amr INDUSTRY ALLIANCE
UNITED AGAINST ANTIMICROBIAL RESISTANCE

PROGRESS REPORT

AMR Industry Alliance 2021 Survey

EXECUTIVE SUMMARY

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RAND EUROPE

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Antimicrobial resistance is one of the most significant public health challenges facing society. Mitigating its risks and managing its impacts requires a collective effort.

Antimicrobial resistance (AMR) is one of the key global public health challenges of our time. At least 700,000 people die each year due to AMR-related causes.[1] Left unchecked, the annual global death toll from AMR could reach ten million by 2050.[2] The emergence of treatment-resistant bacteria, viruses, parasites and fungi threatens to make previously treatable infections more difficult to treat or cure and poses new risks to the safety of existing medical procedures, such as chemotherapy. There are also growing concerns that the COVID-19 pandemic may exacerbate the threat of AMR due to increased or inappropriate antimicrobial use.[3] In addition, evidence suggests that the prevalence of hospital-acquired infections, including treatment-resistant ones, also increased with the burden of COVID-19.[4,5] In recent years, and in recognition of the complexity of the challenge presented by AMR, efforts to tackle the emergence and spread of AMR have been enhanced by governments, international organisations, the life sciences industries, healthcare professionals, academics, not-for-profit organisations and civil society.

The AMR Industry Alliance is a crucial partner in global efforts to tackle AMR.

The life sciences industries are a crucial partner in efforts to curb AMR. Within this context, the AMR Industry Alliance (AMRIA) was established in 2017 and brings together leading biopharmaceutical, biotechnology, diagnostic, generics companies and industry associations to address AMR-related issues.[6] AMRIA's mission is to: 'harness the power of the life sciences industries in the fight against anti-microbial resistance through collective efforts to: promote innovation to prevent, diagnose, and treat infections; address barriers to patient access to the most appropriate vaccine, diagnostic, or test; contribute to slowing the emergence of resistance through appropriate use; and advance responsible manufacturing through standard-setting.'[7]

ABOUT THIS REPORT

This summary report provides a unique snapshot of AMRIA's collective efforts to deliver on their commitments to tackle the rise of AMR across four strategic pillars of Alliance activities: research and science; access; appropriate use; and manufacturing and the environment.

This summary[8] is the third iteration of the Alliance's biannual progress report, documenting AMRIA activities according to its commitments across four strategic pillars. The Alliance's current commitments are highlighted on page 6. The Alliance is also set to commit to specific objectives for 2021–2025.[9]

For each of the four strategic pillars, this report provides an overview of key areas of progress and highlights implications for the future in the context of next steps that Alliance members could consider. The summary report draws on a survey of Alliance members to capture their AMR-relevant activities and progress between 1 July 2019 and 31 March 2021 (see Methodology). A list of AMRIA members is provided at the end of this summary document (**Table 1**). Overall, the Alliance has made significant contributions to tackling AMR in each of the four areas of activity, as outlined in **Box 1** and expanded on in **Boxes 2-9**.

BOX 1. **AMRIA CONTRIBUTIONS TO THE FIGHT AGAINST AMR – A SUMMARY OF KEY ACHIEVEMENTS**

- AMRIA members continue to engage in research and development (R&D), investing US$1.8-1.9 billion in AMR-relevant R&D annually in FY2019 and FY2020. However, this investment remains fragile, with 32% of members expecting to decrease investment if market conditions do not improve.
- Although the R&D investment of surveyed AMRIA members is notable, AMRIA membership is not currently representative of the entire R&D pipeline of industry contributions to AMR. This indicates an opportunity for attracting new members to the Alliance to support a fuller representation of the entirety of the industry R&D pipeline.
- The majority of surveyed companies (81%) were active in supporting access to AMR-relevant products and/or technologies, during the survey reporting timeframe. Companies are also taking action to address substandard and falsified medicines.
- Appropriate use is a key strategic pillar for most Alliance companies. Overall, 92% of surveyed R&D pharmaceutical companies, 89% of surveyed generics companies and 80% of surveyed diagnostics companies have implemented appropriate use and stewardship activities. This percentage was lower (33%) for biotech/small-and-medium-sized entities (SMEs). While the reasons for this merit further research, some biotech/SMEs may not yet have products in late-stage development or on the market and may thus be less engaged with appropriate use and stewardship activities.
- Alliance members have an opportunity to strengthen their work on surveillance and data transparency. During the survey timeframe, slightly more than half (51%) of members reported collecting and/or sharing surveillance data to generate evidence to support appropriate use and stewardship.
- Alliance members are making significant contributions to the appropriate manufacturing of antibiotics. The majority (76%) of antibiotic manufacturing sites owned by Alliance members and assessed against the Common Antibiotic Manufacturing Framework (CAMF) fully met all framework requirements, and almost all (98%) met requirements either fully or partially. Moreover, most products manufactured at Alliance members' sites (88%) have been assessed against Predicted No-Effect Concentration (PNEC) targets, and most of the assessed products (87%) meet these targets.
- Through cross-sectoral and collaborative engagement, Alliance members can continue to support efforts to accelerate adoption of the manufacturing framework across the supply chain and spur continued contributions toward meeting standards, especially for newer and incoming members who will need time to implement actions.

AMRIA COMMITMENTS[10]

RESEARCH & SCIENCE

- Invest in research and development for innovative antibiotics and antibiotic dosage forms, vaccines, new technologies, and diagnostics.
- Continue to advocate for policies that support sustainable investment in AMR-relevant innovation.
- Partner with policymakers, payers and other relevant stakeholders on new reimbursement, valuation and commercial models that support appropriate patient access and a sustainable supply of antibiotics, AMR-relevant vaccines, new technologies and diagnostics.
- Support collaboration and sharing of relevant non-proprietary data with different stakeholders (e.g. academia, consortia, SMEs, public researchers and industry) to help address key scientific and public health challenges.

ACCESS

- Address barriers to patient access to the most appropriate treatment, vaccine or diagnostic.
- Work in collaboration with policymakers to create an economic and regulatory environment that enables the sustainable supply of quality-assured antibiotics.
- Work to reduce the prevalence of substandard and falsified AMR-relevant products.

APPROPRIATE USE

- Contribute to slowing the emergence of resistance by preventing infections through promoting vaccination and reduction of inappropriate use of antibiotics through expanded use of diagnostics.
- Support appropriate use of antibiotics by working closely with other partners on awareness campaigns, continued education for healthcare professionals, and generation of evidence to support appropriate use and stewardship.
- Collect and share surveillance data with public health bodies and healthcare professionals to improve understanding of resistance trends, monitor the effectiveness of antibiotics, inform appropriate antibiotic and vaccine use, and develop adapted infection control strategies.
- Ensure that any promotional activities for antibiotics are aligned with the goal of advancing stewardship.

MANUFACTURING

- Review Alliance members' own manufacturing and supply chains to assess good practice in controlling release of antibiotics into the environment.
- Establish a common framework for managing antibiotic discharge and start to apply it across their own manufacturing and supply chains by 2018 and, in the years that follow, continue to implement the framework to reduce environmental risk due to manufacturing discharges.
- Work with stakeholders to develop a practical mechanism to transparently show that Alliance members' supply chains meet the framework's standards.
- Work with independent technical experts to establish science-driven, risk-based targets for discharge concentrations of antibiotics, develop good practice methods to reduce environmental impacts of manufacturing discharges by 2020 and work with Alliance members to ensure that the discharge targets are met.

METHODOLOGY

The not-for-profit research institute RAND Europe surveyed Alliance members using an electronic survey platform.[11] Alliance members were asked about key activities they undertook to help tackle AMR through research and science and actions targeting access, appropriate use and stewardship and responsible antibiotic manufacturing and the environment. The survey included a mix of quantitative and qualitative questions, with the latter allowing Alliance members the opportunity to elaborate on their activities and provide case examples. All quantitative survey data were analysed using descriptive statistics. Qualitative survey responses were analysed thematically, and key insights were synthesised and incorporated into the report.

A total of 53 out of 93 AMRIA members completed the survey (57% response rate). Participation rates varied between sectors, with 12 out of 12 R&D pharmaceutical companies completing the survey (100% response), 9 out of 9 generics companies (100% response), 5 out of 10 diagnostic companies (50% response) and 27 out of 62 biotech/SMEs (44% response).

The content below and **Boxes 2-9** summarise the key insights related to each of the four areas of Alliance activity and reflect on possible future actions.

There are some limitations and caveats to bear in mind when interpreting the findings of this report.[12] Although we achieved 100% response rates from some sectors, the response rate from other sectors was somewhat lower, as described above. The identity of companies has been protected in respect of commercial sensitivities and in relation to the data presented in this document.

RESEARCH AND SCIENCE

BOX 2: **RESEARCH AND SCIENCE HIGHLIGHTS – KEY INSIGHTS ON PROGRESS**

- **Industry has made a significant investment in R&D to contribute to the fight against AMR. Across 53 AMRIA members, a total of approximately USD$1.8-1.9 billion has been invested in AMR-relevant R&D annually in FY2019 and FY2020.**[13] Alliance-member investment has been enabled by various factors internal to company culture and strategy as well as factors in the external landscape. Key enablers have included company and shareholder commitment to addressing AMR; increased scientific capabilities and know-how; expectations of a reasonable return on specific investments; the existence of conducive partnerships; and attractive push incentives.
- **During the survey timeframe, Alliance members contributed to R&D on 93 products or technologies spanning 54 antibiotics and antifungals, 12 vaccines, 13 diagnostic platforms and assays and 14 non-traditional or other products. Alliance members continue to conduct R&D on AMR priority pathogens,** including products or technologies against microorganisms on the WHO's list of priority pathogens[14] and the CDC's Biggest Threats list.[15] According to the 2021 lists compiled by the Pew Charitable Trust,[16] Alliance members' R&D pipelines account for 42% of antibiotics and non-traditional products for bacterial infections in clinical development. This figure suggests that some non-members contribute to AMR-relevant industry R&D, highlighting an opportunity to further bolster AMRIA membership in the future.
- **The majority of surveyed Alliance members[17] (73%) reported that they would increase investment levels in AMR-relevant R&D if market conditions improved. The most significant challenges to investment were related to a perceived lack of sufficient pull incentives** such as appropriate reimbursement mechanisms, valuation mechanisms and advanced market commitments. Nearly a third (32%) reported that they would decrease investment if market conditions remained as they are today.
- **Collaboration has been an important feature of Alliance members' R&D activities.** Overall, 82% of surveyed companies[18] collaborated with academic institutions, 68% with other private sector organisations, 52% with country-level government bodies and 50% with hospitals and medical laboratories. Part of a collaborative effort also involves sharing data relevant for tackling AMR. Alliance members shared data through various means, including journal publications, conference contributions, workshops/ roundtables and websites. Research protocols, analysis plans or pre-registration plans were shared more rarely, and there is an opportunity to consider greater scope for the timely sharing of such information to support further coordination of global industry efforts.

Alliance members have made notable contributions to advancing research and development of novel AMR-relevant products and technologies, with 93 products or technologies in development during the survey's reporting timeframe.

Alliance members made significant investments in AMR-relevant R&D in the 2019 and 2020 fiscal years, totalling approximately US$1.8-1.9 billion annually. Members continue to build R&D pipelines for AMR-relevant products and technologies, including antimicrobial agents against pathogens prioritised by the World Health Organization (WHO) and the United States Centers for Disease Control and Prevention (CDC). Across the Alliance, 93 products and/or technologies are helping fight AMR.[19] These include antibiotics, vaccines, antifungals, diagnostics and non-traditional products from 12 R&D pharmaceutical members, 62 biotech/SMEs, 10 diagnostic companies and 9 generics companies. Alliance members' R&D activities often involved collaboration with other key actors involved in tackling AMR, including academic institutions (82% of members), other industry actors (68%), government agencies (52%) and local hospitals and medical laboratories (50%).

Alliance members flagged the need for timely improvements to the incentive system for industry investment in AMR-relevant R&D. Continued dialogue between industry and wider stakeholders will be needed to ensure a scalable and sustainable incentive system.

Overall, 80% of surveyed AMRIA members[20] actively engaged in advocacy efforts to strengthen 'push' incentives (e.g. funding to incentivise R&D) to stimulate industry contributions to R&D and 'pull' incentives (e.g. incentives focused on reimbursement and market attractiveness) to help create viable markets and address regulatory, reimbursement and market-access challenges. The global community of actors tackling AMR is making gradual progress in improving incentives.[21] However, many existing efforts are in relatively early stages of implementation and are yet to scale. The incentive system needs to work to reconcile the importance of and need for industry contributions to tackle the burden of AMR with commercial considerations that characterise industry structures and governance. Nearly a third (32%) of survey respondents reported they would decrease investment in AMR-relevant R&D if current market conditions continued, signalling a potential risk to the scale of future innovation that R&D can bring.

There is scope for attracting new members to the Alliance to support a fuller representation of the entirety of the industry R&D pipeline and to reap further benefits of a unified and coordinated approach.

Looking to the future, there is also further potential for the Alliance to build on current progress with research and development on new antimicrobials and diagnostics, through attracting new members to the Alliance to more fully reflect the scale and nature of industry AMR-relevant R&D pipelines. This could also help in efforts to harness the full potential that rests in a collaborative, coordinated and unified endeavour. There is also an opportunity to further expand collaboration between and among Alliance members and continue participation in public-private collaboration between diverse actors united in their commitments to overcoming scientific and technological obstacles to tackling AMR.

BOX 3: **RESEARCH AND SCIENCE – NEXT STEPS**

- **Increase awareness-raising about the urgency of the AMR challenge and the necessity of sustainable and scalable approaches to incentivising R&D.** Advocacy efforts should be evidence-based and rooted in an ethos of collective responsibility and fair and equitable benefit distribution. Efforts should also consider the commercial realities of industry R&D and the high level of scientific and technological risk that industry takes when investing in novel antimicrobials, vaccines and diagnostics.
- **Consider the potential for attracting new members** across biotech/SMEs, diagnostics, R&D pharmaceutical and generics sectors to AMRIA to support a fuller representation of the entirety of the industry R&D pipeline and to reap further benefits of a unified approach and effort.
- **Continue to scale-up collaboration.** This includes working to identify where further collaboration between Alliance members (in R&D and data sharing of pre-competitive, clinical trial results and non-commercially sensitive data) can help leverage synergies in skills, capabilities and resources across member companies. It also includes supporting stronger public-private collaboration and new ways of working to overcome the scientific challenges of creating new antimicrobials and diagnostics.

ACCESS

BOX 4: **ACCESS HIGHLIGHTS – KEY INSIGHTS ON PROGRESS**

- **The majority of surveyed companies (81%) were actively supporting access to AMR-relevant products and/or technologies**, and nearly two-thirds (64%) had formal access strategies or plans in place to support such activities.
- **Alliance members supported access to AMR-relevant products and/or technologies in diverse ways**, with common actions targeting product registration (65% of surveyed companies), affordability (63%), availability (60%), advocacy (53%) and ease of access (49%).
- **Nearly half of surveyed Alliance members (44%)[22] actively pursued collaborative approaches to supporting access**, including through efforts targeting equitable pricing issues, capacity-building to enable improved access to AMR-relevant products and technologies, and product donations with agreements reached through collaboration with national authorities and international organisations.
- **Alliance members in the R&D pharma, generics and diagnostics sectors took actions to reduce substandard and falsified AMR-relevant products or technologies**: 65% of surveyed companies worked to enhance product safety through packaging and serialisation, and 54% took action to improve quality-management systems and controls.
- **Barriers related to the economic and regulatory landscape and prescribing practices have impacted industry efforts to support access to AMR-relevant products or technologies**. Challenges related to appropriate pricing and reimbursement, a lack of timely and appropriate product registration, and prescriber/payer behaviour favouring older, lower-cost antimicrobials.
- **Overall, 60% of surveyed diagnostics companies and 56% of generics companies experienced supply chain disruptions**, for example due to difficulties in sourcing raw materials and supplies, a lack of supplier diversity, and pricing and reimbursement challenges affecting the supply chain. Some companies also linked disruptions directly to the COVID-19 pandemic. Actions to improve supply-chain resilience included improvements to demand-planning and demand-prioritisation systems, capacity-building and tech-transfer initiatives to strengthen supply chains in low and middle-income countries, supplier auditing and supply-chain diversification.

The majority of surveyed Alliance members (81%) engaged in access-related activities. Alliance members worked to reduce regulatory and economic barriers to accessing AMR-relevant products or technologies, made efforts to address supply-chain disruptions and contributed to efforts to remove falsified or substandard products.

AMRIA members are committed to improved patient access to the most appropriate and timely treatments, vaccines and diagnostics. The majority of surveyed Alliance members (81%) engaged in activities to support access to AMR-relevant products or technologies, such as tackling barriers related to timely product registration, affordability, availability and ease of access. Nearly half of surveyed members (44%)[23] collaborated with other stakeholders such as national governments, academia, non-government and international organisations on access-related issues. Alliance members also took actions to improve supply-chain resilience and sustainability and engaged in efforts to remove substandard and falsified antimicrobial products that exacerbate the risks and impacts of AMR from the market.

There is scope to further build on existing efforts to strengthen equitable access to novel and off-patent antibiotics and diagnostics across diverse geographies.

There are opportunities for further collaboration with non-government organisations, healthcare providers and governments to strengthen patient access to novel and off-patent antibiotics and diagnostics, especially in lower-middle income countries (LMICs). There is also scope to continue working in collaboration with other stakeholders to help support a regulatory and economic environment that is supportive of a sustainable supply of high-quality AMR-relevant antimicrobials. Finally, there is scope to further engage with local capacity building efforts in support of access and build on developments made in this regard by some Alliance members.

BOX 5: **ACCESS – NEXT STEPS**

- **Continue investing in capacity-building to support access and put the spotlight on efforts targeting access to novel and off-patent antibiotics and diagnostics in LMICs.** This will require collaboration with non-governmental organisations, healthcare providers and governments. Developing a sustainability framework for off-patent antibiotics to address shortages of urgently needed antibiotics could help in this effort. Such efforts would also benefit from mobilising further activity across a broader range of Alliance members on access-related matters in LMICs. Such activities could be partly targeted towards strengthening local healthcare facilities and diagnostic laboratories and supporting high-quality local manufacturing capacity.
- **Continue to work in collaboration with other stakeholders regarding actions industry can take to ensure a regulatory and economic environment that is supportive of a sustainable supply of quality-assured antibiotics.** This includes continued dialogue about timely product registration for life-saving antimicrobials, engagement related to new payment and pricing models and monitoring of product supply chains and distribution channels. It also entails continuing to help raise awareness about substandard and/or falsified products in collaboration with the healthcare community, regulators and law-enforcement agencies.
- **Encourage Alliance members with access-related activity to make their plans publicly available.** Slightly less than a fifth (17%) of Alliance members with access plans made these publicly available, leaving scope to encourage further transparency in this regard.

APPROPRIATE USE

BOX 6: **APPROPRIATE USE HIGHLIGHTS – KEY INSIGHTS ON PROGRESS**

- **Of those surveyed, 83% of R&D pharmaceutical companies and 80% of diagnostics companies had appropriate use and stewardship strategies or plans for AMR-relevant products and/or technologies.** Significantly fewer biotech/SMEs and generics companies had such plans (33% and 19%, respectively). Although the reasons for this merit further exploration, some biotech/SMEs may not have products on the market or in late-stage development, which may explain comparatively lower engagement of this sector with appropriate use and stewardship issues.
- **Among surveyed Alliance members, 60% implemented appropriate use and stewardship activities across diverse geographies,** regardless of whether they had a formal strategy/plan to guide these activities. This figure includes 11 R&D pharmaceutical companies (92% of all companies in the sector), 8 generics companies (89%),[24] 4 diagnostics companies (80%) and 9 biotech/SMEs (33%).
- **Common ways Alliance members contributed to appropriate use and stewardship included education and awareness-raising (88% of surveyed companies)[25] ;efforts to align antimicrobial promotion with and AMR stewardship through reviewing promotional activities against stewardship commitments (57%); and collecting and/or sharing surveillance data to generate evidence to support appropriate use and stewardship (51%)**, e.g. data on AMR trends and antimicrobial sensitivity. Over half (59%) of companies that collected surveillance data shared it externally as part of their commitment to collaborative efforts to mitigate inappropriate use of antibiotics and vaccines and improve antimicrobial stewardship.[26]
- **Most companies focused their activities on AMR issues relevant to human populations, but some also reported activity related to animal use.** Five companies developed or commercialised products and/or technologies licensed for animal use and promoted responsible use in animals.

The majority of Alliance members engaged in activities to promote appropriate use and good stewardship of antimicrobials, and particularly companies in the R&D pharmaceuticals and diagnostics sectors.

One of the key drivers of AMR is the inappropriate use of existing products. AMRIA members engaged in activities to promote appropriate use and good stewardship of antimicrobials, primarily through education and awareness-raising activities, actions to align antimicrobial promotion practices and AMR stewardship, and activities focused on collecting and sharing surveillance data on antimicrobial resistance trends and antimicrobial sensitivity to ensure evidence-based stewardship activities. The majority of R&D pharmaceutical, generics and diagnostics companies within AMRIA (92%, 89% and 80%, respectively) implemented appropriate use and stewardship for AMR-relevant products and/or technologies. Some contributions to appropriate use and stewardship were also made by biotech/SME (33% of surveyed companies), although comparatively less than other sectors. Some companies who were not active in this space reported reasons that related to their business model (e.g. they may not focus on products requiring appropriate use and stewardship). It may also be because some companies, especially in the biotech/SME sector, may not yet have products in late-stage development when appropriate use and stewardship activity planning becomes more relevant.

There is capacity for Alliance members currently active in this space to share learning with other members who may not yet engage, to support even wider scale engagement in the future.

Looking ahead, there is some untapped potential for the Alliance to build on existing progress. This includes pursuing further stewardship efforts targeting infection prevention and control and raising awareness amongst healthcare professionals about AMR risks and stewardship principles. There is also scope for further advocacy for enhanced AMR surveillance, increased public reporting of surveillance data, and efforts to foster enhanced sharing of surveillance data between Alliance members to support coordinated activity. There is also potential to encourage some Alliance members who do not yet have appropriate use and stewardship plans to establish them in the future, when this is appropriate and aligned to company foci and business models.

BOX 7: **APPROPRIATE USE – NEXT STEPS**

- **Mobilise further efforts related to infection prevention and control:** This includes working with governments and healthcare professionals to support efforts for the expanded use of diagnostics to advance appropriate use and enable better targeted antibiotic prescribing. It also includes continued awareness raising about the importance of developing vaccines and other preventative innovations.
- **Mobilise further contributions to appropriate use activities amongst some Alliance members:** This includes considering untapped potential for some members who do not yet have appropriate use and stewardship plans to establish them in the future where appropriate. It also involves fostering enhanced sharing of surveillance data between Alliance members to support coordinated and collaborative efforts and best-practice sharing.
- **Advocate for enhanced surveillance of AMR through improved data visualisation and for increased public reporting of infection rates, antibiotic use and mortality rates.** The development of an AMR Mortality Index could help support such efforts and highlight the urgency of the challenge. Improved data transparency and sharing of AMR surveillance data, along with greater utilisation of industry data in government reporting of AMR rates, could help support improved stewardship policies and clinical options.
- **Continue building on progress made in raising awareness amongst healthcare professionals about AMR risks and stewardship principles and enhance efforts to support appropriate prescribing and engagement with the general public globally.** This includes efforts to support patient adherence to antimicrobial treatment regimes, educational activities related to infection prevention, and using software and tools to support appropriate antimicrobial prescribing by healthcare professionals.

MANUFACTURING AND THE ENVIRONMENT

BOX 8: **MANUFACTURING AND THE ENVIRONMENT HIGHLIGHTS – KEY INSIGHTS ON PROGRESS**[27]

- **AMRIA members have made significant achievements in implementing Alliance manufacturing requirements at manufacturing sites owned by member companies.** The majority of manufacturing sites owned by companies have been assessed against the Common Antibiotic Manufacturing Framework and meet these requirements (76% meet requirements fully, 98% either fully or partially). Most products manufactured at sites owned by Alliance members with manufacturing operations were assessed on and met PNEC Targets (87%).
- **Alliance members also manufacture products at direct supplier sites. Direct suppliers have also worked to implement Alliance requirements related to appropriate manufacturing.** Alliance expectations have been conveyed to 86% of suppliers. Overall, 44% of supplier sites have been assessed against the Framework. Alliance members reported that 50% of assessed sites meet these requirements fully and 63% meet the requirements fully or partially; Of products made at supplier sites, 42% have been assessed against PNEC targets, with 73% of these meeting these targets.

Alliance members have continued to deliver on commitments to responsible antibiotic manufacturing and to reducing antibiotic emissions from manufacturing activity. The majority of manufacturing sites owned by companies have been assessed against the Common Antibiotic Manufacturing Framework and meet these requirements. The majority of products manufactured at sites owned by Alliance members with manufacturing operations also meet Predicted No-effect Concentrations Targets.

AMRIA members have made a long-term commitment to assess their performance and take action to drive down antibiotic emissions from manufacturing operations across their global supply chains. The Alliance is committed to reducing environmental risk due to manufacturing discharges by following a common risk assessment framework (CAMF, hereafter referred to as 'the Framework') and science-driven discharge targets (PNECs).

The majority of manufacturing sites owned by Alliance members have been assessed against the Framework (85% of sites); over three quarters fully meet the Framework requirements

(76% of assessed sites) and nearly all meet them either fully or partially (98% of assessed sites). Most products manufactured at sites owned by Alliance members (88% of products) have been assessed against PNEC targets, with 87% of assessed products meeting targets. In addition, most Alliance members who engage with manufacturing activity also reported manufacturing at direct supplier sites in addition to at their own sites (90% of manufacturing members). There is progress to be made in assessing direct supplier sites against the Framework requirements and supporting direct suppliers to ensure their products meet PNEC targets. However, it is encouraging that nearly three-quarters of assessed products manufactured at supplier sites met PNEC targets (73% of products).While many advances have been made, there is inevitably scope to do more in support of the Alliance's long-term commitment, particularly in relation to accelerating framework adoption across the supply chain and encouraging Alliance members to address gaps identified during audits. In light of the concerns about potential risk of antibiotic emissions from manufacturing operations increasing the risk of resistance developing in the environment, and absent relevant international standards,[28] the Alliance should continue its work to develop a consensus standard for responsible antibiotic manufacturing.

BOX 9: **MANUFACTURING AND THE ENVIRONMENT – NEXT STEPS**

- **Support efforts to accelerate framework adoption and implementation across members' supply chains.** This includes encouraging all members to audit direct suppliers against Framework requirements and PNEC targets.
- **Continue to work towards developing international standards for responsible antibiotic manufacturing** in collaboration with other international organisations involved with setting standards. Seek to advance mechanisms to enable buyers to identify responsibly made antibiotics more easily.
- **Continue sharing Alliance manufacturing members' work implementing the Framework and PNECs across global supply chains with stakeholders such as policymakers, legislators and regulators.** Use Alliance experience in driving reductions in antibiotic-manufacturing emissions to help inform the development of global and/or national policies and practices that best ensure environmentally responsible antimicrobial manufacturing.

TOWARDS THE FUTURE

Looking beyond the Alliance: industry working within a collaborative and connected landscape

AMRIA seeks to support its members in diverse ways offering both convening and coordinating functions for member activities and working to identify strategic priorities for the companies involved in the fight against AMR. The importance of a coordinated and collective approach for mobilising and focusing member companies' activities is evident in the developments diverse companies are pursuing across all four pillars of Alliance activity.

We have reflected on progress and outlined actions the Alliance can begin to consider in the future. Clearly, many of these actions are not something industry can do alone and depend on collaboration with a wider global community of policy-making bodies (e.g. governments, international authorities and agencies), regulatory bodies, not-for-profits, healthcare professionals and providers, civil society and the general public. Therefore, it is important to consider actions industry can take alongside areas where other stakeholders can help in the collective endeavour and support the scaling up and sustainability of industry contributions. Based on our reflections on key insights and implications from the AMRIA member survey, **Box 10** outlines actions that are also important for other stakeholders to consider in the united global effort to curb AMR. Many of these activities are undoubtedly being considered and pursued as part of key global initiatives such as Combating Antibiotic-Resistant Bacteria Accelerator (CARB-X), the Global Antibiotic Research and Development Partnership (GARDP), Combating Bacterial Resistance in Europe (COMBACTE) and Antibiotic Resistance Leadership Group (ARLG), amongst others. The G7 and G20 also have a vital role in this landscape, including in the context of ensuring the strengthening and full implementation of national AMR strategies.[29] The opportunity ahead lies in connecting key areas of need with the priorities, capabilities, resources and responsibilities of the diverse players committed to mitigating antimicrobial resistance for the health and well-being of current and future generations.

BOX 10: IMPLICATIONS FOR OTHER STAKEHOLDERS: POTENTIAL AREAS TO CONSIDER FOR A UNITED GLOBAL EFFORT

CONSIDERATIONS FOR POLICYMAKING BODIES, REGULATORY AGENCIES & INTERNATIONAL INITIATIVES

Supporting research and science:

- Continue to support public-sector investments in AMR-relevant R&D and clinical trials infrastructure.
- Continue to enable public-private collaboration between traditional actors (e.g. universities, hospitals and R&D pharma) while increasing focus on the role of biotech/SMEs, diagnostics and generics companies in the fight against AMR.
- Engage in dialogue with industry and other stakeholders to establish and embed sustainable and scalable incentives for AMR-related R&D in practice, including pull incentives targeting challenges related to market viability. This requires building on current efforts and recognising the necessity of industry commitments as well as the commercial structures within which industry operates. It also involves leveraging learning from prior efforts and specifying actions with clear timelines for the implementation of pilot incentive programmes.

Supporting access:

- Invest in access efforts through strengthening supply chains and distribution channels and supporting discussions about affordability, especially in LMIC settings.
- Recognise the importance of collaboration between diverse stakeholders (public sector stakeholders such as national governments, international organisations, industry and not-for-profits) and of collective action to improve access.

Supporting appropriate use and stewardship:

- Consider scope for enhanced engagement with healthcare-provider associations to help raise awareness of AMR risk and appropriate prescribing behaviours.
- Engage in communication campaigns to promote behaviours that can mitigate the exacerbation of AMR.
- Enhance efforts to work with local and national authorities to mitigate the use of counterfeits and substandard quality products.

Supporting responsible manufacturing and the environment:

- Continue to drive environmentally responsible antibiotic manufacturing, e.g. through advancing development of a manufacturing standard and recognition of the importance of responsibly made antibiotics in valuation mechanisms.

CONSIDERATIONS FOR HEALTHCARE PROFESSIONALS, NOT-FOR-PROFIT ORGANISATIONS AND THE GENERAL PUBLIC

Supporting appropriate use:

- Consider ways to strengthen contributions to surveillance efforts and data-sharing on resistance trends and antimicrobial effectiveness.
- Raise awareness about how prescribing behaviours can increase the risks of overusing older antimicrobials in priority pathogen areas.
- Continue to support awareness-raising, education and sharing of insights about AMR with healthcare professional communities and patients.
- Invest in grassroots movements that can help support behaviours that mitigate inappropriate use of existing antimicrobials.

TABLE 1. AMR INDUSTRY ALLIANCE MEMBERS (*DENOTES COMPANIES THAT PARTICIPATED IN THE SURVEY)

LARGE R&D BIOPHARMACEUTICALS

* Boehringer Ingelheim, Germany
* F. Hoffmann-La Roche AG., Switzerland
* GlaxoSmithKline plc, United Kingdom
* Johnson & Johnson, United States
* Menarini, Italy
* Merck KGaA, Germany
* MSD (known as Merck and Co. Inc in the US and Canada), United States
* Otsuka, Japan
* Pfizer Inc., United States
* Sanofi S.A., France
* Shionogi & Co. Ltd., Japan
* Sumitomo Dainippon Pharma, Japan

BIOTECHNOLOGY/SMEs

* Aequor Inc., United States
Agile Sciences, United States
* AiCuris Anti-infective Cures GmbH, Germany
* Alaxia Pharma, France
Allecra Therapeutics, Germany
Alphanosos, France
* Amplyx, United States
* Antabio, France
Antibiotic Adjuvant, United States
AntibioTx Aps, Denmark
Ares Genetics, Germany
Athlone Laboratories Lt., Ireland
BioFilm Control, France
* BioVersys AG, Switzerland
* Bugworks Research, India
Cardeas Pharma, United States
* Clarametyx, United States
Combioxin, Swizterland
Contrafect, United States
* Curza, United States
* Da Volterra, France
Deinove, France
* Destiny Pharma Ltd., United Kingdom
Eligo Bioscience, France
* Evotec, Germany
Fastinov, Portugal
Fedora Pharmaceuticals Inc., Canada
* Forge Therapeutics, United States
* Helperby Therapeutics plc, United Kingdom
iNtRON Biotechnology Inc., Korea
La Jolla Pharma, United States
MaaT Pharma, France
* Meiji Seika Pharma Co., Japan
Microbion Corporation, United States
MicuRx Pharmaceuticals Inc.
* Moderna, United States
Mutabilis, France
* Nabriva Therapeutics AG, Austria
NAICONS, Italy
* Northern Antibiotics Ltd., Finland
* Nosopharm, France
* NovaBiotics, United Kingdom
NovaDigm Therapeutics Inc., United States
OJBio Ltd., United Kingdom
Oragenics, Inc. United States
* Paratek, United States

* Peptilogics Inc., United States
* Phare Bio, United States
Pherecydes Pharma, France
Polyphor AG, Switzerland
Rebiotix, United States
* Scynexis, United States
SetLance, Italy
SinSa Labs, Sweden
Soligenix, United States
* Spero Therapeutics LLC, United States
Stochos Therapeutics, United States
Summit Therapeutics, United Kingdom
Synthetic Genomics, United States
Sysmex, United Kingdom
* TAXISpharma, United States
* Venatorx Pharmaceuticals Inc., United States
VibioSphen, France
Vitas Pharma Ltd., India

DIAGNOSTICS

* BD, United States
* bioMérieux SA, France
* Cepheid, United States
Curetis AG, Germany
HemoCue AB, Sweden
* MeMed, Israel
* Mobidiag Oy Ltd., Finland
Nemis Technologies, Germany
QuantuMDx Ltd., United Kingdom
Spectromics, United Kingdom

GENERICS

* Aurobindo, India
* Centrient Pharmaceuticals, The Netherlands
* Fresenius Kabi, Germany
* NGB Laboratories, India
* Novartis AG (Sandoz), Switzerland
* Recipharm, Sweden
* Teva Pharmaceuticals, Ltd., Israel
* Viatris, United States
* Xellia, Denmark

INDUSTRY ORGANISATIONS (NOT SURVEYED FOR THE PROGRESS REPORT)

AdvaMedDx

Association of the British Pharmaceutical Industry (ABPI)

Antimicrobial Innovation Alliance

Association for Accessible Medicines (AAM)

Association Innovative Medicines, The Netherlands (Vereniging Innovatieve Geneesmiddelen)

BEAM Alliance

Biotechnology Innovation Organization (BIO)

British In Vitro Diagnostics Association (BIVDA)

European Federation of Pharmaceutical Industries and Associations (EFPIA)

German Association of Research-Based Pharmaceutical Companies (vfa)

International Federation of Pharmaceutical Manufacturers & Associations (IFPMA)

Japan Pharmaceutical Manufacturers Association (JPMA)

Medicines for Europe

UK Bioindustry Association

ENDNOTES

1 Jim O'Neill. 2014 'Antimicrobial Resistance: Tackling a Crisis for the Health and Wealth of Nations. Review on Antimicrobial Resistance'. HM Government and Wellcome Trust.

2 Ibid.

3 Eric Pelfrene, Radu Botgros, and Marco Cavaleri. 2021. 'Antimicrobial Multidrug Resistance in the Era of COVID-19: A Forgotten Plight?' *Antimicrobial Resistance & Infection Control* 10, 1: 21. https://doi.org/10.1186/s13756-021-00893-z.

4 Meghan A. Baker et al. 2021. 'The Impact of Coronavirus Disease 2019 (COVID-19) on Healthcare-Associated Infections'. *Clinical Infectious Diseases*, no. ciab688. https://doi.org/10.1093/cid/ciab688.

5 Lindsey M. Weiner-Lastinger et al. 2021. 'The Impact of Coronavirus Disease 2019 (COVID-19) on Healthcare-Associated Infections in 2020: A Summary of Data Reported to the National Healthcare Safety Network'. *Infection Control & Hospital Epidemiology*, 1–14, https://doi.org/10.1017/ice.2021.362.

6 In 2021, AMRIA had 109 members: 64 biotech/small-and-medium-sized entities (SMEs), 12 large R&D pharmaceutical companies, 10 diagnostics companies, 9 generics companies and 14 industry associations (note: industry associations were not surveyed for the progress report).

7 AMR Industry Alliance. 'Strategic Plan 2021-2025. '

8 A preview of this summary report titled *2021 Progress Report: Executive Summary* was released in December 2021

9 Ibid.

10 AMR Industry Alliance. Shared Goals, as of 22 October 2021: https://www.amrindustryalliance.org/shared-goals/, with updates to manufacturing commitments.

11 The survey was administered via Smart Survey and was open for approximately ten weeks between 30 March 2021 and 6 June 2021. Two reminders to complete the survey were sent during that period. Companies from each sector received bespoke survey versions depending on the relevance of questions to their sector. A representative from each company completed the survey with informed consent.

12 Whereas 100% response rates were achieved from some sectors (large R&D pharmaceutical and generics companies), response rates from others (biotech/SMEs and diagnostics companies) were somewhat lower. In particular, caution is to be exercised when interpreting data specific to the diagnostics sector due to the relatively small number of respondents. In addition, the number of Alliance members and survey response rates have both changed over the years. Thus comparisons between this report's findings and prior reporting periods would not be meaningful in most cases. Most data was quantifiable; in cases where data was not amenable to quantification, we described reported activities, focusing on diversity rather than relative importance. Finally, although questions were developed with some built-in quality-control checks, auditing the data was outside the scope of this work. In a few cases, clarifications were sought from the AMRIA Steering Committee or member companies. We have protected the identity of companies in respect of commercial sensitivities, unless they provided examples of activity for which they gave permission to be named.

13 Range estimates are based on a combination of companies' data on their investment-value ranges and absolute-value figures, since some companies treat the absolute value of their investments as commercially sensitive information and could only provide a range.

14 WHO. 2017. 'Global priority list of antibiotic-resistant bacteria to guide research, discovery, and development of new antibiotics'. As of 21 October 2021: https://www.who.int/medicines/publications/WHO-PPL-Short_Summary_25Feb-ET_NM_WHO.pdf

15 CDC. 2019. 'Biggest threats and data'. As of 21 October 2021: https://www.cdc.gov/drugresistance/biggest-threats.html

16 Pew Charitable Trusts' list of 'Antibiotics Currently in Global Clinical Development' (March 2021) and Pew Charitable Trusts' list of 'Non-traditional Products for Bacterial Infections in Clinical Development' (March 2021). Most recent data from the Pew Charitable Trusts' list (2021) shows that Alliance members account for 37% of the Pew Charitable Trusts' list of 'Antibiotics Currently in Global Clinical Development' (March 2021). Alliance members also account for 47% of Pew Charitable Trusts' list of 'Non-traditional Products for Bacterial Infections in Clinical Development' (March 2021), equal to 42% of products across both lists.

17 This question was not asked of generics companies; thus, they were excluded from the analysis; the denominator for this question is 44.

18 Ibid.

19 The count of AMR-relevant products and technologies is based on consultation of the Pew Charitable Trusts' lists of 'Antibiotics Currently in Global Clinical Development' (March 2021) and 'Non-traditional Products for Bacterial Infections in Clinical Development' (March 2021), the 'Medicines in Development - Antimicrobial Resistance' (April 2021), and Alliance member responses to the 2021 progress survey.

20 This question was not asked of generics companies, who were thus excluded from the analysis the denominator for this question is 44.

21 The Global AMR R&D Hub provides a useful overview of existing efforts. As of 21 October 2021: https://globalamrhub.org/

22 By sector, 56% generics, 50% diagnostics, 45% pharma and 37% biotech/SMEs actively pursued collaborative approaches to supporting access.

23 Ibid.

24 This data suggests that many surveyed generics companies engage in appropriate-use stewardship but without a formal strategy or plan.

25 This is based on a question asking specifically about the education-related activities of the R&D pharma, diagnostics and generics sectors.

26 These numbers are based on specific questions about these areas of activity.

27 Out of 53 Alliance-member respondents, 20 reported having manufacturing sites, with 211 sites in total.

28 G7. 2021. 'G7 Health Ministers' Communique'. As of 21 October 2021: https://www.g7uk.org/g7-health-ministers-meeting-communique-oxford-4-june-2021/?fbclid=IwAR2IJNBr5NhJaNRd6TRhdgx2ajBXHCRBi_P_e6vFg6a1qSICjfypKz723iU

29 Global Coalition on Aging and Infectious Diseases Society of America. 2021. '2021 AMR Preparedness Index'. As of 21 October 2021: https://globalcoalitiononaging.com/wp-content/uploads/2021/06/GCOA-AMR-Preparedness-Index_FINAL.pdf

ABOUT THE AMR INDUSTRY ALLIANCE

The AMR Industry Alliance is a coalition of over 100 biotechnology, diagnostic, generics and research-based biopharmaceutical companies and trade associations that was formed to drive and measure industry progress to curb antimicrobial resistance. The AMR Industry Alliance will ensure that signatories collectively deliver on the specific commitments made in the Industry Declaration on AMR and the Roadmap and will measure progress made in the fight against antimicrobial resistance.

amrindustryalliance.org