amr INDUSTRY ALLIANCE
UNITED AGAINST ANTIMICROBIAL RESISTANCE

PROGRESS REPORT

AMR Industry Alliance 2021 Survey

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RAND EUROPE

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Foreword

Antimicrobial resistance (AMR) is a threat we have known about for a long time, and it has been on the global agenda many years. In particular, the 2016 UN High-Level Meeting on Antimicrobial Resistance spurred many stakeholders into action, leading to the establishment of the UN Interagency Coordination Group on AMR that released its report three years ago. Since then, the issue of AMR has been raised at every G7 or G20 meeting for the past six years. Many mechanisms and institutions dedicated to tackling the challenge of AMR now exist. Among them, the AMR Industry Alliance is the leading private-sector coalition working to tackle AMR, bringing together R&D pharmaceutical, generic, biotechnology and diagnostics companies together to drive industry progress. Since 2017, the Alliance has consistently documented its activities across several key action areas, demonstrating how its members focus on solutions and lead on AMR among the life-science industry. Captured every two years in our Progress Reports, these achievements provide an important snapshot of what the life-science industry is – and could be – doing better to tackle the rise in antimicrobial resistance.

In our third Progress Report, Alliance members provide detailed data presenting valuable insights into industry progress on AMR and show some encouraging areas of progress and innovation. The Alliance's work focuses on four key action areas, with bold goals and commitments intended to drive progress and curb AMR. We aim to improve access to high-quality antimicrobials, further investments in R&D, promote and support appropriate use and curtail environmental exposures associated with AMR. We are proud of the progress made to date and reassured by the ongoing commitments for future actions.

The Progress Report demonstrates that AMR Industry Alliance members remain committed to the fight against AMR, stepping up to access challenges and implementing appropriate use and stewardship activities – and in a challenging time dominated by COVID-19. Regarding access, four out of five (81%) surveyed member companies report being active in supporting access to AMR-relevant products and/or technologies. Likewise, 92% of our surveyed R&D pharmaceutical member companies, 89% of our surveyed generics member companies, and 80% of our surveyed diagnostics member companies have taken on appropriate use and stewardship activities.

The AMR Industry Alliance's work in addressing the environmental dimension of manufacturing and associated standards has been recognised by the G7 Health Ministers Communique.[1]

The frameworks developed by the Alliance are helping to reduce the environmental impact of antibiotics production and promote best-practice across the wider industry. This year's Progress Report shows that an impressive 85% of Alliance members involved in manufacturing

antibiotics are assessing their sites against the Alliance's Common Antibiotic Manufacturing Framework (CAMF). In addition, the majority of products manufactured at sites owned by Alliance members (88% of products) have been assessed against science-based predicted no-effect concentrations (PNEC) targets, with 87% of assessed products meeting targets.

We also found that investments in AMR have remained steady since our previous report, with over USD 1.8 billion contributed to AMR-related R&D annually by Alliance members. However, we must note that these current investments are in peril if market conditions do not improve.

During these past two years, we have seen that a pandemic can disrupt economic and societal activity and cripple healthcare systems. While antibiotic-resistant infections will not sweep the globe at the pace COVID-19 has, they will bear significant consequences. Antibiotic-resistant infections will continue to take lives needlessly and have the potential to shake modern medicine and healthcare systems to their core. As Dame Sally Davies said late last year, 'COVID's a lobster dropped into boiling water, making a lot of noise as it expires, whereas AMR is a lobster put into cold water, heating up slowly, not making any noise'.[2] That is why it is dubbed a silent pandemic.

During COVID-19, we have also witnessed global stakeholders – policymakers, global institutions, regulators, scientists and the life-sciences industry, to name a few – coming together to fight a clear and present threat. Although we have known about antimicrobial resistance for a long time, the magnitude of the threat is far more significant than predicted. Instead of 700,000 deaths per year, as previously estimated, new data on the global burden of antimicrobial resistance suggests that 1.3 million deaths per year are attributable to resistance, with 3.7 million deaths associated with (but not attributable to) resistance and 3.2 million dying with susceptible infections.[3] It is past the time to act.[4] A landmark report from the UN Interagency Agency Coordination Group on AMR that featured an hourglass on its cover was poignantly titled 'No Time to Wait'. At the Alliance, we know we cannot wait, and we encourage others in the life-sciences sector to utilise the Progress Report as a tool to spur action and encourage greater collaboration in slowing the spread of AMR. We need all stakeholders to work together, move from talking to action, and address the challenge of AMR before the hourglass runs out. We may not be able to turn it over once it does.

THOMAS CUENI, DIRECTOR GENERAL IFPMA, CHAIR, AMR INDUSTRY ALLIANCE

Abbreviations/acronyms

AIDS	Acquired immunodeficiency syndrome
AMR	Antimicrobial resistance
AMRIA	Antimicrobial Resistance Industry Alliance
AMS	Antimicrobial stewardship
API	Active pharmaceutical ingredient
ARLG	Antibiotic Resistance Leadership Group
BARDA	US Biomedical Advanced Research and Development Authority
BD	Becton, Dickinson and Company
BIO	Biotechnology Industry Organization
BSI	Blood stream infections
CAMF	Common Antibiotic Manufacturing Framework
CARB-X	Combating Antibiotic-Resistant Bacteria Accelerator
CDC	Centers for Disease Control and Prevention
CE	European conformity
CETP	Central Effluent Treatment Plant
COMBACTE	Combating Bacterial Resistance in Europe
COVID	Coronavirus disease
CRAB	Carbapenem-resistant Acinetobacter baumannii
DR-TB	Drug-resistant tuberculosis
EBE	European Biopharmaceutical Enterprises
EHS	Environment health safety team
ESBL	Extended-spectrum beta-lactamase
EU	European Union
GARDP	Global Antibiotic Research and Development Partnership
GCOA	Global Coalition on Aging
GNI	Gross national income
GPHF	Global Pharma Health Fund

HCO	Healthcare organisation
HCP	Healthcare professional
HIV	Human immunodeficiency virus
IFPMA	International Federation of Pharmaceutical Manufacturers and Associations
IVD	In-vitro diagnostics
JPIAMR	Joint Programming Initiative on Antimicrobial Resistance
LIC	Low-income country
LMIC	Lower-middle-income country
MD	Medical devices
MDR	Multi-drug resistant
MSD	Merck Sharp & Dohme
NHS	National Health Service
NIAID	National Institute of Allergy and Infectious Diseases
NIH	National Institutes of Health
OIE	World Organisation for Animal Health
PIE	Pharmaceuticals in the environment
PIP	Paediatric Investigation Plan
PNEC	Predicted No-effect Concentration
PSCI	Pharmaceutical Supply Chain Initiative
RR	Rifampicin-resistant
RSV	Respiratory Syncytial Virus
SME	Small-and-medium-sized entities
TB	Tuberculosis
UK	United Kingdom
US	United States
USAID	United States Agency for International Development
USD	United States dollar
WHO	World Health Organisation
XDR	Extensively drug-resistant
ZLD	Zero liquid discharge

EXECUTIVE SUMMARY

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.[5] Left unchecked, the annual global death toll from AMR could reach ten million by 2050.[6] 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.[7] In addition, evidence suggests that the prevalence of hospital-acquired infections, including treatment-resistant ones, also increased with the burden of COVID-19.[8,9] 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 societies.

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.[10] 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.'[11]

ABOUT THIS REPORT

This report provides a unique snapshot of AMRIA's collective efforts to deliver on its 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 is the third iteration of the Alliance's biennial progress report, documenting AMRIA activities according to its commitments across four strategic pillars. The Alliance's current commitments are highlighted on page 13. The Alliance is also set to commit to specific objectives for 2021–2025.[12]

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 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 in **Table 1** on page 27, at the end of this summary. 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 the 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[13]

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 AND THE ENVIRONMENT

- Review Alliance members' own manufacturing and supply chains to assess good practice in controlling the 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.[14] 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.[15] 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 US$1.8–1.9 billion has been invested in AMR-relevant R&D annually in FY2019 and FY2020**.[16] 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 WHO's list of priority pathogens[17] and the CDC's Biggest Threats list.[18] According to the 2021 lists compiled by the Pew Charitable Trust,[19] 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[20] (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[21] 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 the 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.[22] 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[23] 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.[24] 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, the Alliance has further potential to build on current progress with research and development on new antimicrobials and diagnostics by 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.

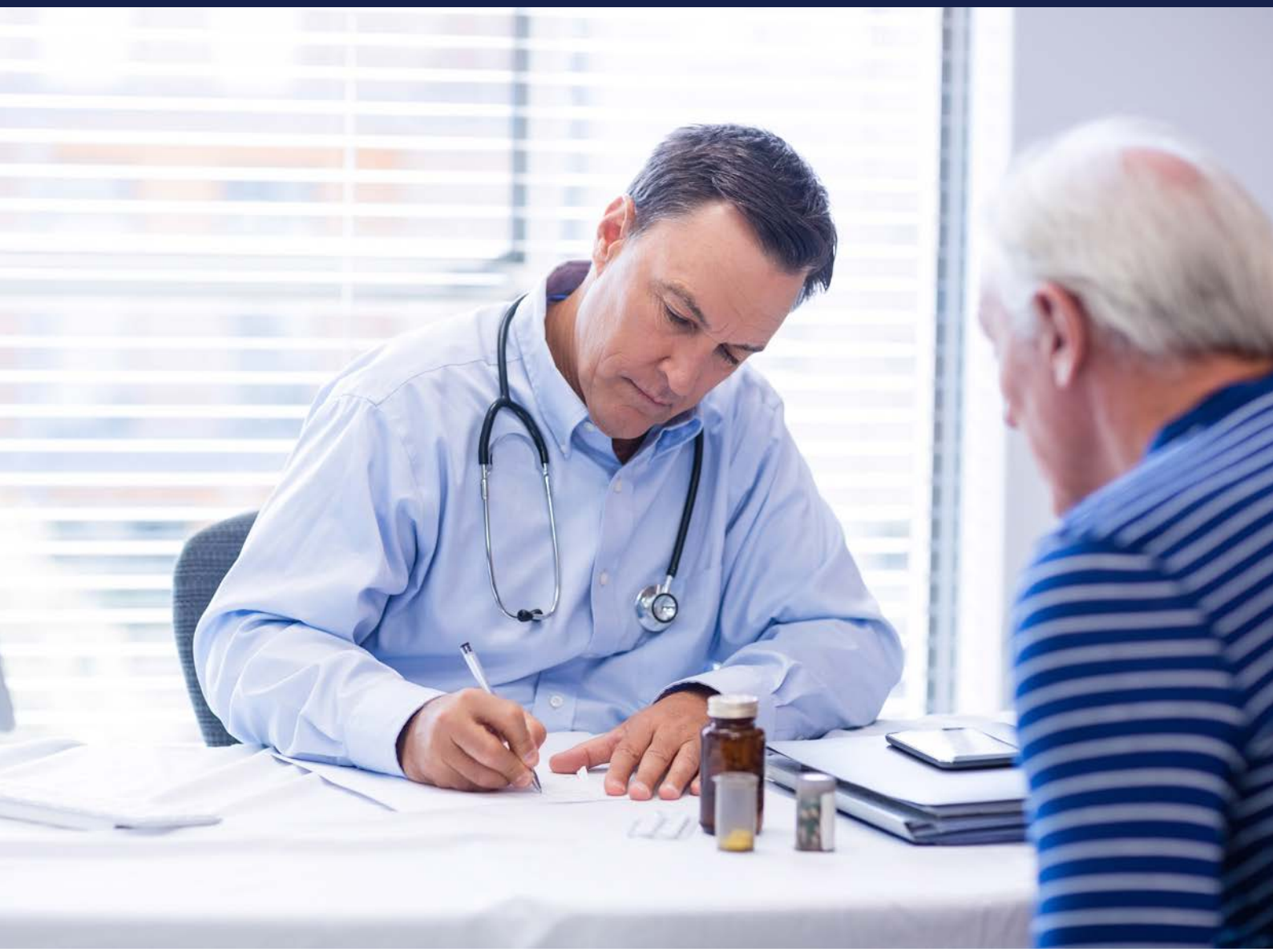
BOX 3: **RESEARCH AND SCIENCE – NEXT STEPS**

- **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 step 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%)[25] 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.** Examples include 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%)[26] 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 step 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%),[27] 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);[28] 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.[29]
- **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, 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. Biotech/SME also made some contributions to appropriate use and stewardship (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 a 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, the Alliance has untapped potential 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 step 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 the 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 the 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 step 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.

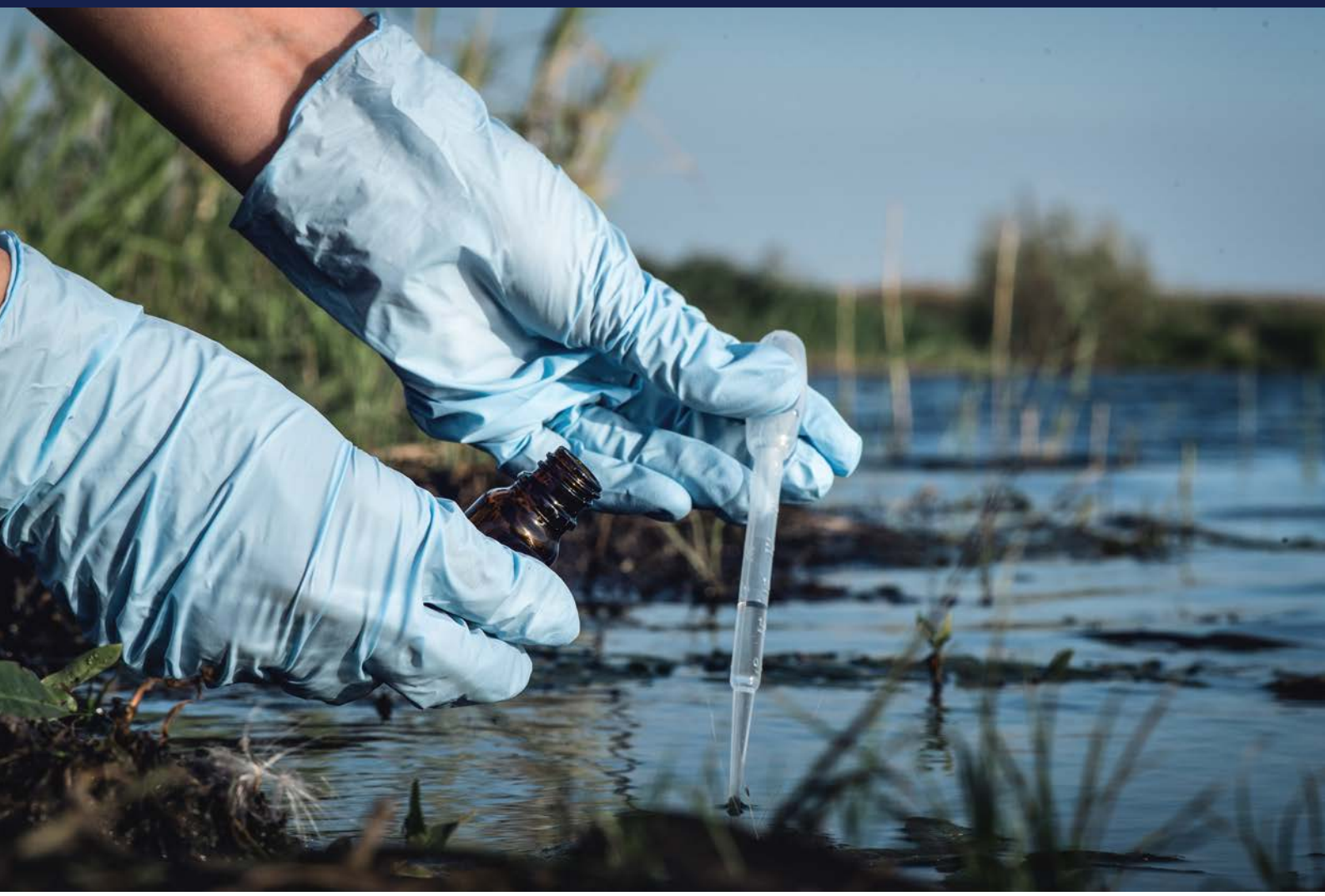
MANUFACTURING AND THE ENVIRONMENT

BOX 8: **MANUFACTURING AND THE ENVIRONMENT HIGHLIGHTS – KEY INSIGHTS ON PROGRESS**[30]

- **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 concerns about the potential risk of antibiotic emissions from manufacturing operations increasing the risk of resistance developing in the environment, and absent relevant international standards,[31] 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 in 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 societies 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.[32] 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.

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

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.

1. INTRODUCTION

1.1. BACKGROUND AND CONTEXT

Antimicrobial resistance represents a major public health challenge.

Antimicrobial resistance (AMR) is a key global public health challenge of our time. The emergence of treatment-resistant microorganisms (bacteria, viruses, parasites and fungi) has led to previously easy-to-treat infections becoming more difficult to treat.[33] Without effective antimicrobials, existing medical procedures, including surgery and cancer chemotherapy, could also become much more dangerous.[34],[35] AMR also threatens to undermine great strides made in managing infectious diseases such as malaria, tuberculosis and HIV.[36] There are also growing concerns that the COVID-19 pandemic may exacerbate the threat of AMR due to an increased or inappropriate antimicrobial use.[37] In addition, recent evidence suggests that hospital-acquired infections, including treatment resistant ones, also increased as the burden of COVID-19 increased.[38],[39] AMR has already reached alarming levels worldwide. At least 700,000 people die each year due to AMR-related causes.[40] Left unchecked, the annual global death toll from AMR could reach ten million by 2050.[41]

Mitigating antimicrobial resistance is a key policy concern.

International organisations have recognised the threat posed by AMR and made plans to mitigate this threat in their global policies. In 2015, the World Health Organization (WHO) adopted a Global Action Plan on Antimicrobial Resistance, which outlines five key objectives for tackling this crisis: (i) improving awareness and understanding; (ii) strengthening knowledge and evidence; (iii) reducing the incidence of infection; (iv) optimising the use of antimicrobials; and (v) developing the economic case for investment in new medical interventions.[42] In 2016, a United Nations (UN) Interagency Coordination Group on AMR was convened to develop a blueprint for the fight against AMR. Their report, published in 2019, called for the adoption of a 'One Health' approach to AMR, recognising that both the drivers and impacts of AMR cut across humans, animals, plants and food.[43]

On a regional level, the European Commission (EC) has also adopted an Action Plan that provides guidance for establishing, implementing and monitoring national action plans within EU countries and sets out three key objectives: (i) making the EU a best practice region; (ii) boosting research, development and innovation; and (iii) shaping the global agenda.[44] Efforts are also underway within individual non-EU countries to develop strategies to combat AMR. For example, in 2019, the United Kingdom (UK) government published a 20-year vision[45] and a five-year action plan[46] for fighting AMR, which recommends building surveillance systems in lower-middle-income countries (LMICs). AMR is also one of the UK's priorities for its G7 presidency in 2021.[47] In April of 2021, WHO launched a call to action on AMR during the closing section of the High-Level Dialogue on Antimicrobial Resistance. A total of 113 member states and 35 supporting organisations signed this call to action.[48]

The life sciences industries are crucial in the fight against antimicrobial resistance.

The engagement of diverse actors across the life sciences industries is key to tackling AMR, alongside the involvement of governments, international organisations, academia, civil societies and other key stakeholders. Areas in which industrial partners can contribute to the AMR challenge are wide-ranging. Such areas include: supporting research and development (R&D) of new antimicrobials, working to prevent infection (either through the development of new vaccines or improving access to existing ones), working with other key actors to improve access to novel products and technologies that mitigate the risks of AMR, promoting global awareness of AMR and encouraging best practice to prevent its further emergence and spread, and reducing the environmental impact of antimicrobials.

Crucially, the AMR challenge also requires engagement between industry and policymakers around innovative financial instruments to incentivise innovation, which can reduce commercial and market risk.[49] Industry is responding to this challenge through individual companies' activities and the support of industry networks and associations, e.g. the 2017 establishment of the AMR Industry Alliance (AMRIA).

AMRIA plays an essential role in tackling antimicrobial resistance.

AMRIA brings together a coalition of leading research-based biopharmaceutical, biotechnological, diagnostic, generics and industry companies and associations in the fight against AMR.[50] For a list of member organisations, see **Annex A.1**. Building on the AMR Industry Declaration[51] signed at the World Economic Forum in Davos in 2016 and a subsequently developed Roadmap to Combat Antibiotic Resistance, AMRIA seeks to drive and measure industry progress on AMR.[52]

As part of their 2021–2025 strategic plan, AMRIA introduced a new mission statement aligned with the Alliance's four key pillars of activity: research and science; access; appropriate use; and manufacturing and the environment.[53] 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 treatment 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.'

AMRIA is a key stakeholder in the global fight against AMR. Tackling AMR is a collective endeavour, and AMRIA sits alongside other cross-industry initiatives on AMR. In July 2020, for example, the International Federation of Pharmaceutical Manufacturers & Associations (IFPMA) launched a new 'AMR Action Fund'. This cross-industry partnership, backed by 20 biopharmaceutical companies alongside the Wellcome Trust and European Investment Bank, aims to bring two to four new antibiotics to patients by 2030. Through the AMR Action Fund, pharmaceutical companies will invest nearly US$1 billion to accelerate antibiotic development and delivery pipelines, working collaboratively with philanthropies, development banks and

multilateral organisations.[54] Regionally, the European Federation of Pharmaceutical Industries and Associations (EFPIA) has partnered with European Biopharmaceutical Enterprises and Vaccines Europe to issue a Joint Statement on Antimicrobial Resistance. The Joint Statement outlines its partners' strong support for multi-stakeholder cooperation on AMR at the EU level while also drawing attention to industry commitments made through the AMRIA.[55]

AMRIA members also contribute to a wider global landscape of other international and multi-stakeholder efforts. Examples include 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.

Progress has been made in the fight against antimicrobial resistance, but many challenges lie ahead.

Alongside efforts of the wider global community of researchers, policymakers, healthcare providers, not-for-profit organisations and civil societies, industry pledges and activities represent a significant step forward. However, they are not without challenges. For example, while optimising both public and industry investment to drive the development of a robust and sustainable R&D ecosystem for antimicrobial development is of key importance, it can be difficult to advance and achieve. The market for antimicrobials is uncertain, and pathogens targeted by new antimicrobials may also develop resistance. Investments made over many years thus run the risk of becoming ineffective, as antimicrobial medicines are sometimes reserved to preserve effectiveness, which can lead to a poor return on investment and limit market sustainability.[56] To limit AMR development, new antimicrobials also need to be used sparingly. This requirement creates the risk of low sales, with implications in terms of reserve stock and lower prices.[57]

The life sciences industries remain committed to tackling this key public health challenge. Scientific advancements are enabling new scientific and technological opportunities. As shown in this report, progress is also being made to ensure appropriate access to the fruits of innovation for populations in need, curb inappropriate use and mitigate against the potential environmental impacts of antibiotic manufacturing while also strengthening the resilience of antibiotic supply. Access to novel treatments and diagnostics for infectious diseases, especially in LMICs where the burden of AMR is disproportionately high,[58] is essential for saving lives and combatting the spread of drug-resistant infections. However, the systemic risks surrounding R&D on new antimicrobials, combined with an uncertain economic environment for the healthcare industry,[59] reinforce the importance of a package of incentives to ensure a sustainable medicines pipeline. This includes continued support for existing push incentives (focused on stimulating research and development) and implementing pull incentives (focused on creating viable markets and ensuring access). These solutions highlight the importance of global collaboration between stakeholders across the public, private and not-for-profit sectors to tackle AMR.

1.2. ABOUT THE PROGRESS REPORT: AIMS AND READERS' GUIDE

Aims

The progress report on the AMR Industry Alliance 2021 survey provides a unique snapshot of AMRIA's collective efforts to deliver on its commitments to tackle the rise of AMR. The report's aims are threefold: (i) to document Alliance members' activities in contributing to the global response to AMR, (ii) identify a variety of antimicrobial products, diagnostic tools and other AMR-relevant technologies that are available on the market or in development (a comprehensive list is provided in the Annex), and (iii) highlight opportunities for industry contributions in the future. The report also highlights the interdependence of industry effort with other global and national initiatives and the policy and regulatory landscape.

More specifically, the report aims to share learnings about AMRIA member contributions across pharmaceutical, biotech/SME, diagnostics and generics R&D sectors in the fight against AMR, focusing on efforts implemented since the most recent AMRIA progress report in 2020.[60] It provides insights and offers a critical reflection on developments across the four pillars of Alliance activities: research and science; access; appropriate use; and manufacturing and the environment. The report is based on a comprehensive member survey (see Section 2. Methods), which tracked Alliance member activity in relation to key commitments.

Readers' guide

This report reviews the methodology used to capture AMRIA activities and progress, provides an overview of Alliance members who responded to the survey and describes caveats for interpreting findings (Section 2). The report then describes, in turn, findings from the survey organised by the Alliance's four pillars: research and science (Section 3), access (Section 4), appropriate use (Section 5) and manufacturing and the environment (Section 6). Finally, the report concludes with reflections on its findings and their implications for the future (Section 7).

Throughout Sections 3–6, key takeaway messages are introduced in summary boxes. Further details on findings from the survey analysis are presented in the narrative that follows each summary box. Case examples from all sectors of the Alliance are provided to illustrate each pillar's diversity of AMR-related efforts and commitments.

1.3. ABOUT THE AUTHORS

The progress report on the AMR Industry Alliance 2021 survey has been researched and produced by RAND Europe. RAND Europe is a not-for-profit policy research organisation that aims to improve policy and decision making through research and analysis. With offices in Cambridge (UK) and Brussels (Belgium), RAND Europe works with a wide range of government, industry, academic and third sector clients to conduct rigorous, impartial and quality assured research. RAND Europe

has an established focus on health and healthcare innovation, including wide-ranging experience researching AMR. The contributing RAND Europe authors are Dr Sonja Marjanovic, Ms Sarah Parkinson, Dr Joe Francombe, Dr Robert Romanelli, Dr Daniela Rodriguez Rincon and Dr Catriona Manville. For further information about this report, please contact Dr Sonja Marjanovic (Director - Healthcare Innovation, Industry and Policy, RAND Europe) at smarjano@randeurope.org. For further information about AMRIA, please email info@amrindustryalliance.org.

The insights presented here result from independent analysis of survey findings by the RAND Europe research team. The team is grateful for AMRIA's open lines of communication and engagement in supporting this work, helping with the clarification of questions and enabling member engagement in consultations on survey design and survey data provision.

1.4. ACKNOWLEDGEMENTS

The authors would like to thank all survey participants for their engagement with the process, as well as the AMRIA Secretariat and Steering Committee for their continued engagement. We also thank Dr Katherine Morley and Gemma Claire-Ali from RAND Europe for their quality assurance of this report.

2. METHODS

2.1. SURVEY DESIGN, ADMINISTRATION AND ANALYSIS

Objective

The 2021 AMRIA survey was designed to capture Alliance member contributions to tackling AMR from 1 July 2019 to 31 March 2021.[61]

Design

The survey focused on Alliance member activities within the key commitment areas of research and science, access, appropriate use and manufacturing for AMR-relevant products and/or technologies,[62] including antimicrobials, vaccines, diagnostics and other non-traditional products.[63] RAND Europe designed the AMRIA 2021 progress survey. The design process involved the following steps:

- Reviews of prior progress surveys for relevance, specificity and clarity of questions asked and consultations with Alliance representatives across R&D pharmaceutical, biotech/SME, diagnostic and generics sectors[64]
- Iteration with the AMRIA Steering Committee on survey drafts to ensure the relevance of questions asked of different sectors as well as sufficient specificity of issues explored
- Design and development of an updated survey, including additional questions addressing previously unasked-about areas of activity that some sectors considered relevant to their efforts in tackling AMR and requested be included. The survey design considered the diversity of companies within any one sector of the Alliance (i.e. within R&D pharmaceuticals, diagnostics, biotech/SMEs and generics sectors).

To the degree possible, RAND Europe was also asked to (i) ensure compatibility with prior survey rounds in terms of the questions explored, (ii) retain some of the questions asked in prior rounds, and (iii) address gaps in response to feedback from sector consultations.

We designed one survey per sector (R&D Pharmaceutical, Biotech/SMEs, Diagnostics and Generics) and used question routing in each survey to ensure that companies only responded to questions that were relevant to their sector and situation.[65]

Participants

The survey was distributed via an electronic platform to 93 AMRIA members comprising R&D pharmaceutical, biotech/SME, diagnostics and generic companies.[66] A representative from each company completed the survey with informed consent. AMRIA industry associations were not included in the survey, as they would not be able to respond on behalf of their member organisations.

Analysis

All quantitative survey data were analysed using descriptive statistics.[67] Qualitative responses from the survey were analysed thematically and key insights gained were synthesised and added as examples of activities for each of the four pillars. Within this

report, we use the term *Alliance members* to refer to companies belonging to AMRIA, and the term *surveyed Alliance members or surveyed companies* to refer to companies that responded to each question in the survey.[68]

Case vignettes

So that they could provide further examples of activities conducted by AMRIA for each of the four pillars, all members were given the opportunity to contribute case vignettes of their activities. These vignettes included information on specific activities' aims, how they were implemented, and their key influences and outcomes and impacts (either realised or anticipated). Although all submissions were considered for inclusion, only those determined by the research team to include sufficient information and clarifications about the activities were included in the final report.

2.2. PROFILE OF SURVEY RESPONDENTS

Out of 93 AMRIA members, a total of 53 completed the survey informing this progress report (57% response rate).[69] However, 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 diagnostics companies (50% response) and 27 out of 62[70] biotech/SMEs (44% response). A list of participating Alliance members can be found in **Table 1,** on page 27.

Of those who participated in the survey, the most common locations Alliance members reported having business units and AMR-related activity were Europe (64% business units, 74% AMR-relevant activity) and North and Central America (64% business units, 72% AMR-relevant activity). However, Alliance members also reported business units and international AMR-relevant activity across all regions: Western Pacific (34% had business units, 42% had AMR-relevant activity), South East Asia (32% had business units, 43% had AMR-relevant activity), Eastern Mediterranean/Middle East (23% had business units, 32% had AMR-relevant activity), South America (21% had business units, 34% had AMR-relevant activity), Africa (19% business units, 30% had AMR-relevant activity) and other regions (19% had business units, 64% had AMR-relevant activity). The survey can be found in **Annex A.1**.

2.2. CAVEATS AND LIMITATIONS

There are some limitations and caveats to bear in mind when interpreting the findings of this report. Whereas 100% response rates were achieved in some sectors (large R&D pharmaceutical and generics companies), response rates from others (biotech/SMEs and diagnostics companies) were lower. Particular caution should be exercised when interpreting data specific to the diagnostics sector due to the relatively small absolute number of respondents. In addition, Alliance members' numbers and survey response rates have both changed over the

years. Thus, comparisons of findings from this report to prior reporting periods would not be meaningful in most cases. Most but not all the gathered data gathered was amenable to quantification. Where data were not amenable to quantification, we described the reported activities and focused on diversity rather than relative importance. Finally, although questions were developed with some built-in quality control checks, data auditing 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.

3. RESEARCH AND SCIENCE

3.1. ALLIANCE COMMITMENTS TO RESEARCH AND SCIENCE TO TACKLE AMR

Innovation through research and science is central in the fight against AMR. Such innovation includes the development of novel antimicrobials, vaccines, alternative products, diagnostics and other technologies used for the prevention and treatment of AMR pathogens. However, as mentioned earlier, incentivising innovation can be challenging due to both scientific/technological obstacles and commercial barriers to ensuring stable and viable markets for novel products and technologies.[71,72]

AMRIA was established as a way of bringing together industry skills, capabilities, resources and commitments to improving population health, in order to help tackle AMR. The Alliance emerged both in the face of scientific, technological and commercial challenges and as a collective effort to respond to them and help shape the way for more sustainable ways to address AMR going forward. The Alliance has a long-standing commitment to research and science in the fight against AMR (**Box 11**). In the following section, we present Alliance member's recent activities on AMR-related research and science.

BOX 11: RESEARCH & SCIENCE COMMITMENTS[73]

- Invest in research and development for innovative antibiotics and 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.

3.2. INVESTMENT IN R&D

BOX 12: **SUMMARY OF INVESTMENT IN AMR-RELEVANT R&D AMONGST SURVEYED ALLIANCE MEMBERS**

HIGHLIGHTS:

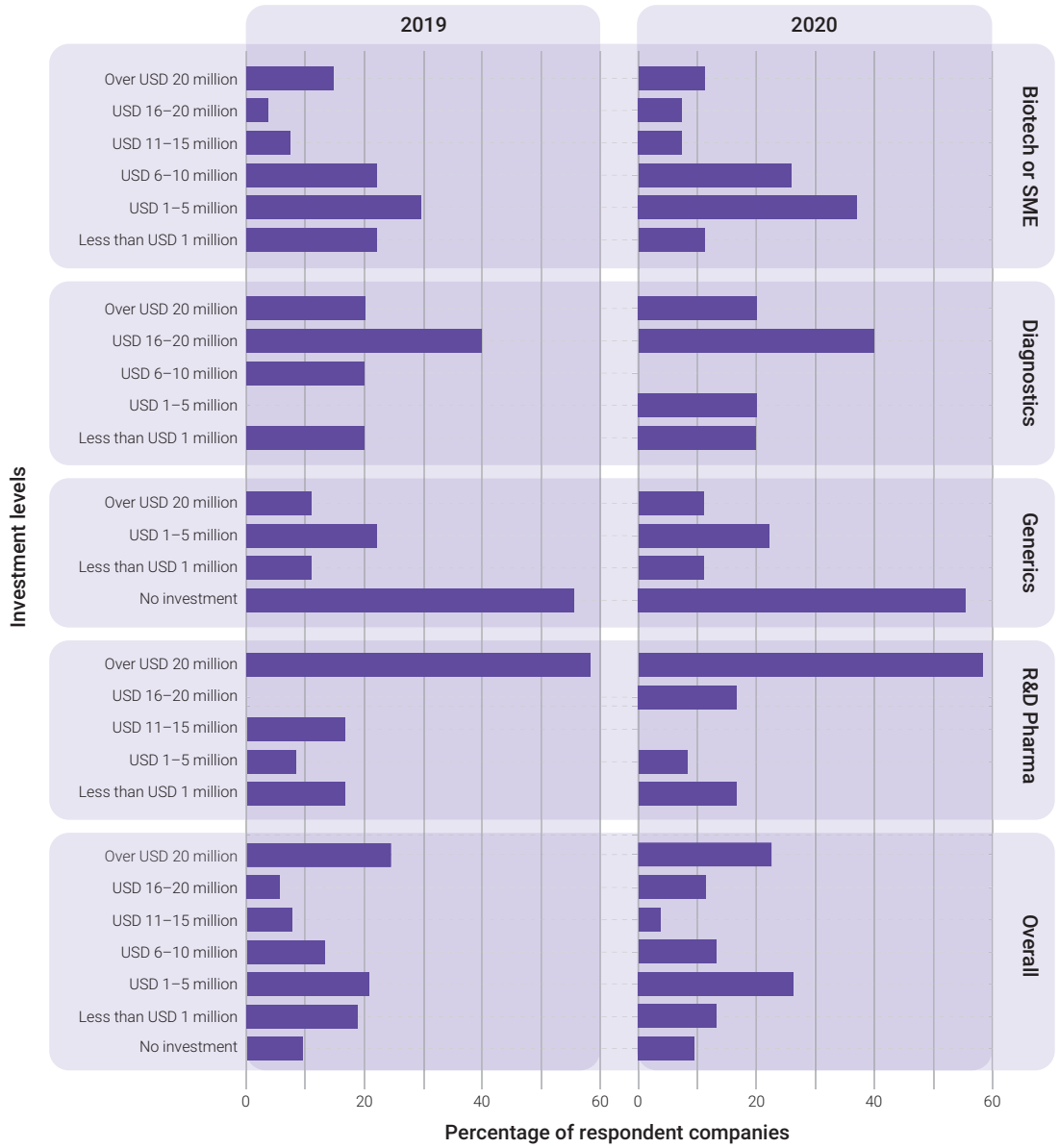
- **The life sciences industry has made significant investments in AMR-relevant R&D,** with 53 Alliance members cumulatively investing US$1.8–1.9 billion in AMR-relevant R&D in FY2019 and FY2020 annually.
- **Companies in the R&D pharmaceutical sector reported the largest investment in AMR-relevant R&D. However, diagnostics, biotech/SMEs and generics companies also make significant financial contributions**, either through R&D on new products and/or technologies or, in the case of generics companies, through R&D related to the adaption of existing products. Levels of R&D investment remained relatively stable between FY2019 and FY2020, with nearly half of Alliance members reporting an increase in AMR-relevant R&D investment in FY2019 compared to FY2018, and only a minority reporting a decrease in their investment.
- **The majority of surveyed Alliance members (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.
- **Looking to the future, Alliance members view new or improved pull incentives as a key factor that will influence the likelihood of increasing investments in AMR-relevant R&D.** Alliance members are committed to working with policymakers and actively engaged in advocacy efforts for improved pull and push incentives that could provide further stimulus for R&D and help in creating viable markets.
- **Member companies contributed to high-level discussions and policy debates and participated in efforts to improve how the value of antimicrobial products is assessed.** Some R&D pharmaceutical companies also engaged in testing new payment models. The global community of actors involved in the fight against AMR are making some progress on strengthening incentives, although many efforts are in the early stages. The Global AMR R&D Hub provides an information resource on existing efforts towards improving the incentives system.
- **The impact of the COVID-19 pandemic on AMR-relevant R&D activity is varied and appears to be context-specific.** Increased global interest in infectious disease prompted some companies to increase AMR-relevant R&D investment. In contrast, others reported decreasing investment and increasing delays in R&D activity due to a need to divert resources to other areas.

Industry has made a significant investment in R&D to support the fight against AMR.

Fifty-three surveyed Alliance members (57% of all members) reported investing US$1,804–1,952 million in AMR-relevant R&D in total in FY2019, and USD$1,798–1,936 million in FY2020.[74] Based on data from FY2018 reported in AMRIA's 2020 progress report, member investment was approximately US$1.6 billion in AMR-relevant activity.[75] Whilst there appears to be a small increase in investment since 2018, direct comparisons of financial investment data across survey years are inadvisable due to the differing number and profile of respondents.[76,77,78]

Figure 1 provides a breakdown of investment levels (according to ranges Alliance members reported on) and by sector (i.e. R&D pharmaceuticals, biotech/SMEs, diagnostics and generics companies) for FY2019 and FY2020, respectively. Unsurprisingly, most investments over US$20 million in FY2019 and FY2020 came from larger R&D pharmaceutical companies, although some companies from other sectors also reported investments of over US$20 million. Further information on the breakdown of investments by sector can be found in **Annex B.1**.

FIGURE 1: INVESTMENT IN R&D FOR AMR-RELEVANT PRODUCTS AND/OR TECHNOLOGIES IN 2019 AND 2020 (N=53)



Source: RAND Europe analysis

Levels of investment in AMR-relevant R&D remained relatively stable between FY2019 and FY2020. However, nearly half of Alliance members reported an increase in investment in FY2019 compared to the previous financial year, and only a minority decreased their investment.[79]

Members were asked about changes in their investment levels between FY2018 and FY2019,[80] the results showed that nearly half (48%) of surveyed Alliance members who invested in AMR-relevant R&D in FY2019 reported that their investment level stayed approximately the same, 44% reported an increase in their investment (either substantially [33%] or somewhat [10%]), and just under a tenth (8%) reported that their investments decreased (substantially [6%] or somewhat [2%]). Based on data provided by participants (summarised in the previous section), R&D investment did not substantially change between 2019 and 2020.

Across the Alliance, 26 companies (49% of survey respondents) provided reasons for changes in investment levels in AMR-related R&D between FY2018 and FY2020. Responses point to a diversity of drivers of increased investment. These relate to the progression of AMR-relevant products and technologies through the R&D pathway, a desire to contribute to cross-stakeholder collaborations and the acquisition of new R&D portfolios as part of corporate restructuring. Several broader factors also enabled increased investment. Examples include company and shareholder commitment to addressing AMR and associated unmet medical needs, increased scientific capabilities and know-how, forecasted abilities to achieve a reasonable return on investment on specific products, the existence of conducive partnerships, and the availability of attractive push incentives. However, Alliance members also flagged the need for improved push-and-pull incentives to incentivise further investment, elaborated on in the following sections.

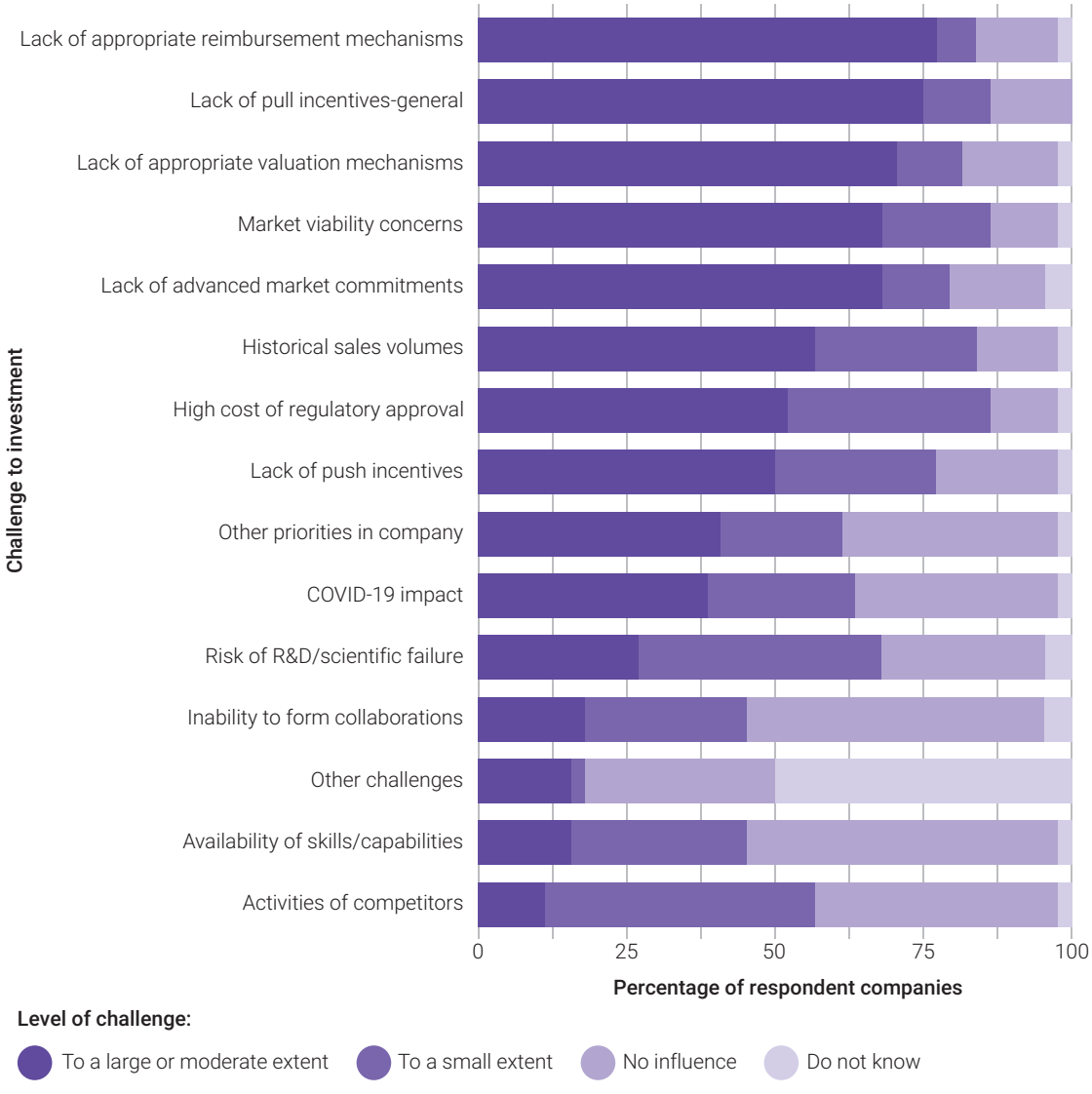
The most significant challenges to investment are related to a perceived lack of pull incentives in general, including a lack of appropriate reimbursement mechanisms, valuation mechanisms, and advanced market commitments, and market viability concerns.

Surveyed Alliance members across the R&D pharmaceutical, diagnostics and biotech/SMEs sectors reported experiencing challenges to investment in R&D for AMR-relevant products and/or technologies.[81] The most common factors that surveyed companies saw as a moderate or large challenge included a lack of pull incentives (identified by 75% of surveyed members as a key challenge) (**Figure 2**). Examples include a lack of appropriate reimbursement mechanisms (reported by 77% of surveyed members), a lack of appropriate valuation mechanisms (reported by 71%) and a lack of advanced market commitments (reported by 68%), and market viability concerns (reported by 68%). Overall, 82% of surveyed Alliance members reported the lack of at least one of these pull incentives as a challenge to investment. In addition, market viability was a common factor reported by Alliance members as a moderate to large challenge (68%

of respondents).[82] It is worth noting that many of these incentives are interrelated (e.g. pull incentives and market viability).

In terms of sector-specific challenges, 83% of the 12 surveyed R&D pharmaceutical companies saw a lack of pull incentives in general and other priorities in the company as a moderate to large challenge to investment levels. Among 27 surveyed Alliance members from the biotech/SME sector, 78% of companies rated a lack of pull incentives in general, a lack of advanced market commitments, a lack of appropriate valuation mechanisms and a lack of appropriate reimbursement mechanisms, respectively, as a challenge to investment levels. Lastly, among five diagnostics companies, 80% rated a lack of appropriate reimbursement mechanisms and the impact of COVID-19, respectively, as a challenge to investment levels.[83]

FIGURE 2: EXTENT TO WHICH FACTORS CHALLENGED COMPANY INVESTMENT LEVELS IN R&D FOR AMR-RELEVANT PRODUCTS AND/OR TECHNOLOGIES (N=44)



Source: RAND Europe analysis

Looking to the future, Alliance members view new or improved pull incentives as a key factor that will influence the likelihood of increasing investments in AMR-relevant R&D. Specific incentives identified as particularly important include improved valuation models for novel products, changes in reimbursement models to support patient access, the wider implementation of guaranteed purchase funds/advanced market commitments and market entry awards. A combination of pull incentives would enable efforts to stimulate further investment in R&D.

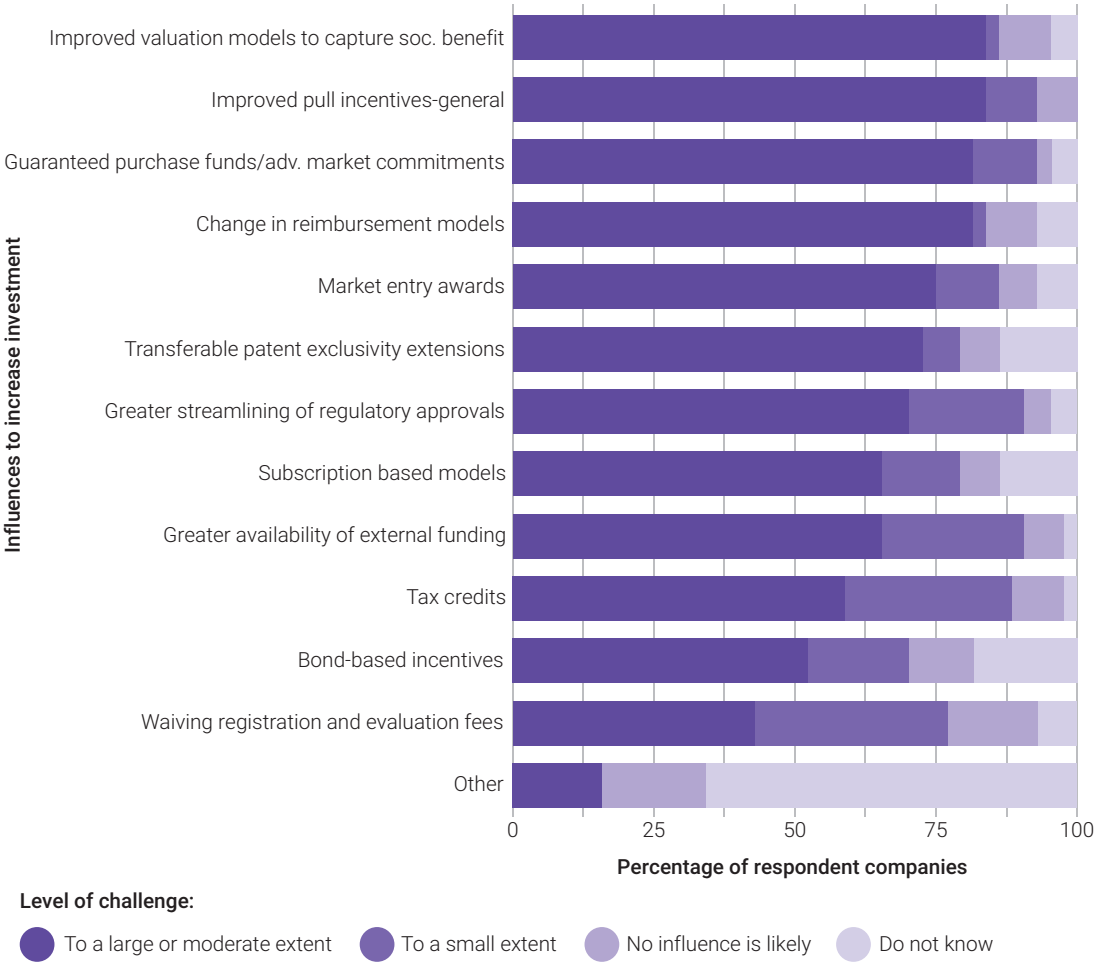
Looking to the future, and according to Alliance members, improved incentives are needed as part of an effort to improve market conditions alongside other factors, including successful innovation outputs, changes in prescribing behaviours to ensure appropriate use and improved surveillance infrastructure (to name a few). Across the R&D pharmaceutical, diagnostics and biotech/SME sectors,[84] the most common need that surveyed members highlighted in relation to positively influencing the likelihood of investment in AMR-relevant R&D in the future was introducing improved pull incentives (84% of surveyed companies saw this as likely to influence their investments to a large or moderate extent). Other factors seen as particularly important by those surveyed included improved valuation models for novel products to capture societal benefit (84%), changes in reimbursement models to support patient access to novel antibiotics (82%), wider implementation of guaranteed purchase funds/advanced market commitments (82%) and market entry awards (75%) (**Figure 3**).[85] It is important to note that there is a difference between reimbursement reform and wider pull incentives to ensure market viability and attractiveness, and efforts to ensure an appropriate incentive system need to tackle multiple needs through a multi-pronged approach. Reimbursement reform and valuation can help bring the market stability needed to improve access but are only seen by Alliance members and industry associations as part of a wider package of pull incentives needed to stimulate a sustainable R&D ecosystem.[86] For example, the International Federation of Pharmaceutical Manufacturers and Associations (IFPMA) has called on countries to take steps towards delivering an implementation roadmap by the end of 2021 to achieve implementation progress by 2023 and ensure full and effective implementation by 2025. Key incentives include new economic incentives to boost the confidence of the private sector to invest in R&D to support a robust antibiotic pipeline, bespoke valuation of antibiotics to recognise their full benefit to society, and reimbursement reforms to support market availability and patient access.[87]

In terms of sector-specific perspectives, 92% of surveyed companies within the R&D pharmaceutical sector reported that improved valuation models for novel products to capture societal benefit, together with a wider set of improved pull incentives in general, would influence the likelihood of increasing investments in AMR-relevant R&D to a moderate or large extent. This was followed by change in reimbursement models (83%), guaranteed

purchase funds or advanced market commitments (83%), and transferable patient exclusivity extensions (83%). Within the biotech/SME sector, 93% of companies reported improved pull incentives in general as positively influencing the likelihood of investment. This was followed by market entry awards (89%), improved valuation models for novel products to capture societal benefit (81%), and subscription-based models to incentivise R&D in exchange for guaranteed access to innovation (81%). Lastly, all surveyed companies in the diagnostic sector (100%) reported guaranteed purchase funds/advance market commitments and greater streamlining/ harmonisation or regulatory approval processes as positively influencing the likelihood of investment.[88]

Through the introduction of new incentives or improvements in existing incentives, more favourable market conditions could increase industry investment in AMR-relevant R&D. In response to hypothetical changes in market conditions, 73%[89] of surveyed Alliance members stated that they would increase levels of investment if market conditions improved, while 61% reported that they would decrease levels of investment if market conditions worsened. This trend was similar across sectors. If market conditions remained unchanged, 61% of Alliance members across R&D pharmaceutical companies, diagnostics companies and biotech/ SMEs reported that they would maintain their current level of investment, 32% that they would decrease investment, and 7% that they would increase investment even under such circumstances.

FIGURE 3: EXTENT TO WHICH INSTRUMENTS/INCENTIVES/ CONDITIONS INFLUENCE THE LIKELIHOOD OF COMPANIES INCREASING INVESTMENT LEVELS IN R&D FOR AMR-RELEVANT PRODUCTS AND/OR TECHNOLOGIES IN THE FUTURE (N=44)



Source: RAND Europe analysis

Alliance members agree on the importance of improving incentives systems and of doing so in a timely manner. Some gradual developments in this space are being pursued, though many are still in the early stages of implementation. Existing initiatives provide a foundation for further progress in the future.

Based on publicly available information on the Global AMR R&D Hub,[90] a resource that provides an overview of initiatives being considered and implemented to incentivise and reward AMR-relevant R&D, there is more to be done. However, gradual progress is being made. Various initiatives are tackling different aspects of incentives for AMR-relevant R&D, though not all directly provide incentives (some signal areas of importance to inform R&D and incentives efforts, rather than all being incentives in and of themselves).[91]

However, different incentives-related initiatives vary in maturity/implementation stage and geographical reach, and there is a need for scaled-up implementation and sustainability. Please see a detailed overview of incentive-related initiatives in **Annex B.2**, compiled based on information available on the Global AMR R&D Hub.

Additional insights shared by some of the AMRIA member companies that responded[92] suggest scope for increased recognition of the urgency of the task at hand. Covid-19 has highlighted the critical importance of recognising and committing appropriate resources to address other infectious disease threats such as AMR. Lessons from the Covid-19 response could help mobilise further global commitments to pull incentives for AMR R&D, especially for innovative valuation models for products aimed at timely prevention and those that can support equitable, appropriate access globally, including the most vulnerable populations. This could support efforts to slow the spread of infections and resistant infections.

Alliance members are actively involved in advocacy efforts to improve incentives for AMR-relevant R&D, in line with their commitment to work with policymakers on actions to respond to the urgent need for innovative products and technologies.

Alliance member respondents have engaged in activities to improve market conditions for AMR-relevant products. Activities include advocacy efforts for improved pull and push incentives (80% of respondents), engaging in high-level discussions and policy debates (66%), and involvement in efforts to improve ways in which the value of antimicrobial products is assessed (52%).[93]

Some Alliance members provided information on the nature of advocacy activities they have engaged with. These activities include participation in working groups, membership of international associations (e.g. EFPIA, MedTech Europe, AdvaMedDx, IFPMA and BIO), engagement with national policymakers, participation in research consortia in support of

advocacy, and private-public partnerships such as the AMR Action Fund. Further detail on engagement with the AMR Action Fund is provided in **Box 13**. Examples of initiatives looking to improve incentives involving Alliance members' participation include the EFPIA AMR Incentives Working Group, the MedTech Europe AMR Working Group, the Fleming Fund project in Africa and Asia, the Antimicrobial Working Group and Europe's Innovative Medicines Initiative (IMI).

The Alliance in Action: collaboration to support an enabling R&D ecosystem

Collaboration is key and is central to AMRIA's mission and strategy. The AMR Action Fund illustrates such a collaboration, and some alliance members participate in the AMR Action Fund (**Box 13**). Some alliance members, mainly from the R&D pharmaceutical sector, also provided examples of how they test new payment models for AMR-relevant products and technologies (**Box 14)**.

BOX 13: **THE AMR ACTION FUND**

AMR Action Fund

In 2020, more than 20 leading biopharmaceutical companies launched a partnership that aims to bring two to four new antibiotics to patients by 2030. This group – the world's largest public-private partnership – is now working to address AMR, acknowledging that immediate action is required. This initiative brings together a broad alliance of industry and non-industry stakeholders, including philanthropies, development banks, and multilateral organisations. It helps encourage governments to create market conditions that enable sustainable investment in the antibiotic pipeline. The Fund expects to invest more than US$1 billion to bridge the funding gap and respond to the AMR threat. Multiple AMRIA companies participate in the AMR Action Fund effort. A list of organisations involved in the AMR Action Fund can be found via: https://www.amractionfund.com/

BOX 14: **EXAMPLE ACTIVITIES CONDUCTED BY ALLIANCE MEMBERS TO TEST NEW PAYMENT MODELS FOR AMR-RELEVANT PRODUCTS**

Engaging in a pilot procurement model with Sweden (Shionogi & Co.)

Despite the rise in antimicrobial resistance, Sweden has experienced relatively few infections caused by multi-drug resistant bacteria. Infrequent resistant infections coupled with restrictive stewardship protocols means that new antibiotics are not often used in Swedish hospitals. As a result, companies may not register their products in Sweden because of low demand. Without new products, and as old products are withdrawn from the market, there is a risk that products will not be available when needed.

To address potential issues with access to antibiotics, the Public Health Agency of Sweden (PHAS) launched a new pilot model to improve the availability of approved antibiotics on the Swedish market. Cefiderocol, an antibiotic for aerobic Gram-negative organisms in adults with limited treatment options, was one of the products selected for participation in this pilot model. As part of this pilot, the pharmaceutical company Shionogi & Co. guarantees rapid availability of Cefiderocol to patients within Swedish healthcare institutions when needed. In return, Sweden will provide Shionogi & Co. with a guaranteed annual revenue regardless of how frequently Cefiderocol is used. Cefiderocol will be purchased and administered through typical channels; at the end of the year, the amount spent by Swedish institutions will be calculated and, if it is less than the agreed amount, the Swedish government will cover the difference.

If successful, this model could potentially be adapted by other countries where demand for new antibiotics is low, providing availability for patients in need and a viable market for new antibiotics. While there has been a concern that the size of the contract may not be large enough to interest companies, participation by multiple countries may allow for enough scale to create a meaningful incentive.

Pilot subscription purchasing model in the UK (Shionogi and Co., Pfizer and GlaxoSmithKline)

In the UK's five-year national action plan to tackle AMR, the UK committed to exploring new procurement mechanisms to ensure access to important antimicrobial products. Following up on this commitment, the National Health Service England (NHS England) and the National Institute for Health and Care Excellence (NICE) announced their intention to establish an antibiotic subscription purchasing model through their UK Project for developing and testing an innovative model for the evaluation and purchase of antimicrobials. The model's principle is that companies are paid for antimicrobials based on the estimated value of benefits to patients and the NHS, which is consistent with good stewardship and value-based care rather than payments based on volumes used. This model would rely on a modified health technology assessment to determine the value of the antibiotics, a framework which the Economic Evaluation Policy Research Unit (EEPRU) developed. This model stresses the value of antibiotics to society rather than the value they might provide to an individual patient.

Three R&D pharmaceutical Alliance members stated that they are participating in this pilot model. Products selected to be part of the pilot include Shionogi and Co.'s Cefiderocol and Pfizer's Zavicefta® (ceftazidime and avibactam). GlaxoSmithKline (GSK) has offered its product Gepotidacin for participation in the model, and discussions regarding its inclusion are currently in progress. In addition, GSK chaired the joint working group between industry and the UK government that led to the pilot's development.

The impact of the COVID-19 pandemic on investment levels in AMR-relevant R&D has varied and appears to be context-specific.

Insights on the impact of the COVID-19 pandemic suggest diverse influences on investment into AMR relevant R&D. Greater global interest in infectious-disease related innovation has been linked to increased investment in AMR-relevant R&D in some companies, e.g. by highlighting the importance of improved diagnostics and the risk of infectious diseases exacerbating the threat of AMR through increased and/or inappropriate antibiotic use. However, some companies also reported decreasing investment levels due to the need to divert resources to other areas. Similarly, though not directly R&D related, some members reported that the pandemic affected other areas of their activities. For example, the pandemic may have limited opportunities for face-to-face antimicrobial stewardship and awareness-raising at events and conferences or led to a decline in surveillance and monitoring of antibiotic use in some settings due to pressures on hospital capacity.

Across the Alliance, a third of respondents (33%) reported that COVID-19 had caused delays in R&D for AMR-relevant products. However, more than a quarter of companies (27%) reported that COVID-19 had no influence on their AMR-related R&D activity (**see Figure in Annex B.3**).[94] In the R&D pharmaceutical sector, nearly a fifth of Alliance members (17%) stated that the pandemic led to an increase in funding for AMR-relevant R&D. However, it is not possible to determine from these data whether some companies included COVID-19 related R&D in this funding. However, the same number of Alliance members also reported that COVID-19 contributed to a decrease in internal funding, reinforcing that such impacts can be diverse and context-specific. Generics companies did not report any impacts from COVID-19 on their AMR-related R&D activity. This is perhaps not surprising given they were not conducting R&D on novel products and technologies (although they do conduct R&D on adapting existing products and technologies and new formulations or delivery models). Some diagnostics companies (60% of respondents)[95] and biotech/SME companies (33%) experienced particular challenges around COVID-19, causing delays in R&D for AMR-relevant products.

The experience of the COVID-19 pandemic also offers learning which could help enable future AMR-related and pandemic preparedness efforts and specifically industry engagement in this space. Survey respondents shared insights on key areas of practical learning. These span themes including:

- The key role of raising public awareness of risks of AMR and scaling political will
- The need for a strong regime of push and pull incentives for industry engagement
- Conducive regulatory infrastructure
- The need for establishing ways to scale industry commitment to AMR-relevant R&D through collaborative working between different professions within a single company, between companies and with other stakeholders, and
- Innovative data-sharing practices.

We expand on these learning themes in **Annex B.4** based on the information and perspectives that survey respondents shared.

3.3. NATURE OF R&D ACTIVITIES

BOX 15: **SUMMARY OF THE NATURE OF R&D ACTIVITIES**

HIGHLIGHTS:

- **Alliance members continue to build R&D pipelines focused on AMR-relevant products and technologies.** Member portfolios account for 37% of The Pew Charitable Trusts' list of 'Antibiotics Currently in Global Clinical Development' (March 2021) and 50% of The Pew Charitable Trusts' list of 'Non-traditional Products for Bacterial Infections in Clinical Development' (March 2021), equal to 42% across both lists. This suggests an opportunity to attract new members to the AMRIA Alliance, supporting a fuller representation of the entirety of the industry R&D pipeline and reaping further benefits of a unified approach and effort.
- **Alliance members conduct R&D on AMR priority pathogens,** including developing products or technologies against bacteria featured in WHO's list of priority pathogens and products or technologies against bacteria and fungi featured in the CDC's Biggest Threats list.
- **Collaboration is a key pillar of the AMRIA Alliance commitments and strategy.** The Alliance is committed to stronger public-private collaboration and new ways of working to overcome the scientific challenges of creating new antimicrobials, vaccines and diagnostics. Overall, 82% of surveyed companies reported collaborating with academic institutions, 68% with other private-sector/industry organisations, 52% with in-country government bodies, and 50% with hospitals and medical laboratories.
- **Part of a collaborative effort also involves sharing relevant data for tackling AMR.** Alliance members engaged with data-sharing and exchange on R&D activities for AMR-relevant products or technologies through diverse means such as journal publications, conference contributions, workshops/roundtables and websites. However, research protocols, analysis plans and pre-registration plans are rarely shared. This points to an opportunity to consider a greater scope for timely sharing of such information to further support the coordination of global industry efforts. According to the surveyed companies, the most commonly shared data types included data related to epidemiology and surveillance, clinical trials results, and new compound leads.

Alliance members continue to build R&D pipelines focused on AMR-relevant products and technologies. In total, member portfolios account for 42% of products on the most recent Pew Charitable Trusts lists. This suggests an opportunity to attract new members to the AMRIA alliance to reap the benefits of a unified approach and effort.

To assess the AMR-relevant R&D pipeline of Alliance members, we examined company products listed in The Pew Charitable Trusts' list of 'Antibiotics Currently in Global Clinical Development' (March 2021) and The Pew Charitable Trusts' list of 'Non-traditional Products for Bacterial Infections in Clinical Development' (March 2021). Products in development from these lists are shown in **Table 2**.

The 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) and 47% of The Pew Charitable Trusts' list of 'Non-traditional Products for Bacterial Infections in Clinical Development' (March 2021). This equates to 42% of products across both lists, with ten products in phase 3 clinical trials. The results suggest an opportunity to attract new members to AMRIA, supporting a fuller representation of the entirety of the industry R&D pipeline and reaping further benefits of a coordinated approach and effort.

In addition, Alliance members who responded to the survey provided information on products or technologies not already featured in The Pew Charitable Trusts' lists mentioned above.[96] A total of 14[97] (26%) member respondents provided information on AMR-relevant products or technologies they understood not to be on these existing lists, accounting for 36 products across the Alliance.

Combining information from the Pew Lists, survey responses and the 'Medicines in Development - Antimicrobial Resistance' list (April 2020), **Annex B.5** shows a breakdown of product types, pathogens targeted and product names (where information is available).[98] The combined list illustrates that 93 AMR-relevant products or technologies are currently being developed by Alliance members,[99] comprising 54 antibiotics and antifungals, 12 vaccines, 13 diagnostic platforms and assays, and 14 non-traditional or other products.[100] Broken down by sector, this comprises 29 products or technologies developed by R&D pharmaceutical companies, 50 by biotech/SMEs, 2 by generics companies and 12 by diagnostics companies.

TABLE 2: PRODUCTS IN DEVELOPMENT ACROSS THE ALLIANCE

	The Pew Charitable Trusts' list of 'Antibiotics Currently in Global Clinical Development' (March 2021)	The Pew Charitable Trusts' list of 'Non-traditional Products for Bacterial Infections in Clinical Development' (March 2021)
Total number of Alliance member products	16 of 43 (37% of products on the list)	17 of 36 (47% of products on the list)
Types of products	Antibiotics (16 products)	Vaccines (9 products) Lysin (2 products) Virulence inhibitor (2 products) Synthetic antimicrobial peptide (1 product) Live biotherapeutic product (1 product) Bacterial replacement (1 product) Antibiotic inactivator (1 product)
Number of products by sector	R&D pharmaceutical (1 product) Biotech/SME (15 products)	R&D pharmaceutical (10 products) Biotech (7 products)
Pathogens targeted	*K. pneumoniae* (8 products) *Enterobacter spp.* (7 products) *A. baumannii* (6 products) *S. aureus* (5 products) *P. aeruginosa* (5 products) *E. faecium* (1 product) *C. difficile* (2 products)	*C. difficile* (4 products) *S. aureus* (3 products) *S. pneumoniae* (2 products) *E. coli* (2 products) Group B *Streptococcus* (1 product) *Shigella sonnei* (1 product) *Shigella flexneri* (1 product)
Phase of research	Phase 1 (9 products) Phase 2 (1 product) Phase 3 (5 products) New drug applications (1 product)	Phase 1 (3 products) Phase 2 (8 products) Phase 3 (5 products) New drug applications (1 product)

Alliance members conduct R&D on AMR priority pathogens, including those featured in WHO's list of priority pathogens and the CDC's Biggest Threats list.

Table 3 provides an overview of the number of Alliance member products and technologies targeting priority pathogens on WHO or CDC's lists, comprising 104 products/technologies in total.[101] The table is based on data on pathogens addressed by Alliance member products as reported in The Pew Charitable Trusts' list of 'Antibiotics Currently in Global Clinical Development' (March 2021), The Pew Charitable Trusts' list of 'Non-traditional Products for Bacterial Infections in Clinical Development' (March 2021), the 'Medicines in Development - Antimicrobial Resistance' list (April 2020), and survey data on AMR-relevant products provided by Alliance member companies.

According to this data, the most common pathogens targeted by Alliance member products and technologies are *Staphylococcus aureus* (15 products), followed by *Acinetobacter baumannii* (13 products) and *Pseudomonas aeruginosa* (12 products) and *Mycobacterium tuberculosis* (12 products).[102] The next most commonly addressed pathogens addressed by Alliance member products or technologies were *Enterobacteriaceae* – ESBL-producing (11 products) and *Enterobacteriaceae* – Carbapenem-resistant (7 products).

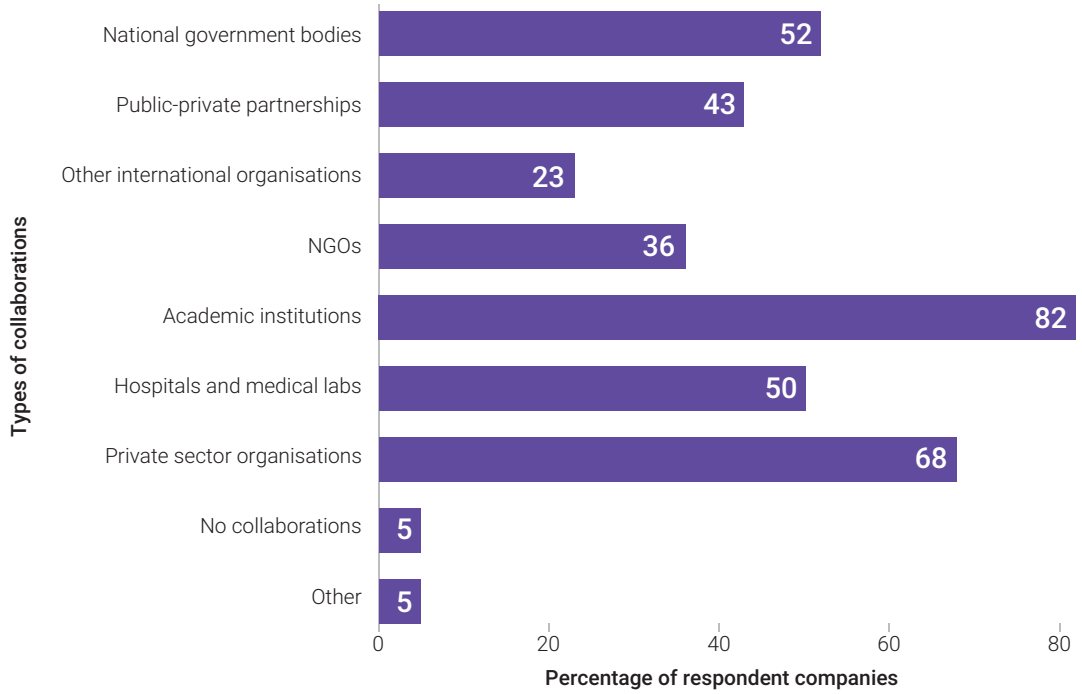
TABLE 3: NUMBER OF ALLIANCE MEMBER PRODUCTS TARGETING AMR PRIORITY PATHOGENS

Pathogen	R&D pharma	Biotech /SME	Generics	Diagnostics[103]	Total (all sectors)	WHO Priority Pathogen List	CDC Biggest Threats List
Staphylococcus aureus	2	13			15	Priority 2: high	
Acinetobacter baumannii	2	11[104]			13	Priority 1: critical	Urgent threats
Pseudomonas aeruginosa		12[105]			12	Priority 1: critical	Serious threats
Mycobacterium tuberculosis	6	2	2	2	12		Serious threats
Enterobacteriaceae- ESBL-producing	1[106]	10[107]			11		Serious threats
Enterobacteriaceae – Carbapenem-resistant	1[108]	3		3[109]	7		Urgent threats
Clostridium difficile	2	4			6		Urgent threats
Streptococci- Streptococcus pneumoniae	3	1			4	Priority 3: medium	
Neisseria gonorrhoeae	1	2[110]			3	Priority 2: high	Urgent threats
Candida spp.		3			3		Serious threats
Aspergillus fumigatus	1[111]	2[112]			3		Watch list
Shigella spp.	1	2[113]			3	Priority 3: medium	Serious threats
Enterococci- Enterococcus faecium		2			2	Priority 2: high	
Salmonellae- Non-typhoidal Salmonella		2[114]			2		Serious threats
Salmonellae - Salmonella serotype Typhi		2[115]			2	Priority 2: high	
Haemophilus influenzae		2[112]			2	Priority 3: medium	
Mycoplasma genitalium				1	1		Watch list
Streptococci- Group B Streptococcus	1				1		Concerning threats

Alliance members actively collaborate with other stakeholders for AMR-relevant R&D efforts to deliver on their commitment to stronger public-private collaboration and new ways of working.

Collaboration is a key pillar of AMRIA commitments and strategy. The Alliance is committed to stronger public-private collaboration as well as new ways of working to overcome the scientific challenges of creating new antimicrobials, vaccines and diagnostics.[117] Among Alliance member respondents, 82% reported collaborating with academic institutions, 68% with other private- sector/industry organisations, 52% with in-country government bodies and 50% with hospitals and medical laboratories (**Figure 4**).[118]

FIGURE 4: TYPES OF COLLABORATORS ACROSS THE ALLIANCE (N=44)[119]



Source: RAND Europe analysis

Part of a collaborative effort involves sharing relevant data for tackling AMR. Alliance members shared and exchanged data through diverse means such as journal publications, conference contributions, workshops/roundtables and websites. However, research protocols, analysis plans or pre-registration plans were rarely shared.

Amongst surveyed Alliance members, over half (57%)[120] of R&D pharmaceutical companies, biotech/SMEs and diagnostics companies facilitate data-sharing and/or exchange of information related to R&D for AMR-relevant products or technologies. By sector type, this includes 83% of R&D pharmaceutical companies,[121] 60% of diagnostic companies and 44% of biotech/SMEs.

The most common way of facilitating data sharing across the three sectors was through journal publications, conference contributions, roundtables and workshops and website content (**see Figure in Annex B.6)**. However, few companies reported publicly publishing research protocols, analysis plans or pre-registration plans. Understanding how these data-sharing trends relate to data-sharing levels in other clinical areas (e.g. oncology or cardiovascular research) would be important for interpreting whether the degree of data sharing is similar or different compared to other therapeutic areas. These data are not available. However, the Alliance is committed to enhancing data-sharing in some areas, including its strategy for the coming years. The most common types of data shared were related to epidemiology and surveillance, clinical trials results and new compound leads related to AMR, although there is some variation across sectors (**see Figure in Annex B.7**).[122]

The Alliance in Action: research and science

Boxes 16–21 provide selected case vignettes, illustrating diversity across AMRIA-member contributions to innovative R&D in terms of the types of R&D being conducted and how innovation is pursued, including collaborative endeavour.

BOX 16: **PFIZER CONTRIBUTES TO ADVANCING THERAPEUTIC AGENTS THAT CAN HELP TACKLE AMR**

Aim: Pfizer continues to advocate creative solutions to help grow the anti-infectives pipeline across bacterial, viral, and fungal infections and combat AMR. The company aims to do so through internal R&D efforts, supporting creative ventures, and seeking out partners with promising candidates in the early stages of development. For example, Pfizer is lending support to creative ventures such as the AMR Action Fund.

Implementation: In October 2020, Pfizer acquired Arixa Pharmaceuticals, Inc.[123], whose lead compound, ARX-1796, is an oral prodrug of avibactam, which, if approved, has the potential to be the first novel oral beta-lactamase inhibitor + antibiotic combination in more than three decades. As an oral agent, this treatment may potentially benefit patients with infections caused by Extended-Spectrum Beta-Lactamase (ESBL)+ pathogens (enzymes that break down beta-lactam antibiotics) by enabling earlier hospital discharge or avoiding the need for outpatient IV antibiotic therapy. Through this acquisition, Pfizer will advance the development program for ARX-1796. Pfizer played an instrumental role in developing a vaccine for SARS-CoV-2, the virus that causes COVID-19, bringing a vaccine to patients in 2020.[124] There are concerns (still being studied globally) that antibiotic overuse to prevent and treat secondary infections related to COVID-19 raises risks of AMR. This flags the importance of vaccines and novel therapeutic agents against COVID-19, which could mitigate against antibiotic use to prevent and treat secondary infections, and thus mitigate AMR risks. During the period covered by this report, Pfizer announced the initiation of Phase 1 studies of novel oral and intravenous antiviral therapeutic agents for SARS-CoV-2.[125] Stopping viral infections such as COVID-19 can play a role in a holistic approach to help prevent AMR.[126] During the AMRIA progress survey reporting period, Pfizer's vaccine portfolio has also focused on developing ways to help prevent infections directly associated with AMR. Examples include the Biologics License Applications (BLA) submission of a 20V adult pneumococcal vaccine (conjugate vaccine that helps protect against 20 serotypes responsible for the majority of invasive pneumococcal disease pneumonia) and commencing phase 3 trials for a paediatric 20V pneumococcal vaccine[127] and Respiratory Syncytial Virus (RSV) maternal vaccine.[128]

Influences on the effort: According to the survey respondent from Pfizer, market dynamics make it difficult for small-and-mid-size companies to compete in the anti-infectives space and progress assets past early-stage development. This, in turn, can impact the overall AMR-relevant R&D supply and influence pharmaceutical company pipelines. Pfizer actively looks for opportunities to collaborate and help progress efforts. However, the market potential for new anti-infective therapies is limited and faced with challenging economic hurdles. According to the survey respondent, there are still relatively few incentives to invest in R&D because of the steep development costs, high risk of failure and long lead times, making it difficult to realise a return. The same respondent also highlighted the lack of significant pull incentives and conducive reimbursement environments as a key challenge.

Outcomes and impacts –realised and/or anticipated: The key outcomes of activity to date relate to commencement of phase 1 trials for novel oral and intravenous antiviral therapeutic agents for SARS-CoV-2 and phase 3 trials for a paediatric 20V pneumococcal vaccine and RSV maternal vaccine. These are all promising efforts to combat AMR through vaccine-related innovation that seeks to prevent the emergence of AMR.

BOX 17: MEMED PURSUES R&D TO DEVELOP A TEST TO DISTINGUISH BETWEEN BACTERIAL AND VIRAL INFECTION AND THUS HELP EFFORTS TO REDUCE THE INAPPROPRIATE USE OF ANTIBIOTICS

Aims: MeMed is a diagnostics company with headquarters in Israel and a subsidiary in the US. MeMed's multi-year AMR-related program aims to develop and productise a rapid and accurate host-protein test for differentiating between bacterial and viral infection (called MeMed BV®), which is important for curbing the inappropriate use of antibiotics. MeMed has also developed a user-friendly and rapid measurement platform (called MeMed Key®) that can be deployed at a wide range of hospital settings to run the test that accurately differentiates between bacterial versus viral infections. The programme started in 2009 and is ongoing. Between 1 July 2019 and 31 March 2021, MeMed aimed to complete clinical and analytical validation studies designed to support regulatory clearance of the Key/BV system in Europe and the US.

Implementation: Individual host-protein biomarkers are inherently limited in their discriminatory performance between bacterial and viral infections. Therefore, MeMed searched for a combination of viral-and-bacterial-induced proteins that complement one another's gaps in differentiating bacterial from viral infection. MeMed then employed machine learning to identify the best performing combination of proteins to serve as a tool to better diagnose patients with suspected acute infection. The diagnostic test's performance has been independently validated in multiple blinded clinical studies, achieving a negative predictive value of 98%.[129,130]

Developing MeMed's solution has been a long-standing effort. However, in the specific period covered by this survey (1 July 2019 to 31 March 2021), MeMed completed a clinical validation study for Key/BV that enrolled over 1,000 children and adults with suspected infection at Emergency Departments and Urgent Care Centres in the US, Israel, Germany and Italy. In addition, MeMed conducted analytical validation of the Key/BV system in line with Clinical and Laboratory Standards Institute (CLSI) guidelines.

Influences on the effort: According to MeMed, dedicated and enthusiastic clinical and laboratory partners in Israel, Europe and the US who are key opinion leaders in infectious disease, emergency medicine, antimicrobial stewardship and point-of-need diagnostics helped support the R&D effort's progress. These individuals conducted clinical studies and helped define the unmet need and workflow, and are supporting adoption activities. Additionally, the Key/BV efforts were supported partially by awards from the Defense Threat Reduction Agency (DTRA) of the US Department of Defense and Congressionally Directed Medical Research Programs (CDMRP) of the US Department of Defense and European Commission. Challenges experienced include those related to regulatory and reimbursement pathways, and awareness-raising and education beyond early adopters.

Outcomes and impacts – realised and/or anticipated: Key/BV is now CE-IVD (CE marking for in-vitro diagnostics). On 20 September 2021, MeMed announced that Key/BV is now FDA cleared. MeMed is gathering real-world data in Europe and Israel to better understand the impact of Key/BV on appropriate antibiotic use. The recent FDA clearance of Key/BV enables the rollout and evaluation of real-world impact on appropriate antibiotic use in the US. Additionally, MeMed is working to achieve the compatibility of MeMed BV to whole blood samples and to additional measurement platforms, which could help increase this novel test's utility and impact on antibiotic stewardship.

BOX 18: **GSK INVESTS IN DEVELOPING VACCINES AGAIN STAPHYLOCOCCUS AUREUS AND CLOSTRIDIUM DIFFICILE TO PROTECT PATIENTS AND REDUCE THE RISK OF AMR**

Aims: Alongside antibiotics, vaccines are an important tool in reducing the spread of antibiotic resistance globally. Vaccines can help prevent both bacterial infections, which are directly treated with antibiotics, and viral infections (such as influenza and varicella), for which antibiotics are often prescribed.[131] In addition, vaccination can help protect unvaccinated individuals through 'herd immunity', helping to reduce the spread of a pathogen and reduce the need for antibiotic treatment and opportunities for resistance development.[132] GSK already has an established portfolio of vaccines and is committed to leveraging its innovative vaccine platform technologies and bringing together leading scientists to investigate potential new tools to fight AMR. During the AMRIA progress reporting survey period, GSK continued to invest in AMR-relevant vaccine R&D to support longer-term aims to prevent and mitigate AMR through vaccine innovation.

Implementation: GSK teams are leveraging new scientific insights and innovative technologies, including mRNA, next generation bioconjugation, structural vaccinology, and generalised module for membrane antigens (GMMA), to target pathogens likely to develop resistance and to create effective vaccines faster and more efficiently compared with traditional approaches. GSK currently have vaccine and medicine projects targeting priority AMR pathogens for WHO, the European Centre for Disease Prevention and Control (ECDC) and the US Centers for Disease Control and Prevention (CDC). For example, GSK began a Phase I clinical study in 2019 to investigate a candidate vaccine against *Clostridium difficile*.[133] In 2020, GSK initiated a Phase I/II study for a candidate vaccine against *Staphylococcus aureus* that is leveraging the company's capacities and expertise in bioconjugation and adjuvant technologies.[134]

Influences on efforts: According to the GSK survey respondent, key enablers of company activity in tackling AMR during the survey period include (i) continued activity from public and private funders focused on AMR (engagement and interest from these funders have had a positive effect on channelling resources to AMR, including for vaccines R&D), and (ii) additional scientific data published reinforcing the importance of vaccines as part of the overall AMR solution. Challenges encountered during the period include (i) the difficulty of building the internal business case for AMR-targeted vaccines given the uncertainty of the future burden and respective market implications, (ii) significant disruption in non-COVID clinical studies due to competing resources resulting in timeline delays, and (iii) lack of attention to the role of vaccines as a tool to fight AMR in the public policy debate.

Outcomes and impacts – realised and/or anticipated: GSK's improved understanding and expanding capabilities in vaccine development may lead to potentially new and effective ways to tackle the problem at the source, aiming to protect more people from infectious diseases and prevent and mitigate AMR. Key achievements during the survey reporting period relate to progressing clinical studies for two major priority AMR pathogens,[135] including the previously mentioned candidate vaccine against *Clostridium difficile* and a candidate vaccine against *Staphylococcus aureus*.

BOX 19: VENATORX PHARMACEUTICALS AND THE GLOBAL ANTIBIOTIC RESEARCH AND DEVELOPMENT PARTNERSHIP IS PARTNERING TO DEVELOP AND PROVIDE ACCESS TO NOVEL ANTIMICROBIALS GLOBALLY

Aim: On 20 April 2020, Venatorx Pharmaceuticals and the Global Antibiotic Research and Development Partnership (GARDP) announced a collaboration to accelerate the development of, and access to, cefepime-taniborbactam.[136] Cefepime is a fourth-generation cephalosporin antibiotic with more than two decades of proven safety and clinical utility against key common susceptible gram-negative bacteria.[137] Taniborbactam (formerly VNRX-5133) is an injectable beta-lactamase inhibitor (BLI) discovered and developed by Venatorx Pharmaceuticals. In combination with cefepime, Taniborbactam is a potential treatment option for patients with serious bacterial infections caused by resistant gram-negative bacteria. Cefepime-taniborbactam has *in vitro* and *in vivo* activity against difficult-to-treat resistant pathogens – including carbapenem-resistant Enterobacterales (CRE) and carbapenem-resistant *Pseudomonas aeruginosa* (CRPA) – that produce extended-spectrum beta-lactamases (ESBL), AmpC beta-lactamases, oxacillinases (OXA), *Klebsiella pneumonia* carbapenemase (KPC), and metallo-beta-lactamases including Verona integron-encoded (VIM) and New Delhi metallo-beta-lactamases (NDM).

Implementation: GARDP is collaborating with Venatorx to complete the development of cefepime-taniborbactam, including a phase 3 complicated urinary tract infection (cUTI) trial, which is already in progress. In addition, the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA) approved Venatorx's initial Paediatric Study Plan (iPSP) and Paediatric Investigation Plan (PIP), respectively, for cefepime-taniborbactam. The PIP approvals enable Venatorx and GARDP to initiate clinical trials for cefepime-taniborbactam in paediatric patients, including newborns.

Influences on effort: The COVID-19 pandemic has made for an extremely challenging R&D environment. The work on cefepime-taniborbactam did not escape the effects of this sweeping crisis, with delays to both the cUTI phase 3 clinical trial and an observational study investigating resistant infections.

Outcomes and impact-realised and/or anticipated: Cefepime-taniborbactam is being evaluated in a global, randomised, double-blind, active-controlled, non-inferiority phase 3 study called CERTAIN-1 (Cefepime Rescue with Taniborbactam in cUTI) in adults with cUTI, including acute pyelonephritis. The trial is assessing the efficacy, safety and tolerability of cefepime-taniborbactam compared to meropenem using clinical cure and microbiologic eradication as the primary composite efficacy endpoint. Venatorx expects to report top-line results in the first quarter of 2022. In support of the PIP and iPSP, juvenile toxicology dose ranging finding studies for cefepime-taniborbactam are ongoing. Additional clinical trials are anticipated in adults with multidrug-resistant infections.

If cefepime-taniborbactam is proven effective, Venatorx is committed to working with GARDP to distribute it on an affordable basis worldwide. Venatorx has granted GARDP exclusive rights to distribute and sub-distribute cefepime-taniborbactam, if and once it is approved for clinical use, in most low-and lower-middle-income countries.

BOX 20: **CLARAMETYX AND AEQUOR TARGET MICROBIAL BIOFILM**

Context: Pathogenic bacteria rapidly form communal, protective biofilm structures as part of establishing infection. Biofilms contribute to AMR in multiple ways. They shield bacteria from antibiotics and the innate immune system, rendering antibiotics less effective, and provide an environment where bacteria can become resistant through horizontal gene transfer and other mechanisms. Every AMR pathogen on WHO and CDC's lists of priority, urgent, pandemic and biothreats is a biofilm-former,[138] but there is no rapid diagnostic for biofilm, delaying immediate treatment.[139] Overall, 80% of chronic wounds and 90% of hospital-acquired infections are associated with biofilm.[140]

Aim: Two AMRIA Alliance members – both biotechnology companies based in the US - reported activities related to biofilm. Clarametyx Biosciences is developing a novel antibody-based therapy that targets biofilm to enable patients' immune systems and first-line antibiotics to kill AMR pathogens more effectively. Aequor Inc has identified innovative compounds that, according to third-party and in-house *in vitro* microbiology data, kill a broad spectrum of antimicrobial-resistant (AMR) pathogens at all stages of growth, including 'biofilm'.

Implementation: Clarametyx Biosciences is developing a humanised monoclonal antibody therapy, CMTX-101, based on scientific discoveries at Nationwide Children's Hospital in Columbus, Ohio. The antibody targets a protein that is ubiquitous across pathogenic bacterial biofilms to collapse the bacterial biofilm structure and render the bacteria more vulnerable to antibiotic or immune intervention. Via private funding and a grant from CARB-X, the company will complete the First-in-Human study of CMTX-101. Clarametyx has advanced preclinical development of CMTX-101 through *in vivo* proof of concept, manufacturing and preliminary toxicology studies.

Aequor Inc. invested in developing a portfolio of small molecules which are, according to the company, third-party validated to kill AMR bacteria and fungi, remove biofilm in minutes and prevent its formation for days. Secured funding support from US National Institutes of Health (NIH)/ National Institute of Allergy and Infectious Diseases (NIAID) and Department of Defense (DOD)/Army Medical Research Institute of Infectious Diseases (AMRIID) will enable pre-Investigational New Drug (IND) trials for Aequor's new drug candidates against AMR and multi-drug resistant (MDR) strains and biothreats.

Influences on the effort: According to the survey respondent from Clarametyx, critical enablers of progress have included state-of-the-art research, researchers and founders, supportive investors and board of directors, and a management team passionate about making a lasting impact on infectious diseases and AMR. Challenges have included overcoming industry scepticism based on recent experiences with the broader category of antibiotic development. According to Aequor, there are a series of challenges related to the regulatory space for biofilm. To the best of Aequor's knowledge, there are also no US reimbursement codes for therapeutics making anti-biofilm claims only.

Outcomes and impact – anticipated and/or realised: Clarametyx has reported progress with preclinical development and drug product manufacturing for initial clinical studies to enable an anticipated clinical trial start in 2022. It is also commencing the development of a prophylactic vaccine, CMTX-301, directed against the same bacterial target as is CMTX-101. Aequor renewed its contract with the NIH/NIAID under the concept accelerator program, which provides pre-Investigational new drug trials for as many novel compounds as Aequor can deliver for testing against high priority pathogens.

BOX 21: **BIOVERSYS FOCUSES ON ONE OF THE HIGHEST UNMET MEDICAL NEEDS IN AMR: CARBAPENEM-RESISTANT ACINETOBACTER BAUMANNII AND VENTILATOR-ASSOCIATED BACTERIAL PNEUMONIA**

Aim: BioVersys AG is a Swiss-based multi-asset biotech tackling nosocomial pneumonia and bloodstream infections (BSI) caused by Carbapenem-resistant Acinetobacter baumannii (CRAB). This is a CDC and WHO priority 1 pathogen with the fewest pipeline programmes available[141] high resistance and a 50% mortality rate in hospital ICUs.[142,143] BioVersys is seeking to develop BV100 as a novel treatment for CRAB in Nosocomial pneumonia and BSI.

Implementation: BioVersys focused on finalising preclinical studies for a novel direct-acting antibiotic and has been progressing phase I trials.

Influences on the effort: According to BioVersys, progress has been facilitated by the sufficient liquidity provided by its investors and team expertise. Liquidity may be a future challenge for AMR-drug development biotechs such as BioVersys, and there are also challenges related to the reimbursement landscape and the need to ensure viable markets. Pull mechanisms rewarding novel antibiotics partially delinked from sales volumes are urgently needed.

Outcomes and impacts – realised and/or anticipated: The drug candidate is in ongoing phase I trials (NCT04636983). BioVersys is preparing to initiate its Phase II/III studies in 2022, focusing on CRAB and aiming to address this unmet medical need. BioVersys expects the read-out from the current FiH trial proving safety and later proof of concept in patients.'

3.4. DISCONTINUED AMR-RELEVANT R&D

BOX 22: **SUMMARY OF DISCONTINUED AMR-RELEVANT R&D AMONGST SURVEYED ALLIANCE MEMBERS**

HIGHLIGHTS:

Just under a quarter of surveyed Alliance members discontinued AMR-relevant R&D projects during the reporting period. The various reasons given included the high costs of R&D combined with poor market conditions, internal commercial requirements, difficulties finding partners for the scaling-up of new drug candidates, scientific factors, or the impact of the Covid-19 pandemic.

Nearly a quarter of Alliance members discontinued some AMR-relevant R&D projects during the reporting period.

Across the Alliance, 23% of respondents report discontinuing some AMR-relevant R&D projects between July 2019 and March 2021. All sectors except diagnostics report doing so.[144] Amongst R&D pharmaceutical companies, 42% report discontinuing some AMR-relevant R&D projects, as did 25% of generics companies and 19% of respondent biotech/SMEs.

Reasons for discontinuing AMR-relevant R&D projects included the high costs of R&D combined with poor market conditions, internal commercial requirements and difficulties finding partners for the scaling-up of new drug candidates. Some Alliance members noted that the reasons for discontinuation were commercially sensitive and could not be publicly shared. Scientific factors also contributed to the discontinuation of some AMR-related projects. These included lack of efficacy in intended indications, inability to achieve targeted product profiles, concern that products under development would not offer solutions to unmet medical needs, and challenges finding candidates with broad pathogen coverage and coverage against emerging resistance mechanisms. Some projects have also been discontinued or postponed owing to the impact of COVID-19 on clinical trial recruitment. The impacts of COVID-19 on clinical trial recruitment are also acknowledged in other innovation areas, extending beyond AMR alone.[145]

For a reflection on the Alliance's next steps in relation to research and science, please see Section 7.1.

4. ACCESS

4.1. ALLIANCE COMMITMENTS TO IMPROVING ACCESS TO AMR-RELEVANT PRODUCTS AND TECHNOLOGIES

Access to novel treatments and diagnostics for infectious diseases, especially in LMICs where the burden of AMR is disproportionately high,[146] is essential for saving lives and combatting the spread of drug-resistant infections. However, there are numerous barriers to access, including market entry challenges, poor antimicrobial stewardship, supply chain disruptions, lack of infrastructure and insufficient quality control.[147],[148] Furthermore, according to WHO, a high prevalence of substandard and counterfeit antimicrobials in LMICs pose a challenge to access.[149]

The life sciences industries have an important role in expanding and sustaining access to much-needed antimicrobials, vaccines, diagnostics and other products used in the prevention, diagnosis and treatment of infectious diseases. Indeed, improving access to AMR-relevant products and technologies is a long-standing commitment of the AMRIA.

The Alliance has long-standing commitments to improving access to AMR-relevant products and technologies (**Box 23**). In the following section, we present Alliance members' recent activity on supporting access.

BOX 23: **ACCESS COMMITMENTS**[150]

- 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.

4.2. ACTIVITIES TO SUPPORT ACCESS TO AMR-RELEVANT PRODUCTS OR TECHNOLOGIES

BOX 24: **SUMMARY OF ACTIVITIES TO SUPPORT ACCESS AMONGST SURVEYED ALLIANCE MEMBERS**

HIGHLIGHTS:

- **Amongst surveyed Alliance members, 81% were active in supporting access to AMR-relevant products or technologies,** and 64% also had formal access strategies or plans in place to support such activities.
- **Alliance members carried out access-related activity across diverse geographies,** with 53% of Alliance members working to support access in LMICs.
- **Alliance members' activities to support access to AMR-relevant products or technologies covered a variety of areas,** with the most common including product registration (65%), affordability (63%), availability (60%), advocacy (53%) and ease of access (49%).
- **Overall, 44% of surveyed Alliance members[151] actively pursued collaborative approaches to supporting access** to AMR-relevant products or technologies and tackled diverse determinants of access issues, including those related to equitable pricing, 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.
- **Challenges related to appropriate pricing and reimbursement, a lack of timely and appropriate product registration and prescriber/payer behaviours that favour lower-cost older antimicrobials were seen by Alliance members as key barriers** in industry efforts to enable wider access to AMR-relevant products or technologies.

The majority of Alliance members are active in supporting access to AMR-relevant products or technologies, and nearly two-thirds also had formal access strategies or plans in place to support such activities.

Across the Alliance, 81% of surveyed members carried out activities to support access to AMR-relevant products or technologies. This figure includes 11 out of 12 R&D pharmaceuticals, 9 out of 9 generics companies, 19 out of 27 biotech/SMEs, and 4 out of 5 diagnostics companies. Nearly two-thirds of Alliance members (64%) reported having formal access strategies or plans

for AMR-relevant products or technologies in place to help guide and support access-related activities, and 17% of those with general strategies or plans made these publicly available. R&D pharmaceuticals and diagnostics companies were more likely to have access strategies in place (83% and 80%, respectively) than companies in the generics or biotech/SME sector (67% and 52%, respectively). Although further research would be needed to understand the reasons for this, the biotech/SME sector might be less focused on access strategies than some other sectors due to the nature of biotech/SME products/technologies and stages of their development, and due to access issues being outside of the business model of some biotech firms.

In addition, some surveyed Alliance members reported having engaged in access-related activities in the absence of formal strategies or plans (17% of members).[152] Further information on access plans is provided in **Annex C.1**.

Alliance members carried out access-related activity across diverse geographies, with slightly over half working to support access in LMICs.

Surveyed Alliance members carried out access-related activities in countries with diverse income levels. Over half worked to support access in LMICs (53%), and 44% worked to support access in low-income countries.[153] Slightly over half (51%) reported activities in high-income countries and 44% in upper-middle-income countries. Nearly a quarter of responding companies (23%) did not target access-related activities according to countries' income levels. There is a potential opportunity to mobilise further activity across a broader range of Alliance members on access-related matters in LMICs going forward.

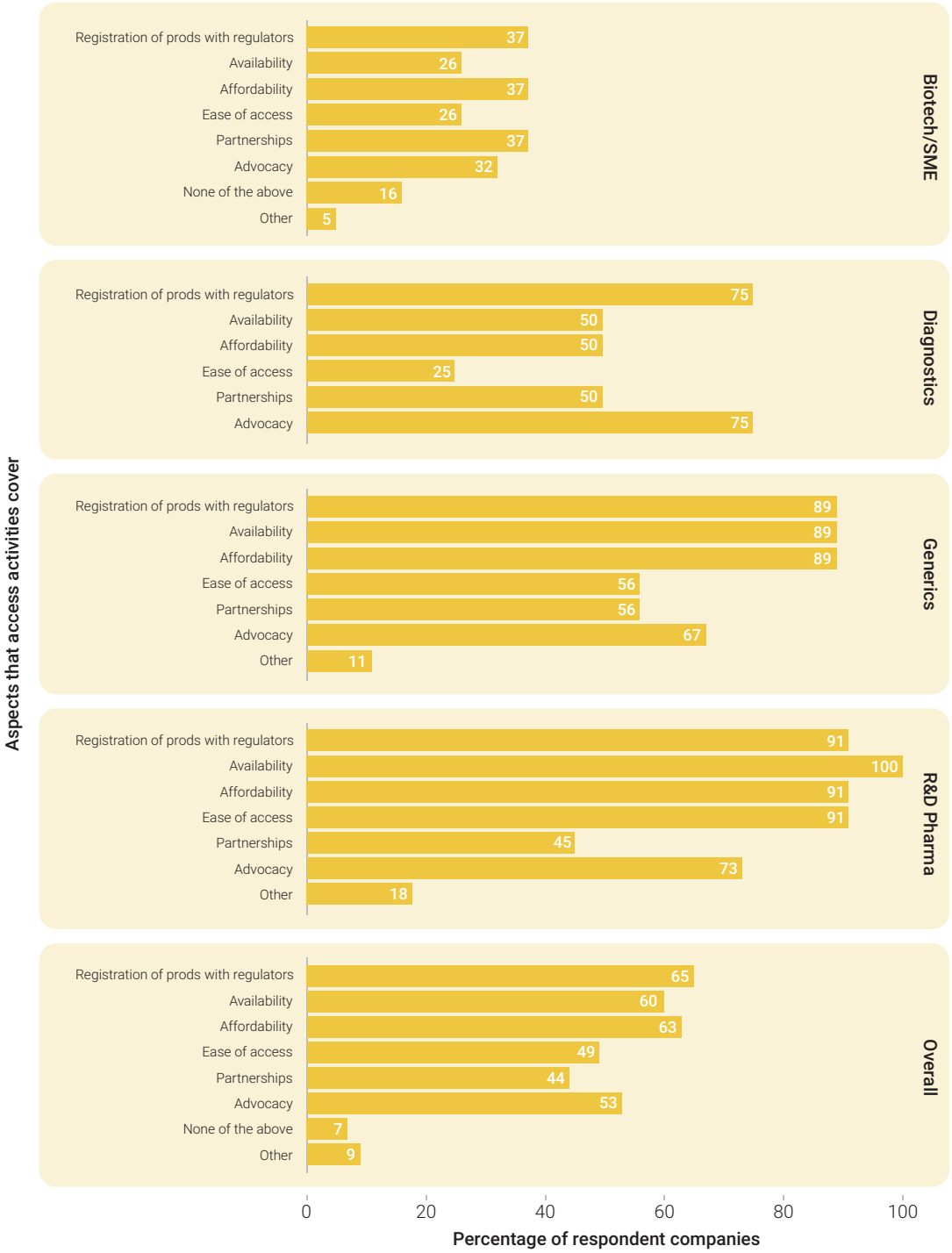
Alliance member activities to support access to AMR-relevant products and/or technologies covered various areas, most commonly product registration, affordability, availability, advocacy and ease of access.

Among the 43 Alliance member respondents that reported having an access plan or engaging in activities to support access (regardless of whether they had a formal plan or not), the most common activities included working to improve product registration related activity (65% of companies), affordability (63%), availability (60%), advocacy (53%) and ease of access (49%).

The focus of access-related activities varied by sector (**Figure 5**). For example, all 11 R&D pharmaceutical member companies that carried out activities to support access[154] to AMR-relevant products or technologies worked on availability (100%), and most (91%) worked on affordability, ease of access and issues related to the registration of products with relevant authorities. Nearly three-quarters (73%) also carried out advocacy activities. Among the nine surveyed generic companies with access-related activities, most (89%) engaged with product registration and efforts targeting affordability and availability of AMR-relevant products and technologies. Over half (56%) focused on ease of access issues and partnership/collaborative access mechanisms. Diagnostics-sector companies with access-related activities (four

surveyed companies) most often focused on activities related to the registration of diagnostics with relevant authorities and advocacy (75%). However, half (50%) also engaged in efforts related to affordability, availability and partnerships/collaborative access mechanisms.[155] Among the 19 companies surveyed, biotech-company activity seemed to span diverse areas with no dominant focal areas emerging based on survey data. Whether this is because individual companies prioritised a smaller range of activity areas due to the variations in stages of product/technology developments between them or for other reasons would merit further research.

FIGURE 5: DIVERSITY OF ACCESS-RELATED ACTIVITIES OF FOCUS AMONGST AMRIA MEMBERS (N=43)



Source: RAND Europe analysis

The Alliance in Action

Box 25 and **Box 26** provide example case vignettes of Alliance member efforts to support access to AMR-relevant products and wider activity supporting improved access.

BOX 25: JOHNSON & JOHNSON'S COMMITMENTS TO TACKLING AMR AND ENHANCING ACCESS TO TREATMENT AND CARE

Aims: One of the biggest impediments to tackling TB has been the growing resistance to common medicines. Today, drug-resistant TB (DR-TB) accounts for nearly one-third of all deaths from antimicrobial resistance (AMR).[156] COVID-19 is posing new challenges for those living with TB.[157] Against this context, Johnson & Johnson (J&J) has built on its longstanding commitment to TB by investing in efforts to develop and support access to treatment and care for patients.

Implementation: In 2012, J&J introduced SIRTURO® (bedaquiline), the first TB medicine with a novel mechanism of action in nearly half a century. Since then, as of May 2021, J&J has provided nearly 400,000 treatments to 145 countries, with more than 133,000 courses delivered in 2020 alone.[158] In 2020, J&J launched several initiatives to help raise awareness about the importance of tackling TB and ensuring continuity of care for people living with the disease during the Covid-19 pandemic. These efforts help mitigate the risks of AMR by ensuring adequate and timely treatment for DR-TB. For example, in May 2020, J&J launched the DR-TB Lifeline QuickFire Challenge[159] to find creative, community-based solutions to help ensure continuity of care for DR-TB patients in high-burden countries during the pandemic. J&J is also supporting global efforts to help find and deliver care to children living with TB who have not yet been diagnosed, as a diagnosis is essential for timely and appropriate treatment.[160] In addition, in 2020, J&J launched the Ending Workplace TB initiative - a multi-sectoral partnership with the World Economic Forum, The Global Fund, the Stop TB Partnership and others. This partnership aims to roll out awareness, detection and treatment programmes in high-burden countries.[161]

Influences on the effort: According to the J&J survey respondent, public-private partnerships have been a key enabler of progress. A dedicated end-to-end Global Public Health Unit within J&J also provides focus and executive-level support for efforts related to tackling TB and TB-related AMR.

Outcomes and impacts – realised and/or anticipated: Examples of impact from J&J's global efforts to end TB and combat AMR during the survey period include: (i) In May 2020, J&J received approval from the FDA for a paediatric formulation of bedaquiline, tackling the need for more effective treatments for children with multi-drug-resistant TB (MDR-TB)[162]; and (ii) In July 2020, supporting new WHO treatment guidelines, J&J joined forces with the Stop TB Partnership, The Global Fund and United States Agency for International Development (USAID) to develop a novel access framework for bedaquiline,[163] to help catalyse LMICs to achieve rapid access at scale.

BOX 26: **VIATRIS MAKES A DIFFERENCE TO THOSE IMPACTED BY TUBERCULOSIS (TB) BY EXPANDING ACCESS TO AFFORDABLE TREATMENTS AND CARE**

Aim: Viatris is a global healthcare company with generics-focused activities to help tackle multi-drug resistant/rifampicin-resistant (MDR/RR) and extensively drug-resistant (XDR) TB, together commonly referred to as DR-TB. While MDR/RR and XDR-TB cases represent less than 5% of the total global TB cases, they account for nearly 15% of all TB deaths.[164] DR-TB is also a major factor in the growth of anti-microbial resistance (AMR). It is estimated that DR-TB cases will account for more than one-quarter of all deaths from AMR over the next 25 years.[165] Despite the significant global burden of TB, research into new therapies has historically been neglected.

Implementation: In 2019, Viatris joined the non-profit TB Alliance as its global commercialisation partner for the first drug approved to treat XDR-TB or MDR/RR-TB that is treatment-intolerant or non-responsive. TB Alliance developed this important treatment from early discovery through to its first regulatory approval. It has since been approved over the past two years by several global regulatory health authorities, including the European Medicine Agency (EMA) and the Drugs Controller General of India (DCGI), where the prevalence of TB is the highest in the world. As the world's largest producer of HIV drugs by volume, Viatris realised that it had a powerful platform to help those living with TB worldwide, including in low- and-lower-middle-income countries where the TB burden is highest. To help reach patients living in countries where the drug was not registered or available, Viatris also developed a Named Patient Access Program. This program aimed to help any physician, regardless of where they live, access the product free of charge as long as their patient meets certain basic eligibility criteria. According to a Viatris survey respondent, the registration of the product in additional low-and-middle-income countries also continues to advance rapidly: the product is filed with 29 regulatory authorities covering 59 countries globally to ensure that treatment is accessible within the same timeframe in high-income countries. In India, for example, regulatory approval was received less than 12 months after the first regulatory approval in a developed market. This achievement marked a new speed-to-market record, as other recently developed MDR-TB drugs have taken more than three years to secure product registration.

In partnership with TB Alliance, Viatris is also advancing key operational research and conditional access programs worldwide. They are now actively working with not-for-profit organisations and governments across many countries in Eastern Europe, Central Asia, South and Southeast Asia and sub-Saharan Africa to further evaluate the safety and efficacy of the treatment.

Outcomes and impacts – realised and/or anticipated: A core focus of Viatris' mission is to help provide access to medicines, regardless of geography or circumstance. Based on the information provided by the Viatris survey respondent, Viatris was able to make the product available to public health programs in 150 LMICs within two months of its first regulatory approval through the Stop TB Partnership's Global Drug Facility.

Close to half of Alliance members actively pursued collaborative approaches to supporting access.

Just under half of the 43 surveyed Alliance members with access-related activities (44%)[166] reported engaging in partnership and collaboration. Some of these companies shared additional information on the nature of partnerships and collaborations that supported their access-related efforts suggesting a diversity of collaborators, including national governments, academia, NGOs and international organisations.[167]

Collaborative activities aimed to tackle diverse access determinants, including:

- **Equitable pricing** (for example, through the sale of products through a non-profit model, tiered pricing structures linked to country's ability to pay, partnerships to ensure the provision of vaccines at the lowest price for Gavi-eligible countries and the freezing of prices for Gavi-graduated countries[168] for ten years after graduation).
- **Capacity-building to enable improved access to AMR-relevant products and technologies** (for example, initiatives to support a new vaccine manufacturing facility and programmes to scale up the use of new pharmaceutical products).
- **Product donations with agreements reached through collaboration with national authorities and international organisations**. Examples include donations of antibiotics to humanitarian relief programmes, donations of antibiotics and antifungals for paediatric cancer patients using a volume-based free goods framework to provide an escalating percentage of free goods once certain annual volume thresholds are reached, and undertaking epidemiological surveys to ensure drug donation efforts align with the needs of global and national programmes.

BOX 27: **EXAMPLES OF COLLABORATIVE ACTIVITIES TO SUPPORT ACCESS**

Collaboration in support of equitable pricing efforts:

- The pharmaceutical company GSK's equitable pricing strategy uses a tiered pricing structure linking prices for pharmaceuticals to countries' ability to pay based on World Bank gross national income (GNI). GSK also establishes pricing tiers for all on-patent vaccines through public-private partnerships, including four tiers based on country GNI for pooled buying mechanisms (e.g. Gavi). Through the partnership with Gavi, vaccines are provided at the lowest price for Gavi-eligible countries and frozen for Gavi-graduated countries for ten years after graduation.
- As part of an ongoing partnership, the biotech company Venatorx granted the Global Antibiotic Research and Development Partnership exclusive rights to distribute and sub-distribute cefepime-taniborbactam, following approval for clinical use, in LMICs.

Capacity-building to enable improved access to AMR-relevant products and technologies:

- A public-private partnership between Pfizer, the South African Government and the Biovac consortium in Cape Town enabled a local partner to manufacture Prevnar for patients in South Africa. The project involved joint assessment of the technical and operational requirements across all areas of vaccine manufacturing. It was implemented through collaboration with partners in South Africa and visits to Pfizer plants.
- Sanofi's Global Health Unit is dedicated to improving the availability and affordability of 30 essential medicines, including anti-infectives, in 40 of the world's poorest countries. As part of these efforts, Sanofi signed a partnership agreement with UNITAID to improve the availability and affordability of treatment against latent tuberculosis infection in Global Fund to Fight AIDS, Tuberculosis and Malaria eligible countries.
- Together with the Stop TB Partnership and support from the Global Fund to Fight AIDS, TB and Malaria, and the U.S. Agency for International Development (USAID), Johnson & Johnson has established a new joint initiative to help low- and middle-income countries rapidly scale up the use of SIRTURO® in support of new WHO treatment guidelines recommending all-oral treatment regimens for drug-resistant TB patients.

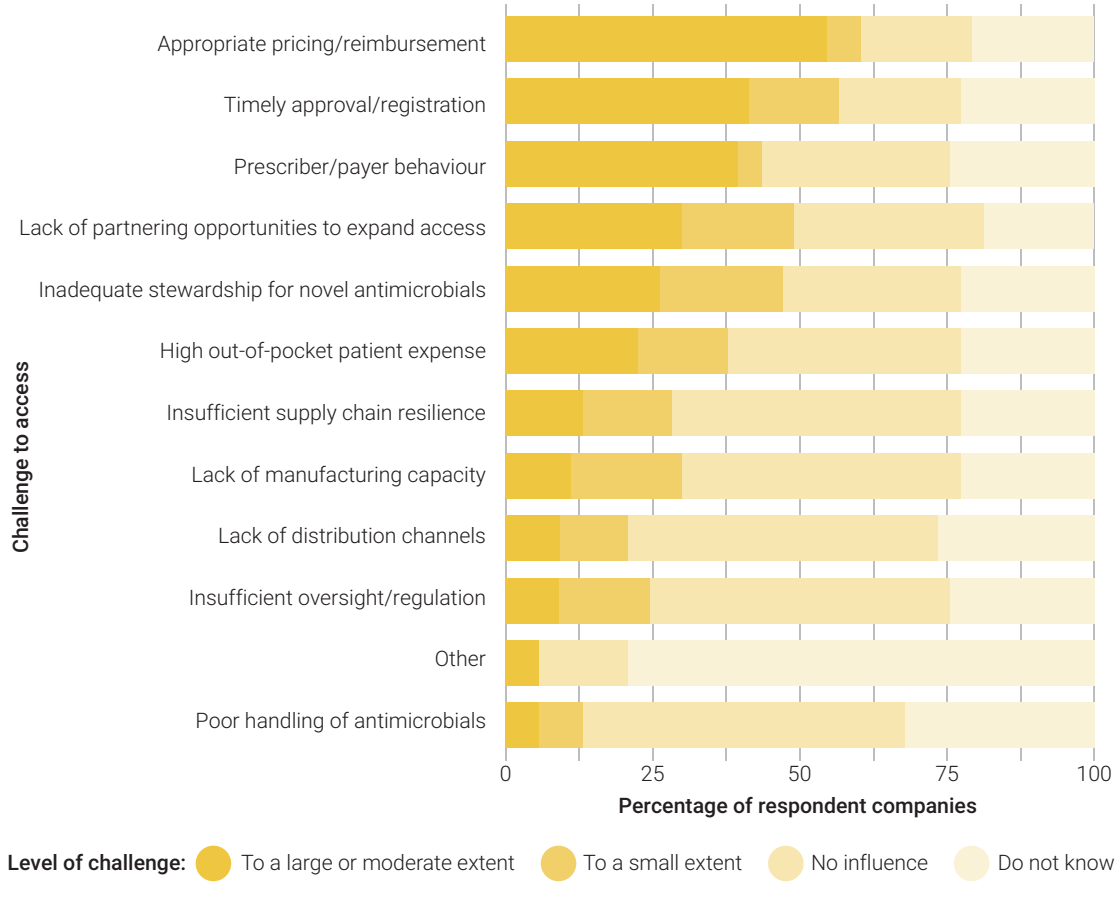
Product donations with agreements reached through collaboration with national authorities and international organisations

- Through its Global Hematology-Oncology Pediatric Excellence (HOPE) access programme for paediatric cancer patients, which is run in partnership with Texas Children Hospital and Direct Relief, Teva Pharmaceuticals donates antibiotics and antifungals in LMICs.

Key barriers to Alliance members' efforts to widen access to AMR-relevant products and/or technologies included challenges related to appropriate pricing and reimbursement, a lack of timely and appropriate product registration and prescriber/payer behaviour favouring lower-cost older microbials.

Surveyed Alliance members reported experiencing barriers related to access to AMR-relevant products or technologies during the reporting period (**Figure 6**). Over half of surveyed Alliance members (55%) saw the absence of appropriate pricing and reimbursement as a barrier to enabling access to AMR-relevant products or technologies (with 36% seeing it as a barrier 'to a large extent' and 19% 'to some extent'). Timely and appropriate registration of products and prescriber/payer behaviours that favour lower-cost older microbials were also seen as important barriers (41% and 39% of surveyed Alliance members saw these as challenging their access-related efforts to either 'a large extent' or 'to some extent', respectively).[169]

FIGURE 6: EXTENT TO WHICH ITEMS WERE BARRIERS TO COMPANIES ENABLING ACCESS TO AMR-RELEVANT PRODUCTS AND/OR TECHNOLOGIES – OVERALL ALLIANCE DATA ACROSS ALL SECTORS (N=53)



Source: RAND Europe analysis

4.3. ADDRESSING SUSTAINABLE SUPPLY CHALLENGES FOR AMR-RELEVANT PRODUCTS AND/OR TECHNOLOGIES

BOX 28: **SUMMARY OF CONTRIBUTIONS TO ADDRESSING SUPPLY CHALLENGES AMONGST SURVEYED ALLIANCE MEMBERS**

HIGHLIGHTS:

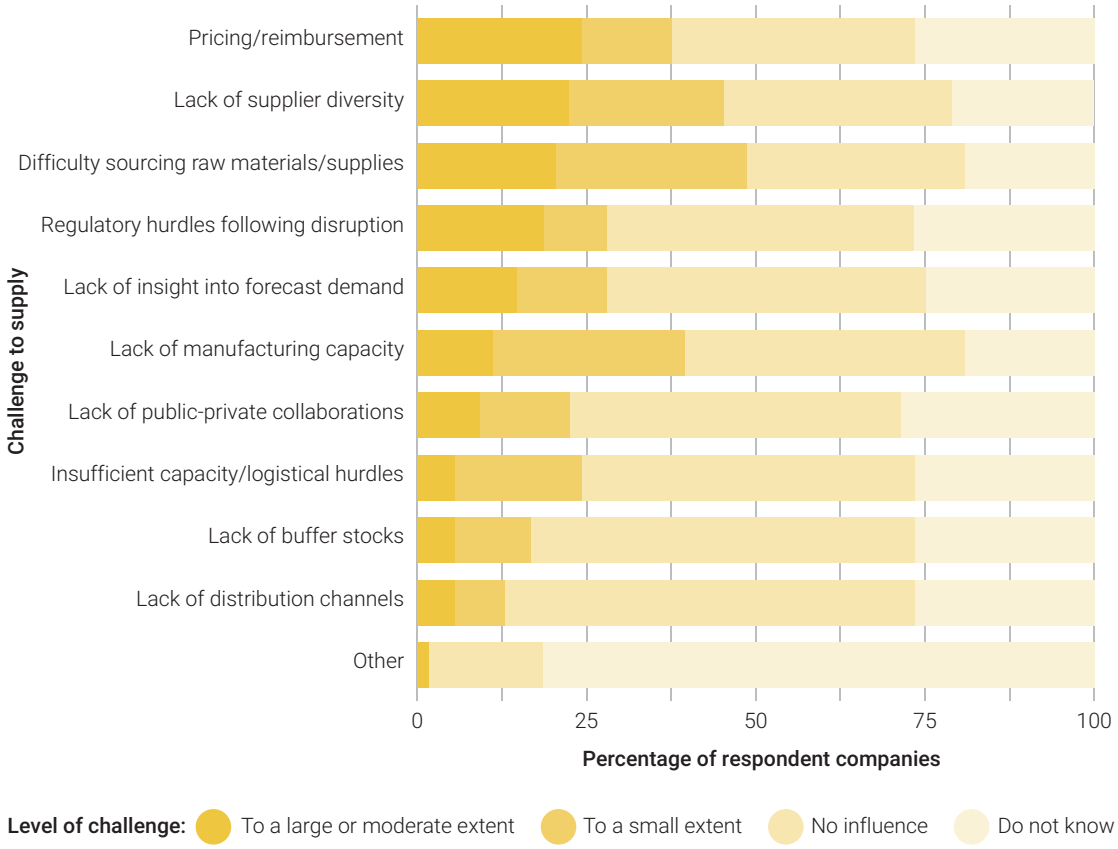
- **Overall, 60% of diagnostics companies and 56% of generics companies experienced supply chain disruptions.**
- **Companies reported a diversity of challenges to supply chain sustainability and resilience:** 21% reported experiencing difficulty (to a large or moderate extent) in sourcing raw materials and supplies, 23% reported being affected by a lack of supplier diversity, and 24% reported pricing and reimbursement challenges affecting the supply chain. Companies also noted that some disruptions related directly to the COVID-19 pandemic.
- **Nearly a quarter (23%) of Alliance members reported taking action to improve supply chain resilience and sustainability.** Examples include improvements in demand planning and demand prioritisation systems, efforts to strengthen supply chains in low-and-middle-income countries through capacity-building and tech transfer initiatives, and supplier auditing and supply chain diversification.
- **Alliance members in the R&D pharma, generics and diagnostics sectors reported taking action to reduce substandard and falsified AMR-relevant products or technologies,** with 65% of companies reporting activities to enhance product safety through packaging and serialisation and 54% reporting activities to improve quality management systems and controls.

Just over a quarter of Alliance members reported supply chain disruptions, with over half of generics companies and diagnostics companies being affected by such disruptions.

Supply chain continuity is key to efforts to ensure populations in need can access AMR-relevant products and technologies in a timely manner. Over a quarter (26%) of surveyed companies experienced supply chain disruptions, including 60% of diagnostics companies, 56% of generics companies, 17% of R&D pharmaceutical companies and 15% of biotech/SMEs.[170] Differences in experiences of supply chain disruption across sectors may, in part, reflect the nature of sector activities. For example, few biotech/SMEs have marketed

AMR-relevant products that would be subject to supply chain disruption, and pharmaceutical companies may have larger-scale resources and capacities to mitigate against supply chain disruptions. However, this would merit further research. Although relatively few companies had supply chains significantly hindered, a diversity of supply chain sustainability and resilience challenges were identified. Just over a fifth of surveyed companies reported experiencing difficulty (to a large or moderate extent) in sourcing raw materials and supplies (21%). Nearly a quarter were affected by a lack of supplier diversity (23%) and pricing and reimbursement challenges affecting the supply chain (24%) (**Figure 7**).

FIGURE 7: BARRIERS AND CHALLENGES TO ENSURING A SUSTAINABLE AND RESILIENT SUPPLY OF AMR-RELEVANT PRODUCTS AND/OR TECHNOLOGIES (N=53)



Source: RAND Europe analysis

Some Alliance members[171] provided further information explaining the disruption to the supply chain of AMR-relevant products and technologies they experienced. These included disruptions relating directly to the COVID-19 pandemic (e.g. COVID-19-related cargo dispatch and clearance issues), disruptions to the supply of laboratory equipment and disruptions to the supply of active pharmaceutical ingredients (APIs). Disruptions to the supply of APIs have been linked to the COVID-19 pandemic and other factors. For example, disruptions have led to price fluctuations, causing pressure on formulation manufacturing and long lead times for API manufacturing. This can limit responsiveness to increases in demand and, more rarely, supplier technical problems and other internal manufacturing challenges, leading to product-recall.

Nearly a quarter of surveyed Alliance members (23%) reported taking actions to improve supply chain resilience and sustainability. These actions included improvements to demand planning systems and responding to the COVID-19 pandemic, for example by establishing additional plans to ensure that patient demand can continue to be met or adopting a strategy of segmenting products into 'medically necessary' and 'medically significant' to manage supply. Other actions included efforts to strengthen supply chains in low-and-middle-income countries (including capacity-building and tech-transfer initiatives), supplier auditing and supply chain diversification.

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Some examples of company efforts to improve supply chain resilience and sustainability are illustrated in **Box 29.**

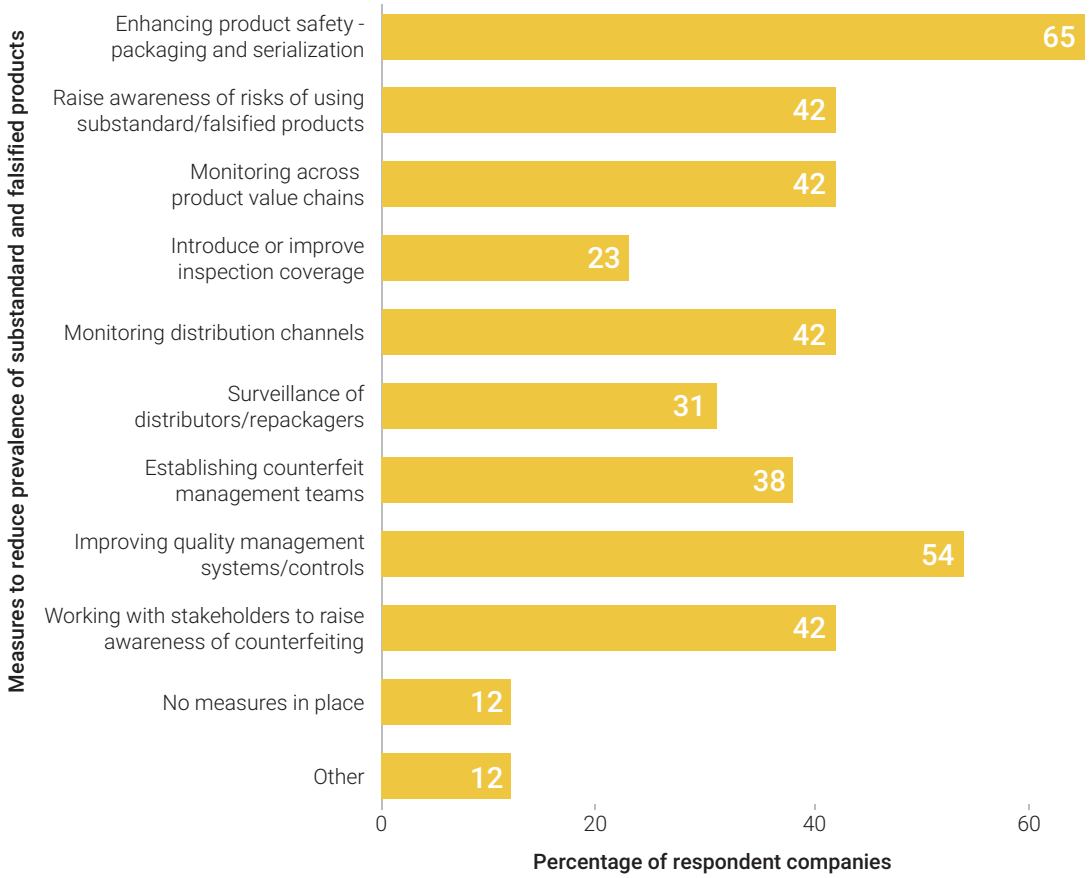
BOX 29: **BUILDING MORE RESILIENT AND SUSTAINABLE CHAINS – KEY EXAMPLES SHARED BY COMPANIES**[172]

- To strengthen the resilience and sustainability of its supply chain, the generics company Centrient Pharmaceuticals launched a revamped supplier qualification programme in 2019. The programme consists of assessing potential critical suppliers together with auditing and multi-year improvement plans for existing approved suppliers, aligned with the Pharmaceutical Supply Chain Initiative (PSCI) principles. Based on the audit outcomes, Centrient developed a corrective and preventive action plan covering ethics, labour, health and safety, and environmental protection.
- GSK's digital value stream mapping compiles end-to-end supply chain data from across the company's resource planning systems into a single dataset, with inventory policies set at each stage of the supply chain. When stock levels are out of tolerance with the agreed policy, alert messages are generated, enabling mitigating action to normalise the levels.
- In the context of the COVID-19 pandemic, Pfizer responded to a global surge in demand for anti-infectives through a global supply chain strategy focussing on the segmentation of key 'medically necessary' and 'medically significant' products. The approach helped the company manage incremental demand from across different regions – including China, Europe, Latin America and India – during different periods of the pandemic.
- The key aim of Johnson and Johnson's global public health (GPH) supply chain team is to address product and customer supply chain needs in low-income countries (LICs) and LMICs. The team conducts a wide range of activities to ensure alignment between demand, inventory and supply and manufacturing plans to meet the specific needs of LIC and LMIC populations. Activities include engaging with local health authorities to quantify patient numbers and developing annual unit forecasts and developing business continuity plans to ensure supply chain resilience in the event of major disruption.

Alliance members in the R&D pharmaceutical, generics and diagnostics sectors took action to reduce substandard and falsified AMR-relevant products or technologies, with nearly two-thirds engaging in activities to enhance product safety and over half engaging in activities to improve quality management systems and controls.

Substandard and falsified products, which often contain subtherapeutic doses of a drug, can increase the risk of drug resistance and exacerbate the threat of AMR.[173],[174] Amongst surveyed Alliance members in the R&D pharmaceutical, generics and diagnostics sectors,[175] the most common measure to reduce the prevalence of substandard and/or falsified products was enhancing product safety through packaging and serialisation (65% of respondents), followed by improving quality management systems and controls (54%). Other notable efforts included raising awareness of the risks of using substandard or falsified products; monitoring product supply chains; monitoring distribution channels; working with the healthcare community, regulators and law enforcement to raise awareness of counterfeiting (42% of member respondents); establishing counterfeit management teams (38%); and introducing or improving surveillance of distributors and re-packagers (31%) (**Figure 8**). Three-quarters (75%) of R&D pharmaceutical companies reported taking actions to enhance product safety through packaging and serialisation and improving quality management systems and controls. Overall, 89% of surveyed generics companies also reported taking actions related to improving product safety through packaging and serialisation. Serialisation across supply chains is likely to matter in assisting efforts to reduce the prevalence of substandard and falsified AMR-relevant products and technologies.

FIGURE 8: MEASURES TO REDUCE THE PREVALENCE OF SUBSTANDARD AND FALSIFIED AMR-RELEVANT PRODUCTS/TECHNOLOGIES (N=26)



Source: RAND Europe analysis

Some companies provided further information on activities undertaken to reduce the prevalence of substandard or falsified AMR-relevant products and technologies, which reflect many of the mechanisms outlined in **Figure 8** (above). Although the nature of the information provided is not amenable to quantification, examples of efforts include: using serialisation systems enabling the unique identification and traceability of items across the supply chain; adopting new safety and security features such as tamper-evident seals; digital authentication through mobile applications and track-and-trace sensors; and investigating the use of blockchain technology to enhance pharmaceutical supply chain security. Other activities related to monitoring efforts included establishing multidisciplinary global anti-counterfeiting teams, monitoring online marketplaces and social media platforms, gathering business intelligence data (including customer complaint and pharmacovigilance data), conducting stock reviews and using prioritisation tools and processes to identify markets at high risk of stockout-related counterfeiting. Monitoring activities were undertaken in close collaboration with law enforcement agencies to enable official investigations and the removal of counterfeit products. Some companies have also supported law enforcement by providing training to help customs officials identify counterfeit products.

Across the Alliance, collaboration with stakeholders was seen as important in tackling the challenge of counterfeit products. Collaborators included other pharmaceutical companies, either directly or through cross-industry networks (e.g. the Pharmaceutical Security Initiative). They also included health authorities, hospitals and healthcare professionals (e.g. in training and awareness-raising efforts or through the development and dissemination of field test kits for detecting counterfeit products), and/or policymakers at the national and international level (e.g. on discussions around the impact of illicit trade and advocacy for legislative reforms to better address illicit pharmaceutical trade). Some companies highlighted their involvement in the 'Fight the Fakes' campaign to raise awareness regarding the dangers of substandard and counterfeit medicines. Where specific detail was provided, illustrative examples of company efforts are shared in **Box 30**.

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BOX 30: **REDUCING THE PREVALENCE OF SUBSTANDARD AND/OR FALSIFIED AMR-RELEVANT PRODUCTS OR TECHNOLOGIES – EXAMPLES SHARED BY COMPANIES**[176]

- **Product safety and security:** In 2020, the generics company Novartis and the Universidad Politécnica de Madrid began co-leading an industry-wide public-private partnership to explore the use of blockchain technology to enhance pharmaceutical supply chain security.
- **Monitoring and enforcement:** Johnson & Johnson's Illicit Trade Analytics (ITA) programme, developed by its Global Brand Protection team, draws on various data sources to identify patterns and trends that expose illicit trade activity. In 2020, a new prioritisation tool was introduced to support the identification of the brands at greatest risk of illicit trade. In the UK, Johnson & Johnson conducts training to help government officials identify falsified products.
- **Detection:** Through its Global Pharma Health Fund (GPHF), Merck Sharp & Dohme (MSD) provides field test kits with simple methods for rapid drug quality verification and counterfeit medicines detection. The GPHF-Minilab provides healthcare professionals with labware, chemicals, reference standards and multilingual operation manuals to support detection. The Minilab works on a range of 100 drugs, including 31 antibiotics, and is used in 98 countries.
- **Awareness-raising:** Pfizer provides training to law enforcement and healthcare professionals to raise awareness on counterfeiting and enhance their ability to distinguish counterfeit from authentic medicines. As of December 2020, Pfizer had provided training to authorities from 164 countries.
- **Advocacy:** Through membership in associations such as the European Federation of Pharmaceutical Industries and Associations (EFPIA) and the Quality Brands Protection Committee (QBPC), GSK advocates for legislative reform to strengthen laws and penalties for dealing in falsified medicines in high-risk markets.

4.4. REMOVAL OF AMR-RELEVANT PRODUCTS OR TECHNOLOGIES FROM THE MARKET

BOX 31: **SUMMARY OF REMOVAL OF PRODUCTS OR TECHNOLOGIES**

HIGHLIGHTS:

- Only a small percentage of surveyed Alliance members (8%) reported removing AMR-relevant products or technologies from the market.
- Reasons for removal of products included regular reviews of portfolio and divestment decisions, the high cost of R&D combined with no or low reimbursement and insufficient capital to continue clinical studies or other unspecified commercial reasons.

Only a small percentage of Alliance members reported removing AMR-relevant products or technologies from the market.

Across the Alliance, only 8% of members reported having removed AMR-relevant products or technologies from the market during the survey reporting timeframe. This percentage included two pharmaceutical companies, one generics company, and one biotech/SME. Where reasons for removal were shared, these included removal as part of regular reviews of portfolio and divestment decisions, the high cost of R&D combined with no or low reimbursement and insufficient capital to continue clinical studies or other unspecified commercial reasons.

For a reflection on the Alliance's next steps in relation to access, please see Section 7.2.

5. APPROPRIATE USE AND STEWARDSHIP

5.1. ALLIANCE COMMITMENTS TO ENSURING THE APPROPRIATE USE OF ANTIMICROBIALS

The development of novel antimicrobials and improving access to these products in the fight against AMR must be complemented with promoting appropriate use through robust antimicrobial stewardship. The goal of antimicrobial stewardship is to ensure that patients receive 'the right drug for the right pathogen at the right time',[177] optimising outcomes whilst minimising unintended consequences (i.e. AMR). Diagnostics are also crucial for achieving this goal, specifically in the interest of surveillance and the early detection of drug-resistant microorganisms.

The Alliance has long-standing commitments to the appropriate use of antimicrobials (**Box 32**). In the following section, we present Alliance members' recent activities on the appropriate use of antimicrobials.

BOX 32: **THE APPROPRIATE USE OF ANTIMICROBIALS**[178]

- Contribute to slowing emergent resistance by preventing infections through vaccination promotion and reducing the inappropriate use of antibiotics via the expanded use of diagnostics.
- Support the 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 align with the goal of advancing stewardship.

5.2. AMRIA CONTRIBUTIONS TO THE APPROPRIATE USE OF ANTIMICROBIALS

BOX 33: **SUMMARY OF CONTRIBUTIONS TO THE APPROPRIATE USE OF ANTIMICROBIALS AMONGST SURVEYED ALLIANCE MEMBERS**

HIGHLIGHTS:

- **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 the 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%),[179] 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)[180]; 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.[181] Several Alliance members provided examples of contributing to appropriate use and stewardship activity by supporting research on the topic to ensure that the best available evidence informs practice.
- **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 surveyed R&D pharmaceutical and diagnostics companies had appropriate use and stewardship strategies or plans for AMR-relevant products and/or technologies. However, fewer generics companies and biotech/SMEs had such plans. In part, this may be related to the fact that not all biotech/SMEs focus on antimicrobial products nor have such products in late-stage development or on the market.

To support appropriate use and stewardship for AMR-relevant products and/or technologies, 42% of surveyed Alliance members reported having strategies or plans in place during the reporting period, and 45% of these were publicly available. 83% of R&D pharmaceutical[182] and diagnostics companies (80%) reported having such plans but fewer generics companies (33%) and biotech/SMEs (19%).

Appropriate use and stewardship are more commonly relevant to companies producing antimicrobials, and hence not relevant to all AMRIA members, which may in part explain the comparatively lower number of biotech/SMEs with such plans. Nearly a quarter of all Alliance member respondents (23%) reported that such plans do not apply to their business models.[183] Nevertheless, the need for appropriate use and stewardship strategies/plans merits further consideration, amongst companies with products in late-stage development or on the market who do not yet have such plans.

Some Alliance member's strategies or plans were product or technology specific. This is important because what constitutes appropriate use for a vaccine, for example, will not be the same as for an antibiotic or diagnostic test. 86% of Alliance members with strategies or plans in place report that their plans apply to antibiotics; 36% reported their plans apply to anti-fungals; 23% reported their plans apply to diagnostics; 18% reported their plans apply to vaccines, 14% reported their plans apply to biologics; and 5% reported their plans apply to other products. The type of product covered by appropriate use and stewardship strategies or plans also varied by sector, in line with what different sectors focus on.

A majority of Alliance members implemented activities to support appropriate use and stewardship, across diverse geographies, regardless of whether they had a formal strategy or plan to guide these activities.

Thirty-two surveyed Alliance members (60%) reported engaging in activities related to appropriate use and stewardship. Of which, 22 companies did so in the presence of a formal strategy and plan, and 10 companies reported implementing activities without having a formal strategy or plan in place to guide them.

AMRIA members are committed to supporting efforts for appropriate use in diverse regions globally and appropriate use and stewardship activities took place in diverse geographies. Two thirds (66%) of surveyed Alliance members engaging in appropriate use and stewardship activities did so in LMICs, 50% in low-income countries, 53% in upper-middle income countries and 59% in high-income countries. Nearly a fifth of surveyed companies (19%) who carried out activities related to appropriate use and stewardship report that their activities were not specific to the income level of countries.

Some members' appropriate use and stewardship activities were product or technology specific, and where this is the case, appropriate use and stewardship was most commonly applied to activities related to antibiotics. For example, 88% of Alliance members who actively support appropriate use and stewardship reported that their activities applied to antibiotics, 38% to anti-fungals, 16% to diagnostics, 12% to vaccines, 9% to biologics and 3% to other products. The type of product covered by appropriate use and stewardship strategies or plans also varied by sector, in line with what different sectors focus on.

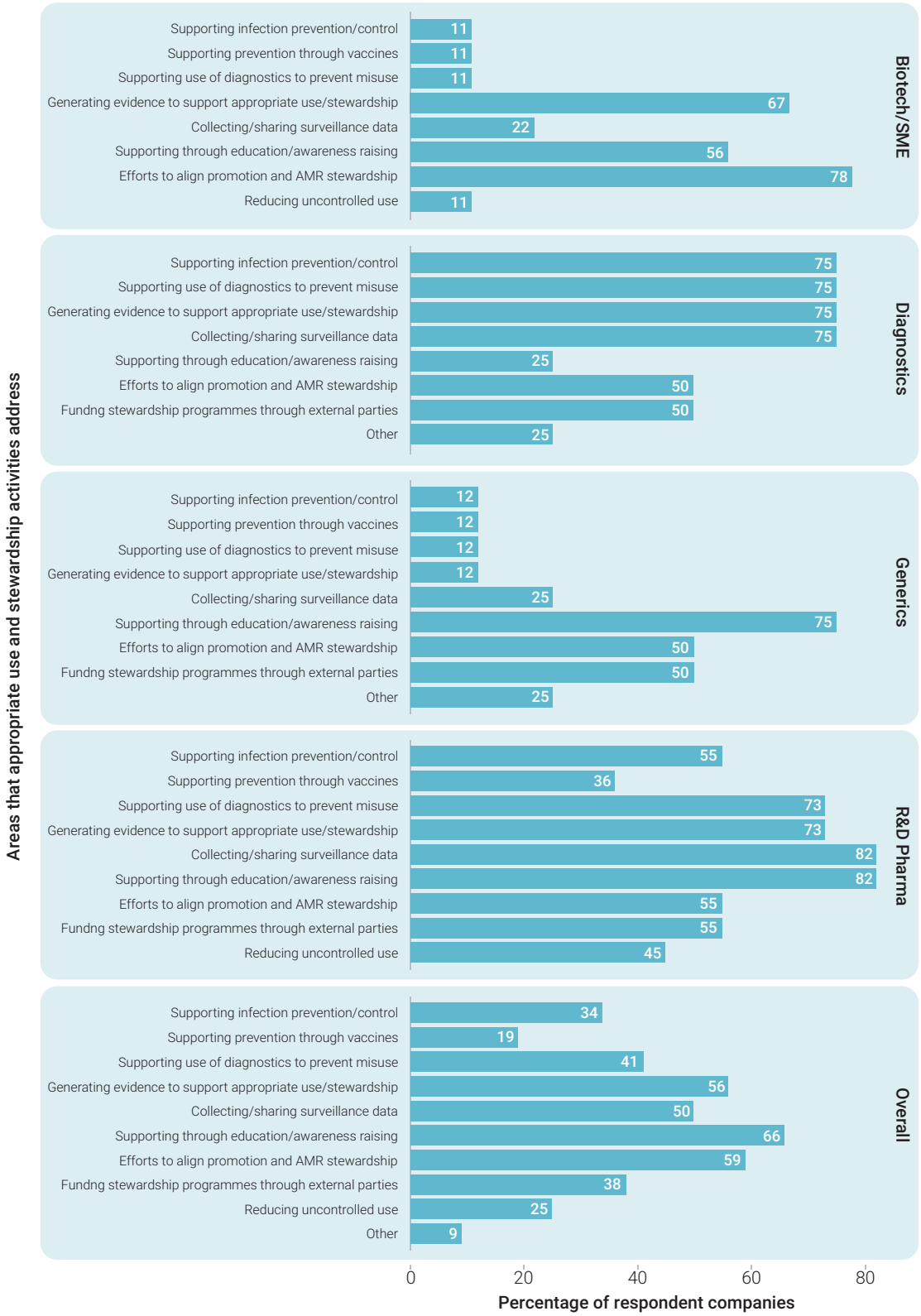
The need for appropriate-use and stewardship activities is considered at different stages of the product development process. Among the 32 companies with activities related to appropriate use and stewardship, 25% reported that they begin to consider appropriate-use and stewardship needs in early or preclinical stages of R&D, 6% in phase I, 13% in phase II and 9% in phase III. For about a quarter (28%) of companies, the stage they considered such issues vary according to the product in question: 9% do so only once R&D is completed, and 9% did not seem to have a strategy of thinking about appropriate use and stewardship at any particular stage of a pathway.[184]

Education and awareness, aligning antimicrobial promotion and AMR stewardship, and generating evidence to support appropriate use were key aspects of appropriate use and stewardship activities.

The most common ways of contributing to appropriate use and stewardship were through education and awareness-raising (66%),[185] efforts to align antimicrobial promotion and AMR stewardship (59%) and generating evidence to support appropriate use and stewardship (56%), including through collecting and/or sharing surveillance data (50%)[186] (**Figure 9).** There are similarities and differences in the types of activities taken by companies in different sectors.[187]

As in previous years' surveys, companies were asked to provide further information on the types of activities they conduct in relation to education and awareness-raising,[188] collecting and sharing surveillance data, and how they align promotional practices with the goal to advance appropriate use and stewardship.

FIGURE 9: TYPES OF CONTRIBUTIONS TO APPROPRIATE USE AND STEWARDSHIP BY AMRIA MEMBERS (N=32)



Source: RAND Europe analysis

Developing and distributing educational and awareness-raising materials, and engaging with diverse stakeholders in these efforts, have been a key part of Alliance members' activities to support appropriate use.

Across the Alliance, 88% of respondents[189] reported engaging in initiatives to promote stewardship through education and awareness-raising during the survey reporting timeframe. Engagement often occurred through developing and distributing education and awareness-raising materials (83% of the 23 companies that reported engaging in education and awareness-raising)[190] and developing materials to explain AMR risks and stewardship principles (70%). There is an opportunity to consider how Alliance members could increase activities related to supporting wider efforts to improve patient adherence (including through information on drug packaging to encourage patients to complete antimicrobial courses) and support appropriate antimicrobial prescribing by healthcare professionals in future years, as these activities were less frequent.[191]

Diagnostics companies were active in initiatives related to deploying diagnostics for pathogen identification and antimicrobial susceptibility/resilience (each reported by 75% of diagnostics companies that engaged in education/awareness-raising initiatives). This finding is aligned with an Alliance commitment to improving infection prevention and control through the expanded use of diagnostics so that antibiotics are only used for those patients who need them. R&D pharmaceutical companies were more likely to pursue additional post-approval indications as part of their appropriate-use and stewardship activity than other sectors, including generics companies. This finding is unsurprising given novel R&D activity on antimicrobials in the pharma R&D sector (reported by 73% of R&D pharmaceutical companies engaged in education/awareness-raising initiatives).

Alliance members engaged diverse stakeholders in education and awareness-raising activities. Twenty-three companies across the R&D pharma, diagnostics and generics sectors provided information on stakeholders with whom they have interacted.[192] Nearly all members engaged with individual healthcare professionals (96%) and the majority engaged at the institutional level with healthcare provider organisations (78%). Over half of Alliance members engaged with patients and/or caregivers (61%), the general public (57%) and others (22%), such as national agencies, farmers and veterinaries, wider company stakeholders and employees and learned societies. Overall, 74% of these companies also employed legal, compliance and internal-quality reviews of educational and awareness-raising material to ensure high quality, and over a third (39%) subjected educational materials to external peer review. In addition, to mitigate the risk of any perceived or actual conflict of interest in their engagements with healthcare providers and other stakeholders, over half of the 23 surveyed Alliance members (61%) partnered with NGOs, educational organisations and/or independent experts to develop educational material and over half also removed product and/or technology branding (57%).

The Alliance in Action: education to support appropriate use and stewardship

Nine companies offered additional information on education activities for patients and/or healthcare professionals (**Box 34**). As the examples show, partnerships with diverse national and international organisations and agencies have been an important component of these efforts.

BOX 34: **EXAMPLES OF EDUCATIONAL ACTIVITIES TO SUPPORT APPROPRIATE USE AND STEWARDSHIP**

- **bioMérieux's Partnership with Medical Education:** The diagnostics company bioMérieux worked in collaboration with the Center for Infectious Disease Research and Policy (CIDRAP), which launched an Antimicrobial Stewardship Project in July 2016 to build an online international community focused on antimicrobial stewardship. The collaboration's goal is to help leverage this valuable information source to raise the awareness of healthcare professionals, particularly antimicrobial prescribers, about the benefits of timely and accurate results to achieve effective antimicrobial stewardship.
- **Becton, Dickinson and Company (BD)'s Prevention Course in Hospital Acquired Infections Knowledge and Control:** BD, a diagnostics company, developed an online infection-control training course in collaboration with The Society for Healthcare Epidemiology of America (SHEA). Launched in 2020, the course consists of half-hour-long modules that provide participants with information on the fundamentals of infections prevention, best practices for preventing device-and-pathogen-associated infections, and disinfection and sterilisation procedures.
- **Viatris's Educational Programs to Update Healthcare Professionals:** Viatris, a generics company, participated in an educational programme in collaboration with the Indian Society of Critical Care Medicine (ISCCM). Topics covered include disease management of bacterial and fungal infections covering antimicrobial resistance and steps to overcome it. Viatris reported that 875 healthcare professionals had enrolled on the program at the time of reporting for this survey.
- **Teva Pharmaceuticals' 'Immunisations in a Pharmacy':** The Canadian generics company Teva Pharmaceuticals supported a campaign to reduce the incidence of viral diseases and, as a consequence, reduce AMR (since patients with a viral infection will commonly need antibiotics to treat parallel bacterial infection insurgence). As part of this campaign, Teva Pharmaceutical developed injection administration videos to instruct pharmacists on vaccine administration.
- **Novartis's Global Medical Affairs Stewardship Education Programme:** Novartis' generics function has designed and implemented online interactive educational modules addressing AMR, antimicrobial stewardship and clinical management of infectious disease to educate internal medical associates on the local implications

of AMR and antimicrobial stewardship. In addition, under the patronage of the Egyptian Ministry of Health and in collaboration with four specialised scientific associations, Novartis is engaged in the Egypt Anti-Infectives Stewardship Program. This scientific educational project seeks to establish consensus and develop national recommendations addressing proper diagnosis and optimal management of different types of infectious diseases and appropriate use of antimicrobial therapy.

- **Centrient Pharmaceuticals' Appropriate Use Campaign in China:** In partnership with the China Association of Health Promotion and Education, the generics company Centrient Pharmaceuticals launched an initiative to educate stakeholders on the importance of following national antibiotic prescription guidelines in China to safeguard the efficacy of antibiotics. The initiative involved designing and distributing brochures and posters for patient classroom training in hospitals and at doctors' conferences. The initiative was rolled out in 70 hospitals across 15 provinces and cities in China.
- **J&J Providing Education and Resources During COVID-19:** J&J is supporting essential vaccine education by organisations such as the American Nursing Association (ANA), National Black Nurses Association, Congressional Black Caucus Foundation, National Urban League and industry associations, such as the Biotechnology Industry Organization (BIO), and the Internal Federation of Pharmaceutical Manufacturers and Associations (IFPMA). They have created the COVID-19 Resources Center, powered by dialogEDU and created by the Johnson & Johnson Institute in collaboration with the Advances in Surgery (AIS) Channel, to help meet the immediate and pressing needs of surgeons and other healthcare professionals (HCPs) in relation to COVID-19.
- **GSK Pharmacist Education:** Pharmacists provide first-line support for patients in self-managing, self-limiting conditions like cold and flu and play a key role in improving patient understanding of the appropriate use of antibiotics. In 2019, GSK's Consumer Healthcare function and the Royal Pharmaceutical Society developed guidance and resources for pharmacy teams to improve consultations and help patients to better self-manage cold or flu in the context of AMR. The aim was to share practical resources for pharmacy teams to improve consultation skills and enable patients to better self-manage cold or flu, rather than resorting to antibiotics for these viral infections. In addition, during World Antibiotic Awareness Week, GSK held an event in collaboration with the Indian Medical Association (IMA) Healthcare Organisation (HCO) aimed at increasing awareness of global antimicrobial resistance and encouraging best practice among the general public, physicians & policymakers.
- **Pfizer Bug Bus:** For several years, Pfizer has conducted in-person and digital engagements around the WHO-sponsored World AMR Awareness Week. In 2020, The Pfizer Bug Bus went virtual, offering healthcare professionals and the general public experiences to educate themselves about AMR and steps to take to reduce the risk of infection. In 2020, the website was deployed in 15 countries – including Ghana, Malaysia, Mexico, Nigeria, Peru and South Africa – across five continents.

Three companies also provided more detailed case vignettes of their education and awareness-raising activities, which further bring to life AMRIA member efforts to support appropriate use and stewardship and how this is being pursued (See Boxes **35–37**).

BOX 35: BIOMÉRIEUX AND BD CONTRIBUTE TO TACKLING AMR IN RESOURCE-LIMITED COUNTRIES THROUGH CONTRIBUTIONS TO SURVEILLANCE INFRASTRUCTURE AND SHARING EXPERTISE IN THE FLEMING FUND SURVEILLANCE PROGRAMME

Aim: In 2019, bioMérieux and BD were selected by the Fleming Fund, a UK Aid Programme, to tackle antimicrobial resistance in LMICs worldwide. Among other aims, the Fleming Fund seeks to strengthen AMR-surveillance systems in LMICs by building laboratory and data management tools to expand AMR surveillance.

Implementation: As part of the programme, bioMérieux and BD support laboratories in LMIC countries where they have been respectively awarded by the Fleming Fund in Africa and the Asia Pacific with systems for the detection of infection and identification of antibiotic susceptibility. The companies' global health departments ensure coordination of all activities related to integrating the pathogen-identification and antibiotic-susceptibility testing systems into the clinical laboratories through meetings and communications with local implementers, regional teams and partner organisations. Ensuring successful integration is a challenging task as different countries have different requirements given lab specificities such as laboratory construction and renovation. As part of the program, bioMérieux additionally supports veterinary laboratories in the 18 countries with diagnostic tools to ensure a One Health approach to surveillance of AMR.

Influences on the effort: Collaboration with local/regional Mott MacDonald and company representatives, grantees and lab managers has been important for sustaining momentum setting up equipment in the laboratory facilities and ensuring ongoing progress during the COVID-19 pandemic.

Outcomes and impacts – realised and/or anticipated: Despite the challenging context of the COVID-19 pandemic, bioMérieux and BD note that significant progress was made in 2020 preparing laboratories to build capacity to engage with surveillance activities. With the support of in-country governments and Fleming partners, the companies continue to support installations of instruments and their routine use in 20 countries. Analyses carried out in these laboratories are expected to help establish robust antibiotic resistance surveillance systems and provide information on the evolution of pathogen resistance. This information is critical for the ultimate aim of improving patient treatment and is expected to contribute to the development of better-informed national policies against bacterial resistance.

BOX 36: SUMITOMO DAINIPPON PHARMA SURVEILLANCE RESEARCH SEEKS TO SUPPORT APPROPRIATE PRESCRIPTION AND USE OF ANTIMICROBIAL AGENTS IN VIETNAM

Aim: Sumitomo Dainippon Pharma has invested in surveillance research to support the appropriate prescription and use of antimicrobial agents in Vietnam. The work is expected to help inform capability-building and evidence-based practice by healthcare professionals and minimise the risk of emerging drug resistance due to inappropriate use. The project focuses on four pathogens: *Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa* and *Acinetobacter baumannii*. It involves five products, including meropenem, imipenem, doripenem, colistin and tigecycline.

Implementation: The company conducts one surveillance study every two years supported by company investment. The work entails collaboration between the Ministry of Health of Vietnam, Sumitomo Dainippon Pharma, the National Center for Global Health and Medicine and ten major local hospitals. The research involves a detailed cohort investigation into the development of resistance to the antibiotics used as the primary treatment option for severe and intractable infections in Vietnam.

Influences on the effort: According to the survey respondents from Sumitomo Dainippon Pharma, implementing the surveillance study required investment in relationship-building between industry and public-sector partners because such relationships enable progress with surveillance activities. The company also compiled training materials on antimicrobial resistance for healthcare professionals and were seen as helpful for enabling the surveillance study. However, the COVID-19 pandemic led to some challenges to in-person related activities in the surveillance study, such as on-site assessments of the appropriate prescription and use of antimicrobial agents and training. Securing sustainable financing for future surveillance research is also a challenge.

Outcomes and impacts – realised and/or anticipated: Since study reporting was not finalised at the time of the AMRIA 2021 survey, it is too early to report on impacts. Some preliminary findings were shared in poster form at ECCMID 2021 (European Congress of Clinical Microbiology & Infectious Diseases), which took place online from 9–12 July 2021. Sumitomo Dainippon Pharma hopes to expand the scope of surveillance research activities in the future to include the animal sector, in line with a One Health approach.

BOX 37: SHIONOGI PARTNERS WITH NATURE TO RAISE AWARENESS ABOUT THE GROWING AMR THREAT AND ADVOCATE FOR INNOVATION IN ANTIBIOTIC DEVELOPMENT

Aim: With headquarters in Japan, Shionogi & Co., Ltd. worked with Nature Publishing Group to contribute to a *Nature Outlook* supplement on AMR ('Antimicrobial Resistance – Preserving the power of life-saving drugs').[193] The supplement covers content related to raising awareness about the threat of AMR, highlights areas in need of policy action and provides educational information on advancements in efforts to tackle AMR. Shionogi's contribution to the supplement aimed to continue building awareness about AMR and to share Shionogi's call for action on policies needed to reduce AMR.

Implementation: Nature approached Shionogi with the opportunity to sponsor an 'Outlook' section of the journal, which would support topics associated with antimicrobial resistance. The content was editorially independent, meaning that Shionogi did not have any influence or input into any of the articles aside from the one article they contributed. Shionogi's article discussed the scientific and economic challenges associated with antibiotic development and advocated for several policy changes to address the AMR crisis. Shionogi also issued a call to action to incentivise the development and commercialisation of innovative antibiotics.

Influences on the effort: According to the Shionogi survey respondent, the profile of the Nature brand and the recognition given to AMR by Nature supported efforts to achieve impact. However, the COVID-19 pandemic has accentuated challenges to dissemination efforts as there have been fewer opportunities for sharing insights at conferences and other events.

Outcomes and impacts – realised and/or anticipated: Both English- and Japanese-language versions of the supplement were made accessible in October 2020 and January 2021, respectively. The supplement has been a helpful tool for Shionogi's efforts to raise awareness about AMR and about policy options that may be needed to address it. Shionogi has been able to share these materials with outside organisations and key opinion leaders, e.g. in the United States Congressional offices when educational content has been requested. This publication has also been shared through other media like the AMR Solutions newsletter.[194] According to the Shionogi survey respondent, many of the articles in the supplement could help readers understand how advocacy activities can contribute to policy actions. This publication is expected to continue to serve as an educational resource and tool for improved AMR awareness.

The majority of Alliance members who engage in educational activities included material for healthcare professionals in promotional activity, and over half reviewed promotional activities against stewardship goals.

As part of the effort to ensure that pharmaceutical promotional practices were consistent with the goal of advancing appropriate use and stewardship, the majority of surveyed Alliance members (87%) that participated in initiatives to help educate and raise awareness about appropriate use and stewardship included AMR educational material for healthcare professionals in promotional activity. Over half (57%) review promotional activities against stewardship goals. Other key efforts pursued by somewhat fewer companies included evaluating promotional material against guidelines (39%), reviewing sales representative incentive schemes (26%) and engaging in risk-benefit assessments of products and/or technologies regarding appropriate use and stewardship (22%). Some examples of initiatives implemented by Alliance members to ensure pharmaceutical promotional practices consistent with the goal of advancing appropriate use and stewardship are shared in **Box 38**.

The Alliance in Action: Ensuring that pharmaceutical promotional practices were consistent with the goal of advancing appropriate use and stewardship

BOX 38: EXAMPLE INITIATIVES TO ENSURE PHARMACEUTICAL PROMOTIONAL PRACTICES WERE CONSISTENT WITH THE GOAL OF ADVANCING APPROPRIATE USE AND STEWARDSHIP

Ethics and Compliance:

- **bioMérieux Ethics & Compliance Program** promotes ethical business conduct per regulations, trains employees on ethical standards, and allows those who have questions or concerns to express them. In order to abide by the multiple local or regional legal requirements and *in-vitro* diagnostics (IVD)/ medical devices (MD) industry code rules, bioMerieux's Compliance Department has developed a robust HCPs/ HCOs interactions Compliance Program. This program involves (i) training all concerned employees on HCPs/HCOs rules and constraints and (ii) implementing a detailed process whereby every interaction with HCPs/HCOs is first controlled and validated by the Compliance Department before being contracted. This directive is applied to all company activity, including AMR activity.
- Based on guidelines from organisations such as WHO and the CDC, MSD's **'Star of Stewardship' framework** guides the pharma company's efforts to support optimal patient-centred antimicrobial stewardship (AMS). The framework ensures that the right drug is given at an appropriate dose for an adequate duration in the ideal care setting based on an accurate diagnosis, and therapy is narrowed when possible. Using this framework, MSD regularly examines, reviews and updates its promotional materials.

The use of unbranded materials:

- **GSK runs its own AMR educational programme** directed at healthcare professionals worldwide, on AMR in the context of illnesses where antibiotics are commonly prescribed, including lower respiratory tract infections and uncomplicated urinary tract infections. Content for these events is developed independently from the pharmaceutical company's marketing department using unbranded materials. In addition, no financial or material incentives are offered to participants.
- **The generics company Fresenius Kabi recently launched an AMS campaign in France.** The campaign took place in November 2020 during the 'World Antimicrobial Awareness Week' and on 'European Antibiotic Awareness Day'. No financial incentive was offered to participants, and no product name was mentioned on any of these tools (although they were company branded).

- When participating in meetings, speakers from the generics company **Viatris need to agree to the following statement as a company requirement:** 'The program is primarily dedicated to promoting objective scientific and educational activities. No product promotion will be done at said program.'

Removing volume-based incentives for anti-infectives sales representatives:

- The pharmaceutical company MSD is exploring new approaches in certain countries to field-sales-representative compensation that supports AMS, including pilots where field sales representatives are not incentivised based on sales volume of antibiotics.
- In 2020, the pharmaceutical **company Pfizer implemented Global Minimum Incentive Standards (GMIS)**. One element of these standards is that sales representatives' incentive plans must be based on at least 15% qualitative rather than quantitative factors. In addition, Pfizer has removed sales incentives for their anti-infectives field force in the UK. Colleagues in the UK are measured through Management-Based Objectives, focusing on generating access to medicines and promoting appropriate use.

Third-party providers to deliver educational activities:

- **Healthcare professional education on TB:** The J&J pharmaceutical company is involved in educational activities directed at healthcare professionals with comprehensive conflict of interest (COI) mitigation in place. Since 2016, J&J has supported training for over 25,000 healthcare workers in 13 countries on treating TB. To mitigate conflicts of interest, J&J provides financial resources to independent third parties to develop the programs. These include unrestricted educational grants in sub-Saharan Africa, providing medical education on the appropriate use of anti-TB drugs in China, a webinar series in Indonesia, and an online learning platform in the Philippines on treating MDR-TB.

Over half of Alliance members collected surveillance data to inform their appropriate use and stewardship activities. Of these, over half shared it externally as part of their commitment to collaborative efforts.

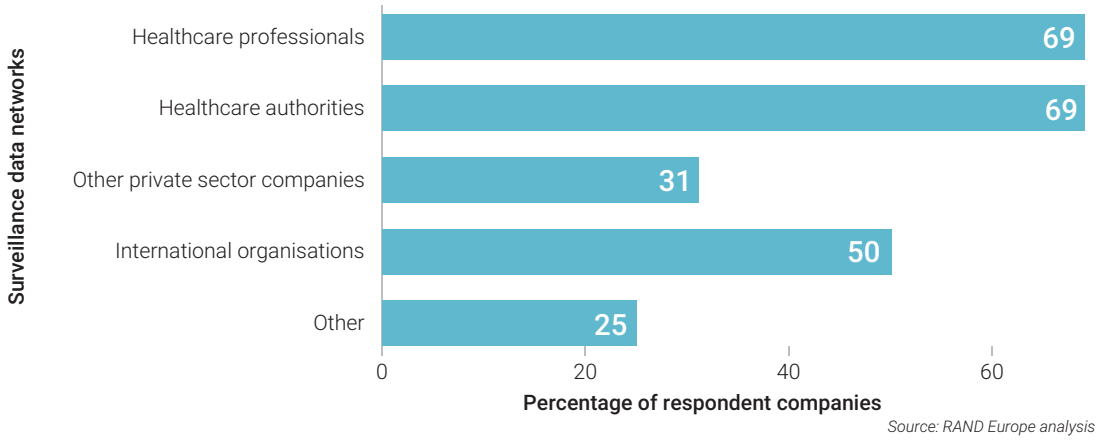
Across the Alliance, around half of surveyed members (51%) reported that they collected surveillance data. For the remainder, companies reported that collecting surveillance data did not apply to their business model (21%) or that they did not engage in this activity during the survey reporting timeframe (28%). Collecting surveillance data was more common amongst R&D pharmaceutical and diagnostics companies (83% of R&D pharmaceutical and 80% of diagnostics companies). A smaller percentage of generics companies reported collecting such data (33%).[195] Similarly, just over a third (37%) of biotech/SMEs reported collecting surveillance data and found it relevant to their activities, while approximately a third felt it was not relevant to their business model.[196]

Among the 27 companies that reported collecting surveillance data, nearly three-quarters collected data on resistance trends (74%), and over two-thirds collected data on antimicrobial sensitivity (67%). Other areas included data on resistance mechanisms (48%), antimicrobial prescription or post-market surveillance (30%), and outbreaks (22%). There is expected variety in the types of data collected across different sectors, in line with the types of activities they focus on and the stages of products in their development pathways. For example, data on resistance mechanisms were not collected by diagnostics-sector or generics-sector companies as they do not develop antimicrobials.

Of the 27 companies that collected surveillance data, 70% collected data on the pathogen species and 48% on the pathogen genus. Over half (52%) of companies that collected surveillance data did so at the hospital level, 41% at the in-country regional level and 41% at the country level.

Over half of Alliance members that collected surveillance data (59%) shared the data externally. Data sharing activities varied by sector, in line with the focus of company activity.[197] Data were shared with diverse stakeholders, most frequently with healthcare professionals, healthcare authorities and international organisations (**Figure 10**). Around a third of companies sharing surveillance data also stated that they shared data with other private sector companies.

FIGURE 10: PARTIES WITH WHICH COMPANIES SHARED SURVEILLANCE DATA (N=27)



Source: RAND Europe analysis

Alliance members shared data through various means,[198] including through conference presentations (81%), peer-reviewed publications (75%), and face-to-face meetings and workshops (56%). Data were also shared through company-owned open-access databases (25% of all companies who engaged in some form of data sharing), white paper publications (25%), company-owned licensed databases (19%) and external open-access databases (6%).

The Alliance in Action: research and surveillance to support antimicrobial stewardship

Box 39 provides an example of how surveillance activities and other factors are helping tackle the threat of AMR and supporting antimicrobial stewardship.

BOX 39: MSD FUNDS RESEARCH TO IMPROVE ANTIMICROBIAL STEWARDSHIP AND MAKES USE OF SURVEILLANCE DATA AS PART OF ITS WIDER EFFORTS TO PROMOTE APPROPRIATE ANTIBIOTIC USE AND EFFECTIVE STEWARDSHIP

Aim: MSD aims to contribute to good antimicrobial stewardship (AMS) by supporting the implementation of AMS programs and funding studies in this area.

Implementation: MSD has also worked with over 1,100 hospitals in 28 countries as an AMS resource and partner to develop and implement patient-centric, product-agnostic AMS programs around the world.[199]

Influences on the effort: MSD serves as an AMS resource, helping hospitals worldwide to develop and implement patient-centred AMS programs that are customised at the local level based on factors including epidemiology, clinical setting and resource availability. The ability to tailor programs to local factors requires the availability of hospital surveillance data, awareness of prescribing patterns, broad recognition of the significant threat posed by antimicrobial resistance and multi-disciplinary collaboration. Subsequently, AMS programs can use a range of strategies customised to the hospital, including prospective auditing of prescriptions, algorithms or empirical therapy flow charts for the prescription or modification of therapy and tools that support therapeutic decision-making.

Outcomes and impacts – realised and/or anticipated: In terms of impacts from activities during the AMRIA progress survey period, MSD supported the early implementation of AMS programs at three hospitals in EsSalud, Peru. Consequently, the consumption of broad-spectrum antimicrobials was reduced by 30-50% in two of these three hospitals following MSD's contributions to enhancing their AMS-program infrastructure through resources and processes. These research results were published in the Chilean Journal of Infectiology and recognised by the Kaelin Research Award in 2020.[200]

Research on antimicrobial use and stewardship is also supported by some Alliance members.

Four Alliance members also offered additional qualitative information showing that they supported stewardship and appropriate use of AMR-relevant products or technologies by funding or contributing to research programmes that supported appropriate use and stewardship agendas (**Box 40**).

The Alliance in Action

BOX 40: **RESEARCH PROGRAMMES ON ANTIMICROBIAL STEWARDSHIP SUPPORTED BY ALLIANCE MEMBERS**

- The diagnostics company bioMerieux funds the Global Point Prevalence Survey of Antimicrobial Consumption and Resistance, designed to provide annual global 'snapshots' of antibiotic use and resistance in hospitals worldwide and managed by the University of Antwerp (Belgium).
- The pharmaceutical company MSD supports Antimicrobial Stewardship Research through Merck's AMS Investigator Initiated Studies program, which generates research to support the implementation of AMS principles across the globe, including over 20% of studies occurring in LMICs.
- The pharmaceutical company J&J has developed the Nurses Innovate QuickFire Challenge Series that invites nurses to develop and share novel treatment approaches, awarding up to US$100,000 in grant funding to nurse innovators alongside access to mentoring from J&J and access to the JLABS ecosystem to develop their ideas.
- The pharmaceutical company Pfizer's Request for Grants program provides external researchers and institutions with funding to support research, education and implementation of stewardship-related programmes.

5.3. PROMOTING THE RESPONSIBLE USE OF AMR-RELEVANT PRODUCTS AND/OR TECHNOLOGIES IN ANIMALS

Five companies (three R&D pharmaceutical companies, one generics company and one diagnostics company) reported that they developed or commercialised products and/or technologies licensed for animal use. To promote responsible use of AMR-relevant products or technologies in animals, three companies described setting corporate policies on animal welfare and developing vaccines in line with a 'One Health' approach to minimise the need for antibiotics. The remaining two companies reported commercialising susceptibility tests for veterinary use, partnering with farmers and veterinarians to promote vaccination/appropriate use/stewardship, and collaborating with animal health and environmental organisations. One company elaborated on their activities (see **Box 41)**.

BOX 41: **AN EXAMPLE FROM THE GROUND: MSD'S ONE HEALTH APPROACH TO TACKLING AMR**

The R&D pharmaceutical company MSD takes on a One Health approach to AMR

MSD collaborates with partners and stakeholders to ensure antibiotics are effective now and in the future for all species to attain optimal health for people, animals and our environment. As such, they have multiple initiatives in place to help farmers protect animal health and ensure a safe food supply:

- **'Time to Vaccinate':** A European program designed to help farmers better recognise the benefits of vaccinating their cattle to prevent disease.
- **Whisper® Veterinary Stethoscope System:** A non-invasive technology that can quickly measure the severity of bovine respiratory disease, allowing appropriate treatment to be selected early and antibiotic use reduced overall.
- **IDAL intra-dermal injection:** An injection system for swine which helps farmers vaccinate large numbers of pigs safely and efficiently while supporting pigs' well-being.
- **Merck Animal Health Intelligence:** An operating unit within the company focused on digital tracking, data collection and management tools to enable farmers and animal caretakers to optimise animal-health-and-well-being management.
- **World Organisation for Animal Health (OIE) and Codex Alimentarius:** Merck Animal Health has a long-standing involvement in OIE and Codex Alimentarius to develop and advance science-based international standards for responsible antibiotic use.

For a reflection on the Alliance's next steps in relation to appropriate use, please see Section 7.3.

6. MANUFACTURING AND THE ENVIRONMENT

6.1. ALLIANCE COMMITMENTS ON ANTIBIOTIC MANUFACTURING AND THE ENVIRONMENT

The primary source of Pharmaceuticals in the Environment (PIE) is via patient excretion following medication taken to prevent, cure or alleviate a medical condition. A comparatively smaller contribution to PIE stems from emissions from industry during the manufacture of pharmaceuticals.[201] While the overall contribution of pharmaceutical manufacturing to PIE is relatively low, there is a potential for localised impacts to be created in cases where manufacturing emissions are inadequately managed.[202] Responsible antibiotic manufacturing is essential for reducing the environmental risks associated with the production of antibiotics and for mitigating the risk of AMR. The AMRIA has been committed to safe and environmentally responsible antibiotic manufacturing across the supply chain. In 2018, manufacturing members of the Alliance developed the Common Antibiotic Manufacturing Framework[203] (CAMF or 'the framework'), which offers companies a methodology for performing risk assessment and providing the minimum site requirements to meet environmental standards, including auditing requirements to ensure adherence to CAMF requirements. Alliance members have also established science-based targets (known as predicted no-effect concentrations [PNEC]) for receiving waters impacted by the production of antibiotics for approximately 120 different agents. PNECs represent exceedingly low concentrations of antibiotics (e.g. microgram per litre [parts per billion]).[204]

The Alliance has long-standing commitments related to antibiotic manufacturing (**Box 42**).

BOX 42: **MANUFACTURING AND ENVIRONMENTAL COMMITMENTS**[205]

- Review Alliance members' own manufacturing and supply chains to assess good practices in controlling the release of antibiotics into the environment.
- Establish a common framework for managing antibiotic discharge and start applying it across their own manufacturing and supply chains by 2018; continue to implement the framework in the following years 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 discharge targets are met.

Over time, the Alliance's antibiotic manufacturing membership expanded from 13 manufacturing members at the start of the Alliance in 2017 to 20 members at the time of the survey in 2021, with some manufactures leaving the Alliance and others joining during this timeframe. At the time of the survey, Alliance founding members had approximately 2.5 years since the Framework and PNECs' publication to meet the stipulated requirements. In contrast, newer members had less time (between 0–2 years) to meet these requirements. Therefore, where appropriate, we have specifically highlighted the performance of the nine founding Alliance manufacturing members when reporting Alliance manufacturing performance in this section, recognising that making progress against the Framework and PNECs is not automatic but takes a dedicated time commitment.

AMRIA members have made significant achievements in implementing Alliance manufacturing requirements at manufacturing sites owned by member companies. As we elaborate on in the contents that follow, 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 Predicted No-effect Concentration (PNEC) Targets (87%). Alliance members also manufacture products at direct supplier sites, and 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% meeting these targets.

6.2. ASSESSMENT OF ANTIBIOTIC MANUFACTURING SITES AND PRODUCTS OWNED BY ALLIANCE MEMBERS

BOX 43: **SUMMARY OF THE ASSESSMENT OF ALLIANCE-MEMBER ANTIBIOTIC MANUFACTURING SITES AND PRODUCTS AMONGST SURVEYED COMPANIES**

HIGHLIGHTS:

- Overall, 85% of Alliance members and 100% of founding members with their own antibiotic manufacturing sites have completed audits on meeting CAMF requirements at least every five years.
- Nearly two-thirds (65%) of Alliance members with their own manufacturing sites met all of the 'Audits of Antibiotic Manufacturers' requirements and followed PSCI audit best practice.
- Some 85% of Alliance members with their own manufacturing sites reported having adequate internal[206] and external reviews[207] of sites in place to verify that the required operating conditions and practices are appropriately followed.
- The majority of antibiotic manufacturing sites owned by Alliance members and assessed against CAMF (76%) met all CAMF requirements fully. Overall, 98% met requirements either fully or partially.
- Some 90% of Alliance members with their own manufacturing sites reported having adequate mechanisms to respond to audit findings.
- Nearly two-thirds (65%) of Alliance members with their own manufacturing sites have assessed *all* antibiotic products produced at their manufacturing sites against PNEC targets.
- The vast majority of products (88% manufactured at sites owned by Alliance members with manufacturing operations; n=1,074 products) have been assessed against PNEC targets, and 87% of assessed antibiotic products meet them.

85% of Alliance members with antibiotic manufacturing operations completed audits on meeting key requirements of the Common Antibiotic Manufacturing Framework at least every five years.

Twenty surveyed Alliance members[208] across large R&D pharmaceutical and generics sectors report that they manufactured antibiotics at their own manufacturing sites.[209] These members reported a range of 1 to 35 own manufacturing sites, with a median of 5 and a mean of approximately 11. In total, Alliance members reported having 211 own antibiotic manufacturing sites.

Most Alliance members (85%)[210] reported that they complete these audits at least every five years, including all founding Alliance members[211] (100%) and nearly three quarters (73%)[212] of newer members. There is opportunity for further progress to be made on this front amongst newer members who do not yet complete audits of this nature.

Nearly two-thirds of Alliance members with their own manufacturing sites met all the of 'Audits of Antibiotic Manufacturers' requirements and followed PSCI audit best practice.

Almost two-thirds of surveyed Alliance members with their own manufacturing sites (65%),[213] including the vast majority of founding manufacturing members (89%),[214] reported meeting all 'Audits of Antibiotic Manufacturers' requirements and followed PSCI-audit best practice, and there is scope for some improvement towards ensuring all Alliance members do so in the future. A quarter (25%)[215] of Alliance members with their own manufacturing sites reported having some 'Audits of Antibiotic Manufacturers' requirements in place and followed some elements of PSCI-audit best practices, and 10%[216] reported having no requirements in place and did not follow elements of PSCI-audit best practice. Based on this information, the Alliance may have an opportunity to engage with newer members on this aspect of Alliance activity.

Of the 20 surveyed Alliance members with their own antibiotic manufacturing sites, the majority (85%)[217] reported that they had an adequate *internal* review of sites to verify that the required operating conditions and practices are in place and appropriately followed, as required by CAMF. All founding members had adequate internal review processes in place. Overall, 15%of companies with their own manufacturing sites reported an inadequate internal review of sites,[218] as some members may need more time to implement these reviews. Similarly, 80%[219] of companies with their own manufacturing sites reported that they had adequate *external* reviews of sites in place (including 89% of founding members).

A majority of Alliance members with their own manufacturing sites have been assessed against CAMF, and 76% fully met CAMF requirements.

Alliance members reported that 179 out of 211 antibiotic manufacturing sites owned by companies with their own manufacturing operations (85%) have been assessed against the CAMF criteria. The majority of Alliance members with manufacturing sites (80%) reported assessing all their sites, 10% reported assessing some but not all, and 10% reported not assessing any sites. Of the Alliance members that have not yet assessed all their sites (n=4), one expected to do so within a year, one within three years, and one reported that this would take more than three years. The fourth site did not provide a timeline for an assessment.

Based on survey responses, a majority (76%) of antibiotic manufacturing sites assessed against CAMF fully met all requirements. A further 22% partially met CAMF requirements, and 2% did not meet CAMF requirements. Therefore, 98% met requirements either fully or partially.[220]

Among the 18 companies that had assessed at least one of their own manufacturing sites against the CAMF criteria during the survey reporting period, the majority (78%; n=14) reported that all their sites fully meet the CAMF requirements. A further 17% (n=3 sites) reported that all their sites either fully or partially meet requirements. Only one company (5%) reported that some of their assessed sites do not meet CAMF requirements.[221], [222]

Nearly half of Alliance members with their own manufacturing sites (45%) provided information on the types of actions they took to ensure these sites meet the CAMF requirements.[223] Examples of such actions include conducting regular audits, developing corrective and preventive action (CAPA) plans or other plans for improvement, implementing a global operating procedure (with global- and site-level responsibility for implementation and training), and closing sites that did not fully meet the CAMF.[224]

Overall, 90% of surveyed companies with their own antibiotic manufacturing sites reported having adequate mechanisms in place to respond to audit findings.

Of the 20 surveyed Alliance members with their own manufacturing sites, 90%[225] reported that they have adequate mechanisms in place to ensure that their sites pro-actively respond to audit findings, as required by CAMF, to minimise environmental impact. All founding members had such measures in place. The survey found that one Alliance member reported inadequate mechanisms, and another reported no mechanisms to enable a proactive response to audit findings.

Nearly two-thirds of Alliance members have assessed all antibiotics produced at their manufacturing sites against PNEC targets.

Surveyed Alliance members reported a total of 1,226 antibiotic products under manufacture at their sites, with a range of 1–551 products per site (median=30.5; mean=61.3). In total, nearly two-thirds (65%)[226] of Alliance members with manufacturing sites – including all founding members – reported assessing all products against PNEC targets. Four companies (20%) reported assessing some, but not all the products manufactured at their own sites and three (15%) reported assessing none of their products against PNEC targets. There is an opportunity for the Alliance to engage with newer members who have not yet assessed all their products, supporting further progress in this area.

A vast majority of products manufactured at Alliance member sites have been assessed against PNEC targets, and most met these targets.

A total of 1,074 out of 1,226 products (88%) manufactured at Alliance member sites had been assessed against PNEC targets, with 87% of the assessed products meeting the targets. Among the 17 Alliance manufacturers that had assessed at least one of the products against PNEC targets, 11 companies (65%) reported that *all* assessed products met PNEC targets. The remaining six Alliance members (35%) reported that between 54% and 95% of their products met PNEC targets.

For the six Alliance members with at least some products not meeting the PNEC targets, two companies reported that they expect all their products to meet PNEC targets within a year, and two companies expected their products to meet the targets in 2–3 years. The remaining two companies reported that products manufactured at their sites would meet PNEC targets in 4–5 years.

The Alliance in Action

Boxes 44–**46** provide illustrative examples of Alliance member activities to ensure responsible antibiotic manufacturing and minimise undesirable environmental impacts.

BOX 44: CENTRIENT INVESTS IN EFFORTS TO IMPROVE THE ANTIBIOTICS MANUFACTURING SUPPLIERS AND OWN ANTIBIOTICS MANUFACTURING PNEC COMPLIANCE

Aims: The global generics company Centrient Pharmaceuticals is a long-standing advocate for industry action against AMR from manufacturing emissions. Centrient's global sustainability strategy includes an AMR-free supply chain as one of its strategic objectives. The company sought to improve its supply chain to mitigate the spread of AMR.

Implementation: Centrient joined AMRIA in 2017. In 2019, Centrient assessed its entire supply chain for compliance with the Common Antibiotic Manufacturing Framework (CAMF). While Centrient's own manufacturing sites were compliant, some of Centrient's antibiotic suppliers were not fully compliant with CAMF, with the lack of quantification of residual antibiotics in wastewater streams being a key challenge.

In 2019, Centrient launched Project PNEC (Predicted No-Effect Concentration) with the objective of making the supply chain fully compliant. PNEC concentrations refer to the concentrations of substances in the environment below which it is unlikely that adverse effects would occur. The results of a compliance assessment were communicated to suppliers with guidance on how to act on the findings. Centrient supported supplier on both mass balance and analytical testing of the residual antibiotics in the wastewater streams. The results of assessments of supplier compliance with PNEC were checked by Centrient, using the guidance document from The Pharmaceutical Supply Chain Initiative (PSCI).

In 2020, Centrient launched a second AMR assessment survey for suppliers, revised according to AMRIA expectations on best practices to comply with CAMF and PNEC target values. The survey results reported significant improvement in practices to minimise AMR risk. Centrient reports that all its suppliers were 100% compliant with PNEC target values in 2020. Centrient asked suppliers to report quarterly in relation to testing methods.

From 2019 onwards, Centrient strengthened its PNEC measurement program through analytical method validation and improved sampling methods to ensure all its own manufacturing sites are fully compliant with PNEC targets (at the time of the survey, all but one of the company's own sites were compliant with PNEC target values). Centrient developed the International Standard Operating Procedure (ISOP) for testing, monitoring and reporting PNEC target values. Centrient Pharmaceuticals is firmly committed to being compliant with PNEC by 2021.

Influences on effort: Centrient experienced challenging technical issues (e.g. identifying partners who could develop and validate analytical testing methods) and natural resistance to implementing changes. However, Centrient's commitment to AMR containment and consistent messaging, guidance and technical support from the AMRIA helped the effort.

Outcomes and impacts – realised and/or anticipated: As a result of this effort, Centrient reports that, with one exception, all its own sites and suppliers' sites are compliant with PNEC target values as published by AMRIA. The last site is expected to be compliant by the end of 2021.

BOX 45: **NBG LABORATORIES INVESTS IN IMPROVING MANUFACTURING FACILITIES TO SUPPORT ZERO DISCHARGE OF ANTIBIOTICS INTO THE ENVIRONMENT**

Aim: Based in India, the generics company NGB Laboratories Pvt. Ltd.[227] engaged in activities to try to eliminate or minimise any antibiotic release in the environment during manufacturing processes.

Implementation: In 2019 and 2020, NGB Laboratories invested in building a zero-discharge plant. In doing so, NGB laboratories collaborated with an environmental testing laboratory[228] and a consultant. This cross-functional team consisted of representatives from internal planning, manufacturing, engineering, environment Health Safety (EHS) alongside an environmental consultant and externally certified analytical environment-testing laboratory.[229] Once it became clear that subscription to the government-approved CETP (Central Effluent Treatment Plant)[230] was not possible (since it was already running at full capacity), the team held a workshop to brainstorm ideas for creating its own effluent treatment plant (ETP) to send the liquid discharge for NGB's effluent treatment. The ZLD (Zero liquid discharge) design was considered to create NGB's own ETP, involving the water balance based on all inputs and outputs and subsequent design. This consisted of pre-treatment, treatment, reverse osmosis and multiple evaporation types, etc.
Influences on the effort: NGB Laboratories' ability to identify appropriate vendors to design and implement the installation and operation of the Effluent Treatment Plant was a key enabler. However, analytical testing of the API proved challenging and was ultimately not possible. Helpful guidance was received from another AMRIA member to develop the mass-balance approach to calculate the quantum of discharge in the ETP system instead.

Outcomes and impacts – realised and/or anticipated: Since building a zero-liquid discharge (ZLD) plant, the NGB survey respondent noted that the company no longer worries about liquid discharge, reducing its concerns about activities and activism taking place in India.[231] The environmental clearance consent and certifications granted to the ZLD after due verification by the authorities are available on record. According to an NGB survey respondent, the company hopes these improvements will give it a favourable position in manufacturing supplier tenders, given its AMR-compliant manufacturing. NGB has installed an electronic flow meter in the inlet of the ETP plant and measures the most efficient consumption of treated water in the cooling towers/boiler; only excess requirements are met using the industrial water supply.

BOX 46: **NOVARTIS' VIRTUAL AUDITING PROGRAMME**

Aims: Novartis' broad internal network of manufacturing sites and a significant external supplier network are supported by the company's auditing program. This programme aims to ensure that Novartis' standards and commitments are achieved, including evaluating this complex network to avoid potential impacts from pharmaceuticals in the environment.

Implementation: To meet the challenge of restricted travel during the Covid-19 pandemic, Novartis set about implementing a virtual auditing programme of their internal and external manufacturing network. The approach included a structured, explicit documentation request in advance of site virtual visits and, where possible, pre-recorded videos of identified areas to supplement live video streams of the sites during the audit. The technology used was a mixture of helmet-mounted cameras and iPhone video links. Novartis utilised the Microsoft Teams platform throughout the process and found it effective in delivering interviews and live streams to assess site infrastructure.

Outcomes and impacts – realised and/or anticipated: The outcome was a complete program planned and delivered in 2021. There was no compromise for the 2021 audit schedule since the virtual plan was in place, a full scope of requirements was set and audits were completed using portable video technology. Being on-site in the traditional sense allows auditors a flexible approach where they can view and inspect the equipment and structure of the site in more detail, whereas the video stream is less dynamic. However, with auditors now gaining much more experience in planning and executing virtual audits using technology, this approach should allow subject matter experts to join audits on a more frequent basis without the inconvenience or environmental impact of travel.

As a result of Novartis' experience during the pandemic, virtual audits will become an integral part of the company's future audit programmes. This strategy allows for a more dynamic approach, enabling a choice between a traditional style or virtual hybrid with the bonus of having additional auditors join for all or part of the audit with minimal business impact while supporting business objectives.

6.3. ASSESSING DIRECT SUPPLIER SITES AND PRODUCTS AGAINST CAMF CRITERIA AND PNEC TARGETS

BOX 47: **SUMMARY OF THE ASSESSMENT OF ALLIANCE-MEMBER DIRECT SUPPLIERS AND PRODUCTS AMONGST SURVEYED COMPANIES**

HIGHLIGHTS:

- Overall, 90% of Alliance member companies engaged with manufacturing activity reported manufacturing at direct supplier sites in addition to their own sites. The majority of direct supplier sites (86%) have had CAMF requirements conveyed to them by Alliance members.
- Two-thirds (67%) of Alliance members that manufacture antibiotics at direct supplier sites report auditing these sites against the Framework requirements at least every five years to ensure they minimise environmental impact. All founding members of the Alliance with direct supplier sites report auditing these sites.
- Some 44% of direct supplier sites of Alliance members with at least one direct antibiotic manufacturing supplier have been assessed against CAMF requirements. Alliance members reported that 50% of the assessed sites fully met CAMF requirements.
- Just under a third (30%) of companies reporting on direct supplier site assessments have assessed all their supplier sites against CAMF requirements.
- Some 42% of products manufactured at supplier sites have been assessed against PNEC targets, of which 73% met the targets.
- An opportunity exists for members to leverage implementation experience to date (their own and supplier sites) to drive greater implementation of both the framework and PNECs at supplier sites. Implementing AMRIA requirements at supplier sites is understood to be more challenging than a member's own sites, typically due to a lesser degree of control. In addition, some members have prioritised implementation of AMRIA requirements at their own sites and focused on their suppliers more recently (which can number in the hundreds in some cases).
- Continual progress over time has been made on responsible antibiotic manufacturing by Alliance members.

Overall, 90% of Alliance members with antibiotic manufacturing sites also manufactured products at direct supplier sites. The majority of direct suppliers have had CAMF requirements conveyed to them by the Alliance.

Across the Alliance, 90%of surveyed members reported that they manufacture antibiotics at direct supplier sites in addition to their own sites.[232] This ranged from 82% of newer Alliance members[233] to 100% of founding members.[234] Alliance members reported a total of 821 direct supplier sites, ranging from 0–250 direct supplier sites per member.

The majority of direct supplier sites (86%)[235] have had CAMF requirements conveyed to them by the Alliance. In total, 59% of Alliance members with at least one direct supplier site[236] reported conveying CAMF to all their direct supplier sites, 29%[237] reported conveying the framework to some sites and 12%[238] reported not conveying it to any of their direct supplier sites.[239]

Ten Alliance members[240] offered additional information to illustrate the nature of actions taken to convey the expectations of CAMF to direct antibiotic manufacturing suppliers. Examples included establishing supplier codes of conduct, incorporating CAMF requirements into supplier assessments and audits, developing questionnaires to all direct suppliers to better understand compliance with the CAMF requirements, and establishing initiatives to better communicate and assess supplier compliance with CAMF requirements (e.g., specifying requirements in written communication to suppliers).

Two-thirds of Alliance members' direct manufacturing supplier sites are audited at least every five years against CAMF requirements. All founding members who have direct supplier sites reported auditing these sites.

Of the 18 surveyed Alliance members that manufacture antibiotics at direct supplier sites, 67%[241] of companies reported they audited these sites at least every five years to ensure that they minimise their environmental impact, as required by CAMF. This percentage ranged from 33% of newer members with direct supplier sites to 100% of founding manufacturing members. Newer members may need more time to enhance activities in this sphere in the years to come.

Alliance members reported that 44% of direct supplier sites had been assessed against CAMF requirements. Half of assessed sites fully meet requirements (50%). These data suggest an opportunity for AMRIA members to share learning and experience in support of improvements at supplier sites that do not currently meet CAMF requirements.

Among 17[242] Alliance members with at least one direct antibiotic manufacturing supplier, two (12%) reported not knowing whether their sites had been assessed or not and are therefore excluded from further analysis. Later in the survey, another two[243] reported not having assessed any sites. Across the remaining 13 Alliance members, 359 out of 821 direct supplier sites had been assessed against CAMF requirements (44%), ranging from 2–102 suppliers per member assessed against CAMF (median=14; mean=27.6). Just under a third (31%) of the 13 companies reporting on direct supplier site assessment reported having assessed all their supplier sites against CAMF requirements. This may represent an area where activity could be enhanced in future years.

A total of 13 surveyed Alliance members reported having assessed at least one of their direct suppliers against the CAMF criteria,[244] accounting for 359 direct supplier sites. However, upon responding to more granular questions, they provided information on 330 sites. Half of these supplier sites (50%; 166 out of 330) met CAMF requirements fully, 12% partially (41 out of 330), and 37% did not meet CAMF requirements (123 out of 330). Two (15%) of the Alliance members who assessed at least one site report that all supplier sites fully met CAMF criteria, four (31%) reported that all their supplier sites either fully or partially meet CAMF requirements, and seven (54%) reported that one or more of their direct supplier sites did not meet CAMF criteria.

Many Alliance members reported assessing some of their direct supplier sites but not all of them. Amongst the 13 companies that reported assessing at least one direct antibiotic

manufacturing supplier, 31%[245] reported that they had assessed all their supplier sites and 69%[246] reported that they had assessed some sites. Among founding members of the Alliance, the percentage of supplier sites per member that have been assessed against CAMF requirements ranged from 66–100%.

Ten Alliance members reported a timeframe within which they expect their direct antibiotic manufacturing supplier sites that have not been assessed to be assessed against CAMF requirements. Three of these companies expect their direct supplier sites to be assessed within a year, four within 2–3 years and two in more than three years. One company reported that they expect that it would take more than three years for all their direct supplier sites to be assessed.

In addition, amongst Alliance members whose supplier sites have been assessed but did not meet the CAMF requirements, one reported that all their supplier sites would meet requirements within a year, and two expected this to happen in 2–3 years. Three other companies reported that their direct supplier sites would meet requirements in 4–5 years. One did not provide a timeframe.

Overall, 42% of products manufactured at supplier sites have been assessed against PNEC targets, and 73% met the targets.

Across the 18 surveyed Alliance members who reported having direct manufacturing supplier sites, a total of 831 products were manufactured at these sites, with a range of 0–195 products per member (median=18; mean=46.2).[247] Of these 831 products, 345 products have been assessed against PNEC targets (42%), of which 252 met the targets (73%). However, three of these 18 Alliance members later reported having produced zero products at direct supplier sites during the survey period.[248] Among the remaining 15 Alliance members that had at least one product manufactured at direct supplier sites, 33% (n=5) report that all their products were assessed against PNEC targets, 40% (n=6) reported that some products had been assessed and 27% (n=4) reported that none of the products had been assessed.[249]

A total of ten Alliance members offered examples to illustrate the types of actions taken to ensure direct supplier sites meet PNEC targets. Such actions include engaging in direct communications with supplier sites about PNEC target requirements to build a shared understanding of the requirements; conducting physical audits either through internal EHS or through third-party audit firms, and in some cases implementing corrective actions plans at select suppliers; offering additional support through the development of toolkits to guide suppliers through key milestones, and engaging with local suppliers regarding PSCI and establishing responsibility standards for suppliers as part of efforts to raise awareness amongst suppliers and openly share standards and expectations.

Continual progress over time has been made on responsible antibiotic manufacturing by Alliance members.

In the 2018 progress report, Alliance members reported developing the Framework and, two years ahead of schedule, the PNEC targets.[250] Alliance members have made progress in implementing Framework requirements and meeting PNEC targets. In the 2020 progress report,[251] R&D pharmaceutical members reported that 52% of their own manufacturing sites and 24% of their supplier sites fully meet Framework requirements, compared with 91% of their own sites (74 of 81 sites) and 54% of supplier sites (162 of 303 sites) in the current progress report on the AMRIA 2021 survey. Similarly, Alliance members from the generics sector reported in 2020 that 38% of their own manufacturing sites meet Framework requirements compared with 48% (62 of 130 sites) in the current progress report; a similar percentage of generic company supplier sites were reported to meet Framework requirements in the 2020 and current progress reports (1% and 0.8% [4 of 518 sites], respectively).[252] In the 2020 progress report, Alliance members provided estimated timeframes for products to be manufactured meeting PNEC targets, reporting that 56% of products manufactured at their own sites and 24% manufactured at supplier sites would meet PNEC targets within three years. In the current progress report, Alliance members report that 77% of products manufactured at their own sites and 31% of products manufactured at their supplier sites meet targets.[253]

For a reflection on the Alliance's next steps in relation to manufacturing, please see Section 7.4.

7. IN REFLECTION AND NEXT STEPS

This report shows that AMRIA member companies across the R&D pharmaceutical, biotech/SMEs, diagnostics and generics sectors have invested significant effort to tackle AMR. Such efforts have been made through a multipronged approach that recognises the complex nature of this public health challenge and the interdependence of activities across research, science, access, appropriate use and responsible antibiotic manufacturing. As well as notable achievements, some areas can help the Alliance make further progress in the coming years and inform the next steps in its work. We reflect on key highlights and outline possible next steps in the content that follows.

7.1. RESEARCH AND SCIENCE: HIGHLIGHTS AND NEXT STEPS

AMRIA members have made significant financial investments to develop new antimicrobials, vaccines, diagnostics, and non-traditional products and technologies (e.g. live biotherapeutic products, monoclonal antibodies, antibiotic inactivators, and lysins, etc.) that can help tackle AMR. As discussed earlier, surveyed companies invested approximately US$1.8–1.9 billion in AMR-relevant R&D annually in FY2019 and FY2020. The generics sector has also engaged in R&D focused on adapting existing products (such as research on new formulations or delivery methods). Across the Alliance, 93 products and/or technologies are helping fight AMR (see **Annex B.5**).[254] These products/technologies include 54 antibiotics or antifungals, 12 vaccines, 13 diagnostic platforms and assays and 14 non-traditional or other products. Of these, 29 products or technologies were developed by R&D pharmaceutical companies, 50 by biotech/SMEs, 2 by generics companies and 12 by diagnostics companies. Alliance member products and/or technologies in development account for 42% of those on the March 2021 Pew Charitable Trusts lists for 'Antibiotics Currently in Global Clinical Development' and 'Non-traditional Products for Bacterial Infections in Clinical Development'. These include products and technologies from 11 R&D pharmaceutical companies and 22 biotech/SME companies, with 10 products across these sectors in phase 3 trials (see **Table 3**).

Although not directly targeting AMR, Alliance member contributions to the fight against COVID-19 (e.g. Pfizer-BioNTech and Johnson & Johnson's vaccines) are also an important step towards mitigating the possible risk of AMR when antibiotics are used to treat secondary infections in patients with COVID-19 or used inappropriately.[255] In this way, the COVID-19-related activities that Alliance members have been pursuing also help combat the AMR challenge.

Survey data suggests that nearly half (43%) of surveyed companies reported increasing investment levels in AMR-relevant R&D compared to the previous reporting period. Alliance members' desire to continue tackling AMR remains strong. At the same time, however, the challenges to sustaining and enhancing industry engagement with R&D in this space are substantial. Nearly one-third of members report that they would decrease investment if market conditions do not improve. As discussed in Section 3.2, the key barriers from an industry perspective relate to a need for a stronger system of pull incentives to help address concerns about appropriate and clear valuation mechanisms, reimbursement pathways and market commitment. Alliance members are committed to working with policymakers

to strengthen the incentive system. At the same time, and as we have shown (see **Annex B.2**), there have been some global developments in this effort with new initiatives working to strengthen both push and pull incentives including (but not confined to) areas such as: supporting early- (e.g. CARB-X, JPIAMR,) and late-stage R&D (e.g. GARDP, AMR Action Fund); streamlining regulatory requirements (e.g. the European Medicines Agency [EMA] and U.S. Food and Drug Administration [FDA]'s parallel scientific advance, WHO's prequalification of essential medicines and health products); market attractiveness (e.g. value-based subscription models, exceptional procurement) and expanding access (e.g. WHO's AWaRe [Access, Watch and Reserve Classification] and Model List of Essential Medicines). Some of these initiatives are in the relatively early stages of development; continued dialogue at national and international levels and between policymakers, academics, industry, not for profits and civil societies will be needed to ensure a sustainable and scalable incentive system going forward.

The scale and pace of innovation in response to the COVID-19 pandemic has shown what can be achieved when governments, academics, industry, not-for-profit organisations, regulators, international organisations, civil societies, patients and the public come together to tackle a key challenge to population health and global wellbeing. In response to the COVID-19 crisis, we witnessed increased financial investment, collaboration, data sharing, regulatory efficiency and innovation in how trials are done and risks are managed (e.g. undertaking trials in parallel rather than sequentially). Not all the lessons learnt from the COVID-19 experience may apply to the fight against AMR, but many are likely to. To mobilise the same scale of global action requires further raising awareness of the urgency of the challenge at hand.

Looking to the future, the Alliance has several windows of opportunity to further build on progress to date on issues related to research and science. Key areas to consider as next steps for the Alliance are overviewed in **Box 48**.

BOX 48: **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. At the same time, they need to 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. This will support a fuller representation of the entirety of the industry R&D pipeline and reap further benefits of a unified approach and effort, while increasing cross-pollination of best practices and innovative approaches.
- **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.

7.2. ACCESS: HIGHLIGHTS AND NEXT STEPS

AMRIA members are committed to improving patient access to the most appropriate treatments, vaccines and diagnostics. As shown earlier in this report (Section 4.2), the vast majority of surveyed Alliance members (81%) carried out activities to support access to AMR-relevant products or technologies. They did this in a variety of ways. Examples include working to ensure timely product registration; working with healthcare authorities in relation to affordability and equitable pricing (e.g. through the sale of products through a non-profit model and tiered pricing structures linked to a country's ability to pay); taking actions to support availability (including through product donations and working on issues of supply chain resilience); pursuing advocacy efforts to improve access; and, investing in capacity building (e.g. supporting new vaccine manufacturing facility and programmes to scale-up the use of new pharmaceutical AMR-relevant products). Access-related activities were rooted in an ethos of collaboration with national governments, academia, NGOs and international organisations.

Efforts to achieve AMRIA aspirations in relation to access are not without challenges. Some of the challenges Alliance members experienced related to the pricing and reimbursement issues discussed earlier, some related to a lack of timely and appropriate product registration,

and others to prescriber/payer behaviours that favour lower-cost older microbials that can exacerbate AMR.

Alliance members also invested time and effort to tackle supply chain sustainability, which is key to access. Over half of surveyed companies in the diagnostics and generics sectors experienced supply chain disruptions. although nearly a quarter of all Alliance members experienced such disruptions (i.e. when R&D pharmaceuticals and biotech/SMEs are included). In cases where disruptions occurred, this was linked to the COVID-19 pandemic and associated disruptions, but occasionally also to wider difficulties in sourcing raw materials and suppliers. Some Alliance members also took actions to improve supply chain resilience and sustainability, such as improvements to demand planning and demand prioritisation systems, efforts to strengthen supply chains in low-and-middle-income countries through capacity-building and technology-transfer initiatives, and supplier auditing and supply chain diversification.

The Alliance is also committed to ensuring patients access to the right high-quality products at the right time (i.e. when they need them). In light of this, companies invested in efforts targeting the removal of substandard and falsified antimicrobial products from the market, given that such products can exacerbate the risks and impacts of AMR. For example, Alliance member efforts related to enhancing product safety through packaging and serialisation and actions to improve quality management systems and controls, as highlighted earlier in the report.

Looking to the future, the Alliance has an opportunity to build on existing progress. Key areas to consider as next steps for the Alliance and related to issues of access specifically are overviewed in **Box 49**.

BOX 49: **ACCESS – NEXT STEPS**

- **Continue to invest in capacity building that can support access and spotlight efforts targeting access to novel and off-patient antibiotics and diagnostics in LMICs.** This step will require collaboration with non-governmental organisations, healthcare providers and governments. Developing a sustainability framework for off-patient 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 going forward. Part of this could also be targeted at efforts related to strengthening local healthcare facilities and diagnostic laboratories and supporting high-quality local manufacturing capacity.
- **Continue to work in collaboration with other stakeholders in relation to actions industry can take to ensure a regulatory and economic environment that supports a sustainable supply of quality-assured antibiotics.** This step includes continued dialogue related to timely product registration for life-saving antimicrobials, engagement related to new payment and pricing models and monitoring product supply chains and distribution channels. It also includes continuing to help raise awareness about substandard and/or falsified products, working together with the healthcare community, regulators and law enforcement agencies.
- **Encourage Alliance members with access-related activity to make their plans publicly available.** Currently, nearly a fifth (17%) of Alliance members with access plans made these publicly available, and hence there is scope to encourage further transparency in this regard.

7.3. APPROPRIATE USE: HIGHLIGHTS AND NEXT STEPS

One of the key drivers of AMR is the inappropriate use of existing products. This is related to a diversity of factors, including a lack of timely or accurate diagnosis, payer/prescriber behaviours, a need for improved patient adherence to antibiotic treatment regimes, the use of substandard or falsified products, the need for improving infection prevention and control efforts as well as needs for enhanced surveillance of resistance trends globally.

AMRIA members are committed to efforts to support appropriate antimicrobial use and to antimicrobial stewardship. As we reported in Section 5.2, the majority of R&D pharmaceutical and diagnostics companies (83% and 80%, respectively) had appropriate use and stewardship strategies or plans for AMR-relevant products and/or technologies in place to guide their efforts. Other Alliance sectors also made contributions to appropriate use and stewardship, although substantially less frequently and occasionally for reasons related to their business models.

Alliance members contributed to education and awareness-raising about the risks of AMR, in line with AMRIA's commitment to collaborate with governments and others to educate healthcare professionals and patients about appropriate use. They pursued actions to align antimicrobial promotion practices and AMR stewardship, e.g. including educational material and information for healthcare professionals in promotional activity and reviewing promotional activities against stewardship commitments. Alliance members also collected and/or shared surveillance data on antimicrobial resistance trends and antimicrobial sensitivity to ensure evidence-based stewardship activities.

All these efforts shine the light on the life sciences industries' understanding of the risks of inappropriate use and the extent to which this can influence the impact of investments in research and science to tackle AMR. There are several opportunities for the Alliance to further build on the progress and achievements realised to date, as highlighted in **Box 50**.

BOX 50: **APPROPRIATE USE AND STEWARDSHIP – 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 the untapped potential for some members who do not yet have appropriate use and stewardship plans to establish them in the future where appropriate. Part of this also involves fostering enhanced sharing of surveillance data between different members of the Alliance in further support of coordinated and collaborative efforts and the sharing of best practices.
- **Advocate for enhanced surveillance of AMR through improved data visualisation and for increased public reporting of infection rates and 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 to build on the 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.

7.4. MANUFACTURING AND THE ENVIRONMENT: HIGHLIGHTS AND NEXT STEPS

As discussed in the AMRIA 2020 progress report, antibiotic manufacturing emissions contribute a relatively small proportion of all antibiotic emissions into the environment, but if poorly controlled, they can exacerbate AMR and lead to undesirable residues in soil and water, as well as sediments around antibiotic-producing factories.[256]

AMRIA Alliance 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 and science-driven risk-based discharge targets.

As introduced earlier in this report (Section 6.1), manufacturing AMRIA Alliance members developed CAMF in 2018 to guide the environmental management of antibiotic manufacturing. The framework is a significant contribution to efforts to minimise the environmental impact of antibiotic production. It offers a methodology for doing risk assessments and sets out the minimum requirements for manufacturing sites to meet environmental standards. In addition, manufacturing members of the Alliance shared scientific data to support the development of science-based targets for antibiotic discharge (known as predicted no-effect concentrations or PNEC) targets into the environment. Good progress has been made in meeting these exceedingly low-concentration discharge targets across the supply chain.

Alliance membership has grown since the establishment of this framework, with 20 members active in antibiotic manufacturing at the time of survey completion for the current progress report, including nine of the founding members. As discussed earlier in this report, Alliance members have made significant advances in implementing the framework at both company-owned manufacturing sites and supplier sites.

The majority (85%) of Alliance members with their own manufacturing sites have completed audits on meeting CAMF requirements at least every five years. The majority of manufacturing sites owned by Alliance members and assessed against CAMF fully met all CAMF requirements (76%), Overall, 98% met requirements either fully or partially.

The majority of products (88%) manufactured at sites owned by Alliance members with manufacturing operations have also been assessed against PNEC targets, and 87% of the products meet these targets. In addition, the majority of direct supplier sites (86%) have had CAMF requirements conveyed through them by Alliance members. Just under half of direct supplier sites (44%) had been assessed against CAMF requirements. Alliance members report that 50% of the assessed sites meet CAMF requirements. Overall, 42% of products manufactured at supplier sites have been assessed against PNEC targets, of which 73% of assessed products met the targets.

Although the number of companies surveyed for the 2020 AMRIA progress report differs from the surveyed companies for the current progress report on the AMRIA 2021 survey (and hence any comparisons require caution), there are signs of significant progress. To illustrate, the percentage of R&D pharmaceutical companies' own manufacturing sites increased (91% in the current progress report versus 52% in the 2020 progress reports), as did direct supplier sites that fully met Framework requirements (54% in the current progress report versus 24% in the 2020 progress report). In addition, the percentage of generic sector companies' own manufacturing sites that fully met Framework requirements increased from 38% in the 2020 progress report to 48% in the current progress report. Furthermore, a larger percentage of products manufactured at members' own sites and supplier sites met PNEC targets in the current progress report (77% and 31%, respectively) than estimated in the 2020 progress report (56% and 24%, respectively).

Finally, since the last report and in the absence of international standards or national mechanisms establishing emission limits for safe concentrations of antibiotics in the environment,[257] the Alliance continues to play a key role in addressing antibiotic-manufacturing emissions. This applies both in the context of the progress here and via sponsoring ongoing work to develop a consensus standard for the responsible manufacture of antibiotics.

Although many advances have been made, there is always scope to do more in support of the Alliance's long-term commitment**. Box 51** summarises key steps that can help support that aim.

BOX 51: **MANUFACTURING AND THE ENVIRONMENT – NEXT STEPS**

- **Support efforts to accelerate framework adoption and implementation across members' supply chains.** This step includes encouraging all members to audit direct suppliers against the Framework requirements and PNEC targets.
- **Continue work towards developing international standards for responsible antibiotic manufacturing** in collaboration with other international organisations involved with setting standards. Seek to advance a mechanism(s) to enable buyers to identify responsibly made antibiotics more readily.
- **Continue to share the work of Alliance manufacturing members in implementing the framework and PNECs across global supply chains with stakeholders, including 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.

7.5. THE ADDED VALUE OF AN ALLIANCE

RAND Europe's engagements with sectors and companies responding to this survey, alongside consultations on relevant issues and feedback on the findings from AMRIA, have shed light on the value of a networked Alliance approach to the fight against AMR. AMRIA seeks to support its members in diverse ways. For example, it is a platform offering convening and coordinating functions for member activities and working to identify strategic priorities for the companies involved in the fight against AMR. It does so across all four pillars of activity: research and science, access, appropriate use and manufacturing and the environment. The importance of a coordinated and collective approach for mobilising and focusing member company activities is evident in developments being pursued by diverse companies across all four pillars of Alliance activity.

At the same time, there are many opportunities ahead. For example, there is scope to further increase the visibility of the Alliance and its work to attract new members to the fight against AMR. There may also be scope to further mobilise the connectivity and reach of Alliance members and their networked structure, engage more actively with the general public to raise awareness of industry efforts, understand the needs and experiences of patients and the public and mobilise them as a partner in the fight against inappropriate antimicrobial use.

There is also scope for AMRIA – as a unified and collaborative entity – to further enhance policymakers' attention to the diversity of AMR-related priorities across geographies, e.g. in relation to falsified products and access in LMICs. There is unique potential in the Alliance to raise further awareness of the critical role that biotech/SMEs, diagnostics and generics companies play alongside large R&D pharmaceutical partners in policymaking circles. The Alliance can do so in a way that encourages dialogue around advancing incentives and supporting the diversity of industry actors contributing across AMR-relevant R&D and product manufacturing.

7.6. BEYOND THE ALLIANCE: INDUSTRY WORKING WITHIN A COLLABORATIVE AND CONNECTED LANDSCAPE

We have outlined actions which the Alliance can consider taking in the years ahead. However, many of these actions are not something industry can do alone. Instead, they depend on collaboration with a wider global community of policymaking bodies (e.g. governments, international authorities and agencies), regulatory bodies, not-for-profits, healthcare professionals and providers, civil societies and the general public. Based on reflections on key insights from the AMRIA member survey and their implications, we outline actions that are important for other stakeholders to consider in the united effort to curb antimicrobial resistance in **Box 52**. Many of these efforts are undoubtedly being pursued as part of key global initiatives, some of which we have referred to throughout this report. The opportunity ahead rests in both sustaining and scaling current momentum and in connecting the key areas of need with the priorities, capabilities, resources and responsibilities of the diversity of players committed to mitigating antimicrobial resistance for the health and well-being of current and future generations.

BOX 52: **ACTIONS FOR WIDER STAKEHOLDERS TO CONSIDER**

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.

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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.

Endnotes

1 G7 Health Ministers' Meeting Communique Oxford, 4 June 2021. As of 18 January 2022: https://www.gov.uk/government/publications/g7-health-ministers-meeting-june-2021-communique/g7-health-ministers-meeting-communique-oxford-4-june-2021

2 Spinney, Laura. 2021. 'The next pandemic? It may already be upon us.' The Guardian. 15 February 2021. As of 18 January 2022: https://www.theguardian.com/commentisfree/2021/feb/15/creating-conditions-next-pandemic-antibiotics

3 Antimicrobial Resistance Collaborators. 2022. 'Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis'. *The Lancet*. 20 January 2022. As of 20 January: https://www.thelancet.com/action/showPdf?pii=S0140-6736%2821%2902724-0

4 Interagency Coordination Group on Antimicrobial Resistance (IACG). 2019. 'No Time to Wait: Securing the future from drug-resistant infections.' Report to the Secretary-General of the United Nations. As of 18 January 2022: https://www.who.int/docs/default-source/documents/no-time-to-wait-securing-the-future-from-drug-resistant-infections-en.pdfsfvrsn=5b424d7_6

5 O'Neill (2014).

6 O'Neill (2014).

7 Pelfrene et al. (2021).

8 Baker et al. (2021).

9 Weiner-Lastinger et al. (2021).

10 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).

11 AMR Industry Alliance (2020c).

12 AMR Industry Alliance (2020c).

13 AMR Industry Alliance (2021).

14 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.

15 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 must 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. In addition, it is worth noting that one company sent contributions to a case-vignette after the survey was completed but during the timeframe of report production and this addition was accommodated.

16 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.

17 WHO (2017a).

18 CDC (2019).

19 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). 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.

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

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

22 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.

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

24 The Global AMR R&D Hub (2021) provides a useful overview of existing efforts.

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

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

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

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

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

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

31 G7 (2021).

32 Global Coalition on Aging and Infectious Diseases Society of America (2021).

33 Ferri et al. (2017).

34 Teillant et al. (2015).

35 Hocking et al. (2021).

36 Ferri et al. (2017).

37 Pelfrene et al. (2021).

38 Baker et al. (2021).

39 Weiner-Lastinger et al. (2021).

40 O'Neill (2014).

41 O'Neill (2014).

42 World Health Organization (2015).

43 UN Ad hoc Interagency Coordination Group (IACG) on Antimicrobial Resistance (2019).

44 European Commission (2017).

45 UK Government (2019).

46 UK Government (2019).

47 UK Government (2021b).

48 World Health Organization (2021).

49 Marjanovic & Feijao (2020).

50 At the time of this report, AMRIA had 108 members: 62 biotech/SMEs, 12 R&D pharmaceutical companies, 10 diagnostics sector companies, 9 generics sector companies and 15 industry associations. Industry associations were not surveyed. A total of 93 companies were eligible for being surveyed at the time of this report.

51 AMR Industry Alliance (2020b).

52 AMR Industry Alliance (2020b).

53 AMR Industry Alliance (2020c).

54 EFPIA/IFPMA (2020).

55 EBE/EFPIA/Vaccines Europe (2020).

56 Wellcome Trust (2019).

57 World Economic Forum (2018).

58 AMR Industry Alliance (2020a).

59 AMR Industry Alliance (2020a).

60 The first Alliance progress report was published in January 2018, and the second in January 2020.

61 For financial investments in R&D specifically, companies reported on FY2019 and FY2020.

62 This covers products and technologies targeting AMR. It covers products and/or technologies that impact the spread of antibiotic-resistant 'priority pathogens' as identified by WHO's priority pathogen list and/or the CDC's AR Threats Report but is not confined to pathogens on these lists alone.

63 In discussion with AMRIA, it was recognised that some products that combat AMR in relation to bacterial and fungal infections might indirectly be related to viruses, impacting antimicrobial use and, as a result, AMR. Therefore, AMR-relevant vaccines (both anti-bacterial and those that impact the inappropriate use of antibiotics, including vaccines for viruses such as influenza, COVID-19, RSV and other respiratory infections) were in scope. Similarly, diagnostics tests that help distinguish between viral and bacterial infections were in scope as long as there was a clear link to AMR.

64 RAND Europe conducted two rounds of engagement sessions in the form of workshops with Alliance members. All member companies were invited to participate in the consultations. A total of 27 individuals were consulted overall.

65 This was done in light of sector consultation feedback.

66 Sector-specific surveys were uploaded to the Smart Survey platform (https://www.smartsurvey.co.uk/), and a unique, password-protected link for each sector was shared in an email invitation to all AMR Industry Alliance members. The survey was open from 30 March 2021 to 6 June 2021, a window of approximately ten weeks. During this period, member companies received a maximum of two follow-up reminders after their initial invitation to complete the survey. Each member company was also provided with detailed guidance on each question's meaning and scope and an email address to contact the RAND Europe team with any questions regarding the survey. They were

also provided with a Microsoft Excel sheet to help count the products and sites that meet requirements for manufacturing and the environment. Before beginning the survey, participants were informed of the purpose of the survey, how survey data would be used, and details regarding privacy and data protection. In addition to participation consent, respondents were asked to indicate their consent for their company to be listed in this report, for the synthesis of survey information here, and for the sharing of de-identified data with the AMR Industry Alliance Secretariat. As some of the survey questions asked for examples and case vignettes, company representatives responding to the survey were asked not to disclose commercially sensitive information and informed that any examples they provided as linked to their company could be used in the public report.

67 The analysis included calculating the number and percentage of respondent companies (overall and within each sector) that selected each answer option within the survey. For numerical responses, we looked at the median and mean values, the distribution of values across member companies and the overall total (where relevant) across respondent companies.

68 Due to the survey's routing and consideration of issues relevant to different Alliance sectors, not every Alliance member will have seen every question. However, we indicate the total sample size (n) for each question within the narrative and graphs in this report.

69 This participation rate represents a decrease from the 2020 progress survey, when 65 out of 91 members completed the survey (71% response rate). However, it is higher than the response rate recorded in the 2018 report, when 36% (36 of 101) of member companies participated. As such, it is worth noting that some members have left the AMRIA Industry Alliance over time, while other new members have joined.

70 AMRIA had 62 biotech/SME sector members at the time of the survey. Since then, three new members joined AMRIA and one left (the total number of current biotech/SME sector members is 64).

71 Simpkin et al. (2017).

72 Årdal et al. (2020).

73 AMR Industry Alliance (2021).

74 These range estimates are based on a combination of data provided by companies on ranges of investment values and some absolute-value figures. Some companies treat the absolute value of their investments as commercially sensitive information and could only provide a range.

75 AMR Industry Alliance (2020a).

76 The AMRIA 2020 progress report and survey had a different number and percentage of responding companies, and generics companies were not asked about R&D activities. In the current report, the generics sector included questions about financial investment, as sector consultations revealed that generics companies do invest in AMR-relevant R&D. Examples include the adaption of existing products through new formulations or new delivery methods, identifying new uses or indications and repurposing existing products, and R&D related to dosing.

77 The lower end of the range (referred to as the lowest potential investment) was calculated assuming that all companies that reported investments within a particular range invested at the lowest possible value (e.g. US$6 million in the range US$6–10million). One exception was companies that reported exact figures for investments, in which case the exact value was used for the calculation. The upper end of the range (referred to as maximum potential investment) was calculated assuming that all companies that reported investments within a particular range invested in AMR-relevant R&D at the

range's highest value (e.g. US$10 million in the US$6–10million range), except for companies that reported exact figures for investments. In these cases, the exact value was used for the calculation.

78 Three companies reported investments over US$20 million but did not provide an absolute value for investment. In this case, US$20 million was used as the lowest range and US$40 million as the highest range.

79 In the 2021 progress survey, we asked companies about changes in investment levels in AMR-relevant R&D between FY2018 (progress report 2020) and investment levels in FY2019. We did not ask about changes in investment between FY2019 and FY2020, as respondents were asked to provide information on their investment levels for both FY2019 and FY2020 and therefore we could deduce variation in these two financial years from the survey questions asked in this round (as per previous section). This question was not asked of generics companies as they did not report on R&D investment for FY2018. Our analysis of the difference between years was based on self-report for 2018 vs 2019 and estimated based on available data for 2019 vs 2020.

80 Generics companies that did not report investment in AMR-relevant R&D in FY2019 and FY2020 were not asked this question, so they were excluded from this analysis. A total of 48 companies responded to this question. The 2021 progress survey only asked about changes in the levels of investment between FY2018 and FY2019.

81 Generics companies were not asked this question, so they were excluded from this analysis; the denominator for this question is 44.

82 All values in this paragraph represent the percentage of companies that considered each factor a challenge to a moderate or large extent.

83 It is worth flagging the relatively small number of survey respondents from the diagnostics sector; this section's results should be interpreted with that caveat in mind.

84 Generics companies were not asked this question, so they were excluded from this analysis; the denominator for this question is 44.

85 All values in this paragraph represent the percentage of companies that considered each factor likely to positively influence investment to a large or moderate extent.

86 International Federation of Pharmaceutical Manufacturers and Associations (IFPMA, 2021).

87 International Federation of Pharmaceutical Manufacturers and Associations (IFPMA, 2021).

88 All values in this paragraph represent the percentage of companies that considered each factor likely to positively influence investment to a large or moderate extent.

89 Generics companies were not asked this question, so they were excluded from this analysis; the denominator for this question is 44.

90 Global AMR R&D Hub (2021).

91 Examples of initiatives in this space include: *supporting early-stage R&D* (e.g. CARB-X, JPIAMR); *enhancing clinical trial conduct* (e.g. ECRAID's [European Clinical Research Alliance on Infectious Diseases] clinical trial network, CITI's [Clinical Trials Transformation Initiative] clinical trial system); *supporting late-stage R&D* (e.g. GARDP, AMR Action Fund); *streamlining regulatory requirements* (e.g. European Medicines Agency [EMA]'s and U.S. Food and Drug Administration [FDA]'s parallel scientific advance, WHO's prequalification of essential medicines and health products); *encouraging earlier and broader uptake of AMR-relevant products* (e.g. IDSA's [Infectious Disease Society

of America] difficult-to-treat infections guidance series; BARDA's [Biomedical Advanced Research and Development Authority] strategic national stockpile and reserve fund); *enhancing relative market attractiveness* (e.g. value-based subscription models, exceptional procurement); *signalling importance to help inform efforts to expedite sustainable global patient access* (e.g. WHO's AWaRe [Access, Watch and Reserve Classification] and Model list of Essential Medicines); *signalling and orienting priorities for AMR-relevant activity* (e.g. Pew pipeline review; WHO's priority pathogen list); and *improving continuity of supply* (e.g. fostering green, diverse and sustainable sourcing; securing and stabilising supply and demand continuity).

92 Six companies offered additional narrative information on this topic.

93 Generics companies were not asked this question as the focus was on novel R&D, so these companies were excluded from this analysis. The denominator for this question was 44.

94 Please note that companies could select multiple options. 'Other' refers to additional options not listed.

95 Please note that this is a small number of diagnostics companies (n=3).

96 While the information available from a review of the product lists provide an overview of the status of products across the Alliance, products available through the survey responses only provide information on the products in development for 53 Member companies (i.e. companies that responded to the survey).

97 This number includes two companies that provided information on AMR-relevant R&D activities without specifying product names or details.

98 From the information provided by survey respondents, we were unable to consistently assess the pathogens that these products or technologies targeted as well as the phases of research these products or technologies were in.

99 Although The Pew Charitable Trusts' March 2021 lists are mutually exclusive, products/technologies mentioned by the survey or the April 2020 'Medicines in Development' may not be mutually exclusive with each other or The Pew Charitable Trusts' March 2021 lists.

100 Products and technologies classified as 'adjuvant – new chemical entity', 'antimicrobial (antiviral and antibacterial) and immunomodulatory', 'antibody', 'anti-virulence agent – new chemical agent' and 'nasal cell membrane modulator'.

101 It is important to note that the number of unique products/technologies listed in prior sections (i.e. 93) is lower than the 104 products reported here because a unique product/technology can address more than one pathogen.

102 There may be other pathogens being targeted by diagnostics and generics companies based on survey data (Enterococci- Vancomycin-resistant Enterococci; Streptococci- Group A Streptococcus; Campylobacter spp; Bordetella pertussis). However, we don't have sufficient data on numbers and types of products/technologies, hence they cannot be included in Table 4.

103 Three products were reported to target all pathogens but have been excluded from this count due to lack of specificity.

104 Two products were reported to target *Acinobacter* but did not explicitly use the term *Acinetobacter baumannii*.

105 Three products were reported to target *Pseudomonas* but did not explicitly use the term *Pseudomonas aeruginosa*.

106 Product was reported to target *Enterobacter spp* but did not explicitly use the term ESBL-producing *Enterobacteriaceae*.

107 Eight products were reported to target Enterobacter spp., one product was reported to target *Enterobacteriaceae* and one product was reported to target Enterobacterales. The term ESBL-producing *Enterobacteriaceae* was not explicitly used.

108 Product was reported to target MDR-*Enterobacteriaceae* but did not explicitly use the term *Carbapenem-resistant Enterobacteriaceae.*

109 These three products were reported to target *Carbapenemase-resistant organisms* but did not explicitly use the term *Enterobacteriaceae* – Carbapenem-resistant.

110 One product was reported to target *Gonorrhoea* but did not explicitly use the term *Neisseria gonorrhoeae*.

111 Product was reported to target *Aspergillus* but did not explicitly use the term *Aspergillus fumigatus*.

112 One product was reported to target *Aspergillus* but did not explicitly use the term *Aspergillus fumigatus*.

113 One product was reported to target *Enterobacteriaceae* and one product was reported to target *Enterobacterales*. The term *Shigella* spp. was not explicitly used.

114 One product was reported to target *Enterobacteriaceae* and one product was reported to target *Enterobacterales*. The term *Salmonellae* - non-typhoidal Salmonella was not explicitly used.

115 One product was reported to target *Enterobacteriaceae* and one product was reported to target *Enterobacterales*. The term *Salmonellae* - Salmonella serotype Typhi was not explicitly used.

116 One product was reported to target *Influenza* but did not explicitly use the term *Haemophilus influenzae*.

117 AMR Industry Alliance (2020c).

118 As generics companies were not asked this question (the focus was on R&D for novel products and technologies), these companies are excluded from this analysis. A total of 44 companies across R&D pharmaceutical companies, biotech/SMEs and diagnostics companies responded to this question.

119 Excluding generics companies (given the focus of the question on collaborations related to R&D for novel products).

120 As generics companies were not asked this question, they were excluded from this analysis. A total of 44 companies across R&D pharmaceutical companies, biotech/SMEs and diagnostics companies replied to this question.

121 Most pharma companies are involved in some form of data sharing, but a minority of companies stated they were not (i.e. answered 'no' to the associated question). They may not have published during the survey reporting period, for example.

122 Overall, 28% of companies engaged in data-sharing activities other than those listed in the survey question. Data-sharing activities reported as 'other' included direct exchanges with consortium partners, responding to specific data requests from rating agencies (e.g. AMR Benchmark), webinars, podcasts and newsletters, and creating designated data-sharing websites.

123 Business Wire (2020).

124 Pfizer (2020b).

125 Pfizer (2021).

126 Kwong et al. (2009).

127 Pfizer (2020a).

128 ClinicalTrials.gov (2020).

129 Ashkenazi-Hoffnung et al. (2018), Kapasi et al. (2016), Leticia Fernandez-Carballo et al. (2021) and Oved et al. (2015).

130 This is the probability that an individual with a negative test result truly does not have a disease.

131 Doherty et al. (2020).

132 Doherty et al. (2020).

133 ClinicalTrials.gov (2021a).

134 ClinicalTrials.gov (2021b).

135 Further detail is not available.

136 Ventanorx Pharmaceuticals (2020).

137 US FDA (2021).

138 Costerton et al. (1999).

139 Wannigama et al. (2020).

140 Jamal et al. (2018).

141 World Health Organization (2017c).

142 Inchai et al. (2015).

143 Paul et al. (2018).

144 Generics companies that did not report investment in AMR-relevant R&D in 2019 and 2020 were not asked this question, so they were excluded from this analysis. The denominator for this question is 48, covering R&D pharmaceutical companies, diagnostics companies, generics companies and biotech/SMEs.

145 PWC (2020).

146 O'Neill (2016).

147 Frost et al. (2019).

148 Pokharel et al. (2019).

149 World Health Organization (2017b).

150 AMR Industry Alliance (2021).

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

152 This includes 9 of the 22 companies (41%) that stated they did not have formal strategies or plans in place to address issues related to access to AMR-relevant products.

153 This question was asked of the 43 companies that either had a formal access plan or strategy or reported engaging in activities to support access.

154 This includes 11 companies in the R&D pharmaceuticals sector that reported on such activity.

155 Please note that this data needs to be interpreted cautiously due to the small number of responding diagnostics companies reporting access-related activity (n=4).

156 The Global Fund (2019).

157 Stop TB Partnership (2020b).

158 Johnson & Johnson, (2021c).

159 Johnson & Johnson (2021a).

160 Johnson & Johnson (2021b).

161 Stop TB Partnership (2020a).

162 Johnson & Johnson (2020).

163 Stop TB Partnership (2020b).

164 World Health Organization (2019).

165 O'Neill (2016).

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

167 Examples of collaborators mentioned in response to this question include the Global Antibiotic Research and Development Partnership (GARDP); The Global Fund to Fight AIDS, TB and Malaria; The Center for Disease Dynamics, Economics & Policy's Global Antibiotic Resistance Partnership; USAID Medicines Sans Frontiers; Save the Children; Direct Relief; UNICEF; Gavi; the AMR Action Fund, the World Health Organization; International Trachoma Initiative; TB Alliance; the Stop TB Partnership, the Global Drug Facility (GDF); KNCV Tuberculosis Foundation;

Unitaid; and diverse hospitals and national governments.

168 The are countries graduating from Gavi alliance support.

169 A 2019 report conducted by the Center for Disease Dynamics, Economics & Policy (CDDEP) identified three major barriers to antimicrobial access: (i) the unaffordability of drugs and health services, (ii) a lack of regulations and processes for bringing new drugs to local markets, and (iii) weak local and national drug supply chains (Frost et al. 2019). Alliance members provided supporting evidence for the CDDEP's findings that the unaffordability of products and limited regulatory/registration processes represent significant barriers to access, while also highlighting additional access barriers surrounding prescriber/payee behaviour. Challenges raised by the CDDEP report regarding supply chain disruption and impacts for ensuring access to AMR-relevant products and technologies are also reflected in Alliance member companies' responses to the survey, as described in the next section of this report.

170 Overall, 60% (n=3) of diagnostics companies reported experiencing disruptions, 56% (n=5) of generics companies, 17% (n=2) of R&D pharmaceutical companies and 15% (n=4) of Biotech/SME companies. Please note that the small number of responding diagnostics companies indicates the need for caution in interpreting these numbers.

171 Overall, 21% of respondents provided this optional additional information.

172 The examples presented in this box are based on information provided by survey respondents and are intended to be illustrative only. Although actions taken by one company may well have been taken by other companies, they did not provide specific examples.

173 Zoufaly et al. (2014).

174 Kelesidis & Falagas (2015).

175 The 27 Biotech/SME companies were not asked this question; hence, the denominator for this section is 26.

176 The examples presented in this box are based on information provided by survey respondents and are intended to be illustrative only. Although actions taken by one company may well have been taken by other companies, they did not provide specific examples.

177 AMR Industry Alliance (2020).

178 AMR Industry Alliance (2021a).

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

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

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

182 It is possible that those without such plans may not have marketed products, but we cannot be certain of this based on the data received.

183 Overall, 33% of biotech/SMEs (n=9), 20% of diagnostics (n=1), 11% of generics sector (n=1) respondents and 8% of R&D pharma respondents (n=1) felt appropriate use and stewardship plans do not apply to their business models. In addition, some companies reported not having plans, but did not state that such plans do not apply to their business models.

184 Percentages in this section add up to 99% rather than 100% due to rounding.

185 This is a conservative estimate of the number of companies that participated in education and awareness-raising activities, as this question was only asked of a subset of respondents (n=32) that

reported activities for appropriate use and stewardship. When all participants (excluding those in the Biotech/SME sector, n=26) were asked directly about their participation in education and awareness-raising activities, 88% indicated that they had conducted this type of activity. See the section below for more detail. The disparity may be due to different interpretation of the word 'support' vs 'engagement' by some survey respondents.

186 This is a conservative estimate of the number of companies that collected surveillance data, as this question was only asked of a subset of respondents (n=32) that reported activities for appropriate use and stewardship. When all participants (n=53) were asked directly about whether they collect surveillance data, 51% indicated that they had conducted this type of activity. See the section below for more detail.

187 Supporting education, awareness-raising and activities related to collecting and sharing surveillance data was particularly common for R&D pharmaceutical companies. Generics companies engaging in appropriate use and stewardship were also highly active in education and awareness-raising. Biotech/SMEs that conducted activities related to appropriate use and stewardship were most active in efforts to align antimicrobial promotion and AMR stewardship and generating evidence to support appropriate use and stewardship. Diagnostics companies' activities were most common in relation to supporting the use of diagnostics to prevent antimicrobial misuse, generating evidence to support appropriate use and stewardship and collecting and sharing surveillance data (and supporting infection prevention and control).

188 Biotech/SME companies were not asked this question, so they are excluded from these analyses.

189 R&D pharma, diagnostics and generics sectors were asked this question. In future years, it may be worth consulting with biotech/SME companies about relevance for this sector.

190 In addition to these 23 companies in the R&D pharmaceutical, generic and diagnostics sectors, there were also an additional five companies in the biotech/SME sector that had reported education/awareness-raising in relation to their activities related to appropriate use and stewardship more generally, asked in response to an earlier question. There are at least 28 companies in the Alliance that conduct activities around education and awareness-raising.

191 Using tools or software to improve patient adherence (n=1, 4%) or to support prescription-related decision making by healthcare professionals (13%, n=3). Efforts focused on including messaging on drug packaging to encourage patients to complete antimicrobial courses were less frequent (n=5, 22%).

192 Biotech/SMEs were not asked this question; hence, they are excluded from the analysis. The decisions to do so were made post sector consultations. However, in future survey reporting years, it may be helpful to ask biotech/SME sector representatives this question, given they reported engaging with education and awareness-raising activities.

193 Nature (2020).

194 AMR.Solutions (2020).

195 Approximately a fifth of generics sector respondents (22%, n=2) felt such data was not relevant to their business model, and 44 % (n=4) stated they did not collect data over the survey timeframe.

196 Approximately a third of biotech/SMEs (30%, n=8) felt such data was not relevant to their business model, and a third (33%, n=9) stated they did not collect data over the survey timeframe. It is likely that many biotech/SMEs at an early stage of development will not yet be collecting surveillance data.

197 For example, biotech/SMEs tended to engage less in data-sharing activities with healthcare professionals and healthcare authorities than other sectors who were more likely to have antimicrobials later in the development pipeline or on the market.

198 A total of 16 companies provided information on this aspect of activity.

199 MSD (2020).

200 Hernández-Gómez et al. (2019).

201 Tell et al. (2019).

202 Bengtsson-Palme et al. (2018).

203 AMR Industry Alliance (2018).

204 Tell et al. (2019).

205 AMR Industry Alliance (2021).

206 All founding members reported having adequate internal review processes in place. A small minority of newer members with manufacturing operations (15%) are yet to put in place internal review processes.

207 Overall, 80% of surveyed Alliance members with manufacturing operations reported an adequate external review of sites (89% for founding manufacturing members).

208 This includes nine founding members with 2.5 years to meet the Framework and PNEC requirements and 11 newer members with 0–2 years to meet the Framework and PNEC requirements.

209 All manufacturing companies within the R&D pharmaceutical sector and the generics sector were asked about their activities related to manufacturing and the environment. However, detailed questions were only asked of companies that reported that they had manufacturing activities at their own sites or at direct supplier sites.

210 Overall, 85% of members with manufacturing operations said that they complete audits every five years (n=17). However, in a later question, 18 companies (90%) reported completing an audit during the survey period – it may be that one company may not audit every five years but did audit during the survey timeframe. Auditing the data is outside the scope of the report, however.

211 This corresponds to nine founding members.

212 This corresponds to eight newer members.

213 This corresponds to 13 companies.

214 This corresponds to eight companies.

215 This corresponds to five companies.

216 This corresponds to two companies.

217 This corresponds to 17 companies.

218 This corresponds to three companies.

219 This corresponds to 16 companies.

220 At the beginning of the CAMF-related survey questions, Alliance members initially reported assessing 179 sites. When subsequently asked how many specific sites met CAMF requirements fully, partially or not at all, this question's reported data would suggest that 194 sites were assessed or that some companies introduced an error in answering this question, resulting in a difference of 15 sites. As auditing the data is outside the scope of this survey analysis and report, we have caveated potential inconsistencies in the reported data. Based on the answer to the specific question of whether sites meet CAMF criteria, the majority of manufacturing sites assessed against CAMF (70%; 136 out of 194) fully met all requirements. A further 28% (55 out of 194) partially met CAMF requirements, and 2% (3 out of 194) did not meet CAMF requirements.

221 Overall, 85% of members with manufacturing operations said that they complete audits every five years (n=17). However, in a later question, 18 companies (90%) reported completing an audit during the survey period. It may be that one

company did not audit every five years but did audit during the survey timeframe. Auditing the data is outside the scope of the report, however.

222 For Alliance members with manufacturing sites, the percentage of sites per member that met CAMF requirements range from 0–100% of sites assessed, with a median value of 100% and a mean value of 81.2%. The percentage of sites per member that partially met CAMF requirements ranges from 0–100% across Alliance members, with a median value of 0 and a mean of 20.8%. The percentage of sites per member that do not meet CAMF requirements ranges from 0–38% across companies, with a median of 0 and a mean of 2.1%.

223 This was in response to an optional qualitative question.

224 Of the four Alliance members whose sites did not yet meet CAMF requirements fully, one expected all their sites to meet them in 2-3 years and another expected this to be achieved in 4–5 years. One Alliance member reported that some of their sites would meet requirements in 2–3 years but did not provide a timeframe for when the remainder of their sites would meet CAMF requirements. One Alliance member did not provide any timeline for when their sites will meet CAMF requirements.

225 This corresponds to 18 companies.

226 This corresponds to 11 companies.

227 NGB Laboratories (2021).

228 Indiamart (2021).

229 Gujarat Pollution Control Board (2021a).

230 Gujarat Pollution Control Board (2021b).

231 Nation News Desk (2021).

232 A total of 18 companies.

233 This corresponds to 9 out of 11 newer members.

234 This amounts to nine companies.

235 This corresponds to 706 out of 821 direct supplier sites.

236 This corresponds to ten companies. The total number of companies who reported having at least one direct supplier site in this question is 17. One company which in a previous survey question said they have a direct supplier site, in response to the current question said they had zero sites and hence there is a small inconsistency between this information and information provided at the beginning of this section. Auditing this data was not possible within the scope of the work conducted.

237 This corresponds to five companies.

238 This corresponds to two companies.

239 Among founding manufacturing members, the minimum percentage of supplier sites per member that have been conveyed CAMF requirements was 75%.

240 Ten companies took up the opportunity to answer this optional survey question. It is plausible that other companies may also take actions of a similar or different nature, but since they did not respond, we cannot ascertain this.

241 This corresponds to 12 companies.

242 The total number of companies who reported having at least one direct supplier site in this question is 17. One company that reported having a direct supplier site in response to a previous survey question said they had zero sites in response to the current question. Hence there is a slight inconsistency between this information and the information provided at the beginning of this section. Auditing this data was not possible within the scope of the work conducted.

243 In response to a follow-on question.

244 Two out of 15 companies reported assessing zero sites.

245 This corresponds to four companies.

246 This corresponds to nine companies.

247 We do not know why some companies reported an option of zero products. It may be because they have an established relationship with a direct supplier site but do not yet manufacture there. However, this would warrant further investigation, which is outside the scope of this work.

248 In a subsequent question.

249 Eleven Alliance members had at least one of the products manufactured at their direct supplier sites that have not been assessed against PNEC targets. Of these, three reported that they expect all to be assessed within a year, two within 2–3 years and four reported in more than three years. The two remaining Alliance members did not provide a timeline for assessing the products manufactured at direct supplier sites against PNEC targets. In addition, eight Alliance members provided timelines within which they expect products manufactured at direct supplier sites that do not meet PNEC targets to meet them. Three of these companies expected the products to meet PNEC targets within 2–3 years, and two expected this to happen in 4–5 years. Two additional members reported they expected that almost all the products manufactured at direct supplier sites (besides one product per company) would meet targets; one expected this would occur within a year, and the other expected this would occur in 2–3 years. Lastly, one member reported that more products would meet targets in 4–5 years but did not provide a timeline.

250 AMR Industry Alliance (2018).

251 AMR Industry Alliance (2020a).

252 These percentages reflect values relative to all sites, not only those that were assessed against CAMF.

253 These percentages reflect values relative to all products, not only those that were assessed against PNEC targets.

254 Information from: (i) PEW (2021a), (ii) PEW (2021b), (iii) 'Medicines in Development – Antimicrobial Resistance' list (April 2020), and (iv) survey responses.

255 Pelfrene et al. (2021).

256 AMR Industry Alliance (2020).

257 UK Government (2021b).

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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