicrobials were identified.

The survey highlights the lack of targeted reimbursement processes to support research, development, and production of novel antimicrobials, with only one economy having a specific reimbursement process in place. Inadequate pull incentives for innovative research and development (R&D) initiatives are also evident, as only two economies (Russia and the United States) have such incentives. The World Health Organization (WHO) advocates for augmenting pull incentives and other financing mechanisms to foster sustainable antimicrobial development, benefiting both health and the economy. Insufficient cost offsets for antimicrobial production and maintenance through push incentives persist, hindering progress. While most reporting economies use data for decision-making within AMR coordination mechanisms, there's room for improvement in reviewing and updating National Action Plans (NAPs) with a focus on accountability, transparency, flexibility, and responsiveness. Financial provision for NAP implementation is included in the economy-wide plans and budget of several economies.

Bringing new antimicrobials to market faces multiple challenges, including scientific hurdles, high R&D costs, complex regulatory processes, market uncertainties, and financial constraints linked to reimbursement, market access, and limited usage to prevent resistance. Policies to support sustainable investment and access to antimicrobials encompass push and pull incentives and reimbursement and Health Technology Assessment (HTA) reform. Push incentives, like public-private partnerships and tax credits, aim to reduce R&D costs upfront, while pull incentives, such as subscription models and market entry rewards, reward market success. Simultaneously, HTA reform focuses on adequately compensating for the broader societal value of antimicrobials and reconsidering payment models to encourage improved access of new antimicrobial drugs.

¹ The full gap analysis report may be accessed on the APEC Meeting Document Database at:
http://mddb.apec.org/Documents/2023/HWG/HWG2/23_hwg2_003.pdf

To address these challenges and capitalize on opportunities, it is essential to strengthen financing mechanisms and resources for sustainable antimicrobial R&D and broader access. This includes supporting public-private partnerships like CARB-X and GARDP, evaluating the effectiveness of pull incentive pilot approaches, examining how changes to reimbursement and HTA can improve antimicrobials access, and exploring international collaborative mechanisms. Furthermore, integration of AMR into international development cooperation initiatives and provisions within push funding agreements can enhance equitable and global access to essential health products, including diagnostics and vaccines.

Identified Gaps and Opportunities:

Insufficient targeted reimbursement processes exist to support R&D, manufacturing, and the creation of a reserve of novel antimicrobials. Our survey reinforces this concern, revealing that **only one economy has implemented a specific reimbursement process for antimicrobials.**

Insufficient pull-incentives currently exist to motivate and reward innovative R&D initiatives. Our survey reports that **only two responding economies responded that they have pull-incentives in place (Russia and The United States).** WHO contends that an augmentation of pull incentives, along with other innovative financing mechanisms, would effectively bolster the development of a sustainable pipeline for novel antimicrobials. Such measures would also reinvigorate innovation within the broader life sciences ecosystem, yielding positive outcomes for health and the economy.

Most reporting economies do not provide sufficient cost offsets for antimicrobial production and maintenance through push incentives. According to WHO, government or regulatory interventions that directly reduce the costs of development have helped alleviate certain challenges associated with antimicrobial development. However, these interventions, in their current scale and isolation, are inadequate to meet R&D objectives and bring a satisfactory number of products to the market.

The majority of reporting economies stated that data is analyzed and used by the AMR multisector coordination mechanism for decision making. The Philippines highlighted their Antimicrobial Resistance Surveillance Program (ARSP) which monitors the current levels and developing trends of antimicrobial resistance.

All economies reported having an AMR National Action Plan (NAP), all < 5 years old. While certainly a positive development that all reporting economies indicated that they had a NAP in place, these should be reviewed and updated with a particular focus on accountability and transparency, flexibility and responsiveness, and continuous improvement. According to the Global Database for Tracking Antimicrobial Resistance (AMR) Country Self- Assessment Survey (TrACSS), financial provision for the AMR action plan implementation is included in the economy-wide plans and budget in Malaysia; the Philippines; Russia; Thailand; and the United States.

Workshop Meeting Summary

APEC Health Working Group (HWG): “Incentives to Bring New Antibiotics to APEC Markets”

31 July - 1 August 2023, Seattle, United States

On 31 July – 1 August 2023 on the sidelines of the 13th Asia-Pacific Economic Cooperation (APEC) High-Level Meeting on Health and the Economy (HLMHE), governments, private sector, and non-governmental stakeholders gathered to advance understanding and further align on key priorities related to incentives for antimicrobials in APEC markets. There were 46 total participants, representing 8 economies, with 24 private sector participants and 22 government participants. The participants included 26 females, 19 males, and 1 other gender.

The two-day workshop featured five expert panels highlighting “**Push Incentives for Early-Stage Development**”; “**Push Incentives for Advanced-Stage Development**”; “**Pull Incentives and Conditionalities**”; “**Access and Stewardship in LMIC APEC Economies**”; and “**2024 and Beyond**”. Panelists provided remarks on the role of multi-stakeholder contributions to unlock transformative innovations and foster effective partnerships. After each panel, participants had the opportunity to engage in a question-and-answer period. This workshop reinforced the need for collaboration to finance critical gaps and ensure that the path to advancement in antimicrobial development can be forged through collaboration and innovation.

Panel Discussion Highlights

Push Incentives for Early-Stage Development. This panel session delved into how push incentives can effectively replenish the clinical pipeline with relevant antimicrobial products for all APEC economies, encompassing both high-income and low and middle-income economies. The session emphasized push incentives, global stewardship, diagnostic testing, and investment needs. According to CARB-X, there is a significant funding gap in early-stage development, with an estimated total investment requirement of USD5.6 billion over the next ten years. Current anticipated investment levels of funding are projected to be USD1.9 billion over the next ten years, leaving a funding gap of USD3.7 billion over the next ten years, or a gap of USD370 million per year.

The session concluded with a discussion covering several topics:

- **Tips for Action:** Panelists shared practical advice, suggesting that economies should conduct internal assessments to identify needs, understand the local innovation landscape, and pinpoint gaps. This process can involve engaging with trade associations, embassies, and relevant local stakeholders.
- **Global Access:** The concept of global access was discussed, noting the challenges of navigating this issue for emerging economies. This session highlighted that many existing push incentives, such as those from CARB-X, set obligations to support global access, which may present an opportunity for emerging APEC economies.
- **Current Challenges:** Challenges faced by the industry in bringing products to market were discussed, highlighting funding, and retaining talent as primary obstacles.
- **Generating Interest:** Regarding the political nature of the topic, discussants shared insights on how to garner interest including making the issue personal to connect with broader audiences and stakeholders.

Push Incentives for Advanced-Stage Development. The panel session explored the potential of push incentives to facilitate advanced development, clinical trials, and access

within APEC economies. It brought to light concerns about pediatric needs, the challenges of global manufacturing, and the imperative to foster innovation and collaboration to address growing health threats. The importance of addressing AMR as a public health failure, particularly concerning children and neonatal cases, was highlighted.

The session concluded with a discussion covering several topics:

- **Revisiting Funding:** A discussion ensued regarding the allocation of funds within the current pipeline. Disappointment was expressed with the lack of innovation to promote novel and impactful solutions.
- **Pediatric Formulations:** The issue of pediatric formulations was raised, highlighting the challenge of obtaining accurate market intelligence and gauging global demand – specifically for the neonatal and pediatric populations.
- **Global Manufacturing Collaboration:** The discussion turned to global manufacturing collaboration. The importance of moving manufacturing to local levels was stressed, while some emphasized the need for a secure end-to-end supply chain and the continuity of facility operations. It was highlighted that many small and medium-sized enterprises (SMEs) rely on third-party manufacturing facilities which can hinder innovation and speed.

Pull Incentives and Conditionalities. The panel provided comprehensive insights into the implementation of pull incentives, balancing financial sustainability with responsible stewardship, and the challenges and successes experienced by different economies and companies with pull-incentive pilots. Speakers noted that pull incentives provide a sustainable return on investment that makes early R&D work feasible, highlighting that pull incentives address both market and public health issues. However, a speaker shared that in order to create an ‘ideal’ pull mechanism, the following must be considered: the mechanism must be rapidly implementable; it must delink revenues from sales; and it must be predictable and of sufficient magnitude.

The United Kingdom (UK) and Swedish models were examined, with the following successes and challenges shared:

- **UK Model:** Successful elements included using spectrum, transmission, enablement, diversity, and insurance (STEDI)²; decoupling payment; and addressing unexpected issues. Challenges included capped payment levels and the need for volume caps.
- **Swedish Model:** Successes included pioneering new procurement/payment methods to promote access, enhancing access, and adaptability for other economies. Challenges encompassed global fairness concerns and short timelines.

The speaker from Japan highlighted their own challenges with justifying pull incentives publicly, evaluating value, encouraging investment by pharmaceutical companies, assessing subsidy scale, evaluating new drugs, ensuring financial sustainability, and fostering global collaboration. At the conclusion of the panel, pull incentive priorities were suggested including: data driven public health priorities; leaning into the interplay of push and pull incentives; and balancing short- and long-term objectives.

² **Spectrum:** Benefits of being able to treat with a narrow-spectrum agent in some settings (note how this use of *Spectrum* has a very specific meaning); **Transmission:** Benefits from avoiding spread of infection; **Enablement:** Benefits from making it safe to receive medical care; **Diversity:** Using varied antibiotics reduces resistance pressure; **Insurance:** Value of having an antibiotic to hand in case of sudden need

Access and Stewardship in Lower- and Middle-Income Economies (LMIE). The session addressed access and stewardship challenges related to antimicrobial development in LMIE economies. Insights ranged from global collaborative efforts to local data utilization, highlighting the significance of both international and community-based approaches to fostering equitable access and responsible use of antimicrobials. Specifically, there was a call out to ensure patients are engaged in these dialogues moving forward. Additionally, data on the local AMR burden needs to zoom in to highlight pathogen-drug combinations and pinpoint regions with the most significant resistance patterns. Suggestions around market intelligence forecasting, coordinated and pooled procurement, and antimicrobial portfolio optimization were provided. The session underscored the importance of diverse partnerships, collaboration, and strategies in confronting the growing issue of antimicrobial resistance.

2024 and Beyond. This panel session brought together insights from different APEC economies on potential strategies and initiatives to drive change in antimicrobial market access. The presentations highlighted the importance of establishing targets, appropriately valuing AMR solutions, fostering innovation, enhancing access, and fulfilling international commitments. Specifically highlighted were potential approaches for the future such as an increase in pooled investing and pooled procurement. We heard specifically from Australia, about their plan forward with clear steps to implement pull mechanisms within the economy. The AMR acronym was also creatively reworded by a speaker to express A = “action-based with ambitions”, M = “multi-stakeholder”, and R = “reflective response with respect”. The session emphasized the collaborative efforts required across economies to address the complex challenges posed by antimicrobial resistance for 2024 and beyond.

Key Takeaways from Workshop

The workshop examined push incentives for early-stage and advanced stage development; pull incentives and conditionalities; access and stewardship in developing economies; and potential areas for future work. The workshop highlighted the crucial need for collaboration, financing, and innovation in advancing antimicrobial development across APEC economies. Speakers called attention to the need for additional funding for push incentives amounting to approximately USD370 million annually to support the pipeline, from CARB-X estimations. Speakers also highlighted how pull incentives demonstrate a substantial return on investment. There are existing incentive models that can serve as valuable lessons and may be scalable for a larger scope. Adjusting stewardship practices to align with the specific attributes of each local economy and situation is also essential. Additionally, all economies, regardless of their income level (whether low, middle, or high), have a role to fulfill.

Potential Areas for Future Work

Speakers and attendees noted the following as possible areas for future work within APEC and more broadly:

- Further explore lessons learned from current subscription programs (e.g. UK and Sweden), such as how the UK approached engagement with industry through a consultation period³ to encourage a collaborative environment to make improvements to the subscription program from the pilot to the full program
- Develop principles on reimbursement reform (with a focus on developing economies) to help improve broader access of innovative antimicrobials to all economies

³ antimicrobial-products-subscription-model--c <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6123552/onsultation-document--1.pdf> (england.nhs.uk)

- Incorporate APEC finance and economic ministries more in future activities related to AMR
- Encourage economies with ongoing programs to join or integrate with CARB-X
- Engage patient groups, including groups not specifically related to AMR, and incorporate AMR into healthy aging
- Harmonize requirements across pull incentive awards
- Increase data collection by strengthening economy-wide or international AMR surveillance systems⁴ in developing APEC economies to understand ongoing trends in resistance and help identify unmet medical needs within each economy
- Explore possible follow up activities related to new subscription pilots under consideration by Australia; Canada; and Japan to promote information sharing and lessons learned

We acknowledge that the participation and conduct of the workshop was largely targeted for established economies which would be considered upper middle to high-income. Many LMIEs may be unable to pursue the possibility or practicality of economic incentives for antimicrobials.

LMIEs experience greater burdens due to higher infection rates, inadequate infection prevention and control, poor water and sanitation infrastructure, fragile healthcare systems, and competing health priorities.⁵ It is important to recognize that vaccines represent a valuable health intervention for AMR mitigation in LMIEs, helping to prevent infections and reduce the need for antimicrobial treatments, thereby contributing to the overall effort in combating antimicrobial resistance.⁶

We therefore, would conclude that some of the economic incentives discussed may be more easily utilized or implemented by higher income economies. While much research has generated successful, evidence-based solutions to mitigate AMR, a critical gap remains in adapting and adopting this evidence in LMIEs. Furthermore, despite the existence of AMR National Action Plans (NAPs) in numerous economies, the persistent challenge lies in effectively prioritizing and implementing NAPs on AMR in resource-limited settings, like LMIEs. As addressing AMR must be a concerted, global effort, LMIEs may be better placed to contribute using policies such as reimbursement and HTA reform, improving data collection to strengthen surveillance and applying best practices to bolster stewardship programs. While it is outside of the scope of this project to specifically focus on LMIEs, these are important conclusions to include as numerous gaps remain in this area.

APEC High-Level Meeting on Health and the Economy

APEC ministers responsible for health agreed to the following statement⁷:

We recognize the threat of antimicrobial resistance (AMR) globally, and the associated mortality and economic costs which will continue to rise if mitigating actions are not taken, and we encourage economies to collaborate with all government sectors, academia, civil society, and the private sector to explore push and pull incentives that promote investment in R&D of antimicrobials. We also strongly support efforts to preserve the antimicrobial pipeline and to

⁴ <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6123552/>

⁵ <https://pubmed.ncbi.nlm.nih.gov/34225545/>

⁶ <https://onehealthtrust.org/wp-content/uploads/2023/10/AMRandVaccinesOHTReport.pdf>

⁷ The full 13th APEC High-Level Meeting on Health and the Economy statement may be found here: <https://www.apec.org/meeting-papers/sectoral-ministerial-meetings/health/chair-s-statement-of-the-13th-apec-high-level-meeting-on-health-and-the-economy>

maximize the effectiveness of existing antimicrobials through antimicrobial stewardship and to create robust surveillance of AMR.

Recommendations for APEC Economies from APEC Ministers Responsible for Health

The following recommendations are from APEC ministers responsible for health:

- APEC ministers responsible for health encourage economies to collaborate with all government sectors, academia, civil society, and the private sector to explore push and pull incentives that promote investment in R&D of antimicrobials.
- APEC ministers responsible for health encourage economies to collaborate with all government sectors, academia, civil society, and the private sector to promote broader access to antimicrobials, including reforms to HTA and reimbursement.

Additional Recommendations for APEC Economies:

The following recommendations are based on results from the survey, gap analysis, and workshop.

- APEC economies are encouraged to seek feedback and meaningfully incorporate views from private sector, civil society (i.e. patient groups) and academia when developing AMR policy and incentives.
- APEC economies are encouraged to examine current incentive programs and explore policy measures that may be relevant to their specific circumstances recognizing the resources and capabilities of each economy.
- APEC economies are encouraged to consider possible options for future work within APEC to create a more enabling environment for AMR R&D.
- APEC economies are encouraged to consider continued collaboration through the creation of a Trans- Pacific Task Force on Antimicrobial Resistance (TPTFAR).
- APEC economies are encouraged to participate in a brief survey in Q4 2024 to track progress in implementing the recommendations.

Annex A. Meeting Agenda

Day 1 – July 31	
12:30 – 12:45pm 15 minutes	<p>Welcome Remarks and Objectives of the Workshop</p> <p>Speaker – Dr. Miranda Smith, Project Overseer, USA</p>
Session 1 12:45 – 13:45pm 60 minutes	<p>Push Incentives for Early-Stage Development</p> <p><i>This session will examine how push incentives can replenish the clinical pipeline with products that are relevant for all APEC economies, which include HICs and LMICs.</i></p> <p>Speaker/Moderator – Kevin Outterson, Executive Director, CARB-X</p> <p>Panel –</p> <p>Brian Finrow, CEO, Lumen Bioscience</p> <p>Dani Peters, Senior Advisor, Canadian Antimicrobial Innovation Coalition</p> <p>Alison Todd, Chief Scientific Officer, SpeedX</p> <p>Discussion</p>
Session 2 13:45 – 14:30pm 45 minutes	<p>Push Incentives for Advanced Development</p> <p><i>This session will examine how push incentives can support clinical trials and prepare for access in all APEC economies.</i></p> <p>Moderated by: Joel Denis, Director General, AMR Task Force, Public Health Agency of Canada</p> <p>Speaker – Mark Albrecht, Chief, Antimicrobials Branch, Division of CBRN Medical Countermeasures, BARDA</p> <p>Speaker – John Alter, Head of External Affairs, AMR Action Fund</p> <p>Speaker – Dr. Jennifer Cohn, Global Access Director, GARDP/SECURE</p> <p>Discussion</p>
Session 3 15:00 – 17:00pm 120 minutes	<p>Pull Incentives and Conditionalities</p> <p><i>This session will examine how pull incentives can be used in HICs while ensuring access and stewardship in all APEC economies.</i></p> <p>Speaker/Moderator – Kevin Outterson, Executive Director, CARB-X</p> <p>Panel –</p> <p>Dr. Greg Frank, Director, Global Public Policy, Merck/MSD</p> <p>Dr. Monika Schneider, Director, Global AMR Policy, Shionogi</p> <p>John Alter, Head of External Affairs, AMR Action Fund</p> <p>Itani Tetsuya, Director for Global Health, International Affairs Division, Japan Ministry of Health, Labour and Welfare</p>

	<p><i>5-minute break/transition</i></p> <p>Speaker – Joel Denis, Director General, AMR Task Force, Public Health Agency of Canada</p> <p>Speaker – Caitlin MacLean, Senior Director of Innovative Finance, Milken Institute</p> <p>Speaker – Dr. Mike Hodin, CEO, Global Coalition on Aging</p> <p>Discussion and Wrap Up</p>
Day 2 – August 1	
9:30 – 9:35am 5 minutes	Recap/Welcome Day 2 – Dr. Miranda Smith, Project Overseer, USA
Session 4 9:35 – 11:30am 115 minutes	<p>Access and Stewardship in LMIC APEC Economies</p> <p><i>This session will examine how APEC economies can address local barriers to access new antimicrobials.</i></p> <p>Moderated by: John Alter, Head of External Affairs, AMR Action Fund</p> <p>Speaker – Dr. Mohsen Naghavi & Dr. Erin Chung, University of Washington, Institute for Health Metrics and Evaluation</p> <p>Speaker – Rachel Silverman Bonniel, Senior Fellow, Center for Global Development</p> <p>Speaker – Dr. Jennifer Cohn, Global Access Director, GARDP/SECURE and Dr. Monika Schneider, Director, Global AMR Policy, Shionogi</p> <p>Speaker – Jessica Martinez, Senior Program Officer, Industry Engagement and Sustainable Access, Bill & Melinda Gates Foundation</p> <p>Speaker – Patrick Holmes, Head, Global Innovation Policy & Geopolitical Risk, Pfizer</p> <p>Discussion</p>
Session 5 11:30am – 13:25pm 115 minutes	<p>2024 and Beyond</p> <p><i>This session will examine how APEC economies may be able to implement change in antimicrobial market access for 2024</i></p> <p style="text-align: center;"><i>Break for buffet luncheon</i></p> <p>Economy presentations</p> <p>Speaker – Joel Denis, Public Health Agency Canada</p> <p>Speaker – Andrew Bowskill, MTPConnect/Australian AMR Network</p> <p>Speaker – Yui Kohno, HGPI Japan</p> <p>Speaker – Dr. Lynn Filpi, U.S. Office of Science & Technology Policy</p>
13:25 – 13:30pm 5 minutes	Closing Remarks – Dr. Miranda Smith, Project Overseer, USA