



THE 2023 AMR INDUSTRY ALLIANCE PROGRESS SURVEY: Manufacturing and the environment





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Context and Approach

Antimicrobial resistance (AMR) is a serious global public health concern, identified as one of the top three health threats by the Health Emergency Preparedness Authority (HERA) according to the European Commission (2022) and as one of the top ten global public health threats facing humanity by the World Health Organisation (WHO)(Murray et al. 2022). Recent estimates suggest that 4.95 million deaths were associated with bacterial AMR alone in 2019 (Dadgostar 2019). In addition to health-related impacts on populations, AMR also has significant economic impacts, with some estimates suggesting that AMR could cost from US\$300bn to US\$1 trillion annually at a global level by 2050 (AMR Industry Alliance 2023a).

The life sciences industry is a crucial partner in the effort to tackle AMR. In this context, the AMR Industry Alliance (AMRIA) was established in 2017 to provide sustainable solutions to curb AMR (Marjanovic et al. 2022) and brings together 77 leading biopharmaceutical (n=12), diagnostic (n=4), biotechnology (n=51) and generic-sector (n=10) companies,¹ as well as ten industry associations, to harness the know-how, resources and infrastructure of industry to help with this effort. It does so by focusing on contributions to four key areas of activity, each of which represents a key part of the complex AMR puzzle. These are (i) contributions to **research and science to develop innovative products and technologies to help tackle AMR**, (ii) efforts to support **access to antimicrobials**, (iii) activities to **support appropriate use** and (iv) actions to help ensure **responsible antibiotic manufacturing**.

This report provides a snapshot of AMRIA's efforts to deliver on their commitments in the pillar of responsible antibiotic manufacturing specifically. This is the fourth iteration of the Alliance's biannual progress reporting. It is based on a survey of Alliance members designed, administered and analysed by the not-for-profit research institute RAND Europe. The survey (see Annex A2) examines AMR-relevant activities of Alliance members between 1 April 2021 and 31 March 2023. Further details on the key findings can be found in Annex A1.

Of the 77 Alliance members, a total of 22 were eligible to complete the parts of the survey related to responsible manufacturing by virtue of engaging with antibiotic manufacturing through their own and/or direct supplier sites. This included 12 research and development (R&D) pharmaceutical and ten generics companies with manufacturing operations. The overall response rate was 100% for the 22 eligible members (100% for R&D pharma and 100% for generics companies). All responding companies did so with informed consent.

Although the report captures diverse member contributions to responsible antibiotic manufacturing and reflects on future considerations, there are some caveats to bear in mind when interpreting the findings. For example, while most companies could provide the data requested in the survey, a minority could not do so for each question due to not having data

at the requested level of detail. We have flagged where this is the case when presenting the findings. In addition, although questions were developed with some built-in quality-control checks, auditing the data was outside the scope of this work. It is also worth noting that, where feasible, we have provided comparisons with key insights obtained on Alliance member contributions to responsible manufacturing in the prior survey round and progress report (Marjanovic et al. 2022).

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A list of Alliance members invited to respond to the manufacturing part of the progress survey is provided below (Table 1).

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

LARGE R&D BIOPHARMACEUTICALS	
* Boehringer Ingelheim	* Otsuka
* F. Hoffmann-La Roche AG.	* Pfizer Inc.
* GlaxoSmithKline plc	* Sanofi S.A.
* Johnson & Johnson	* Shionogi & Co. Ltd.
* Menarini Ricerche	* Sumitomo
* Merck KGaA	
* MSD (known as Merck and Co. Inc. in the US and Canada)	

GENERICS	
* Aurobindo	* Recipharm
* Centrient Pharmaceuticals	* Teva Pharmaceuticals, Ltd.
* Cipla	* Venus Remedies
* Fresenius Kabi	* Viatris
* Sandoz	* Xellia



AMRIA contributions to tackling AMR through responsible manufacturing

The presence of antibiotics in the environment, particularly in wastewater, may contribute to the emergence of antimicrobial resistance if the concentrations of antibiotics are not kept below certain levels, potentially leading to bacterial mutations that could, in turn, result in antibiotic resistance developing (AMR Industry Alliance 2018a). The discharge of antibiotic emissions into the environment is not currently explicitly regulated in terms of limits for antibiotic discharge concentrations. As a large industry group focused on AMR, AMRIA aims to set the standards for industry manufacturers in this regard. These standards are deliberately ambitious, and Alliance members are encouraged to take appropriate actions to achieve intended responsible manufacturing aims.

To support these commitments, AMRIA's R&D pharmaceutical and generics sector members follow a standard risk assessment framework known as the Common Antibiotic Manufacturing Framework (CAMF) (AMR Industry Alliance 2018b). As discussed in the prior AMRIA progress report, the Alliance developed CAMF in 2018 to help guide the environmental

management of antibiotic manufacturing by offering a methodology for doing risk assessments and setting out the minimum requirements for meeting environmental standards by manufacturing sites. Alliance members also supported the development of science-driven discharge targets, Predicted No-Effect Concentrations (PNEC) (AMR Industry Alliance 2023b), for minimising environmental impact from antibiotic discharge into the environment. More recently, AMRIA published the AMR Industry Alliance Antibiotic Manufacturing Standard 2022 (AMR Industry Alliance 2022), which formalises the AMR Industry Alliance 2018 Common Antibiotic Manufacturing Framework.

During the survey timeframe, Alliance members have continued to focus on commitments to responsible antibiotic manufacturing and reducing antibiotic emissions into the environment across their supply chains globally. The Alliance assesses progress against CAMF and PNEC for both members' own manufacturing sites, i.e. sites under the direct control or ownership of the company in which an antibiotic Active Pharmaceutical Ingredient (API) or drug products (i.e. formulated products) are manufactured and direct supplier sites (i.e. sites outside of the direct control or ownership of the company that supply an Alliance member company with an antibiotic API and/or drug products).

The contents below provide an overview of Alliance activities in light of these assessments and in consideration of member commitments to pursue and assess good practices in controlling antibiotic release into the environment. The findings from the survey of member activities in the responsible manufacturing sphere between 1 April 2021 and 31 March 2023 point to notable progress on several fronts related to implementing the CAMF and PNEC targets at their owned manufacturing sites and direct supplier sites. Going forward, they also highlight opportunities for further concerted efforts in select areas.

Overall, the findings show that the percentage of Alliance members with their *own manufacturing sites* who have assessed these sites against CAMF criteria has increased relative to the results of the prior survey round. The percentage of surveyed Alliance members assessing *all* the products manufactured at their own manufacturing sites against PNEC targets has also increased. However, the percentage of assessed products that met PNEC criteria is slightly lower than in the prior reporting period.

Alliance members have also made progress in ensuring *direct supplier sites* are assessed against CAMF, with a greater percentage of sites assessed against CAMF criteria than in the prior survey round but with a lower percentage of assessed sites fully meeting CAMF requirements. Improvements have been made in direct supplier site assessment against PNEC targets, with a higher percentage of products assessed against these targets than in the prior reporting period and a somewhat higher percentage of the assessed products meeting PNEC criteria.

The following contents (Sections 2.1 and 2.2) elaborate on these findings. The section thereafter (Section 3) reflects on the insights in terms of progress relative to results in the prior survey round, explicitly drawing out the comparisons and reflecting on what they show regarding progress and future implications.



Assessment of owned antibiotic manufacturing sites and products

BOX 1. SUMMARY OF THE ASSESSMENT OF SURVEYED ALLIANCE-MEMBER ANTIBIOTIC MANUFACTURING SITES AND PRODUCTS AGAINST CAMF REQUIREMENTS AND PNEC TARGETS



The vast majority (95%) of antibiotic manufacturing sites owned by Alliance members have been assessed against CAMF criteria.



Overall, 90% of surveyed members with their own manufacturing sites assessed against CAMF reported that all their sites either fully or partially met CAMF requirements, with 50% of assessed sites fully meeting requirements.



Most products (88%) manufactured at sites owned by Alliance members with manufacturing operations have been assessed against PNEC targets. The vast majority of products made at manufacturing sites owned by Alliance members and assessed against the PNEC targets met these targets (84%).

Of the 22 surveyed AMR Industry Alliance members across large R&D pharmaceuticals and generics sectors, 21 reported that they manufacture antibiotics at their own manufacturing sites (95%). By sector, this represents ten generics companies and eleven R&D pharmaceutical companies.

Alliance members from the 21 companies reported a total of 199 own manufacturing sites. This ranged from 1–33 manufacturing sites per surveyed company, with a median of five and a mean of nine. One R&D pharmaceutical company reported not owning any manufacturing sites that manufactured products during the timeframe covered in the survey.²

TO WHAT EXTENT ARE ALLIANCE MEMBER MANUFACTURING SITES ASSESSED AGAINST CAMF CRITERIA, AND DO THEY MEET THEM?

AMRIA manufacturing members commit to assessing their own manufacturing sites against the requirements of the CAMF. The CAMF includes (i) compliance with regulatory requirements and permit conditions, (ii) a robust environmental management system to ensure responsible antibiotic production and associated management and treatment of waste, and (iii) risk assessment of antibiotic discharge and assessing these discharges against risk-based targets for discharge concentrations. Sites, including safely accessible perimeters, must be audited at least every five years to verify that operating conditions and practices are in place and appropriately followed.

Among the 199 own manufacturing sites reported from 21 surveyed companies, two-thirds were owned by generics companies (67%, n=134) and one-third by R&D pharmaceutical companies (33%, n=65). The vast majority (95%) of Alliance members' own manufacturing sites (189 of 199) have been assessed against CAMF criteria in the last five years. The assessment rate was 95% for both the generics sector manufacturing sites (127 of 134) and those owned by R&D pharmaceutical sector companies (62 of 65).³

Among the 21 surveyed members with their own manufacturing sites, the majority (86%, n=18; eight generics and ten R&D pharmaceutical companies) had assessed all of their sites against CAMF. A further 10% (n=2; two generics companies) assessed some but not all of their own sites, and 5% (n=1; one R&D pharmaceutical) assessed none. Of the 20 companies that had assessed at least one site, 50% (n=10) reported that all of their manufacturing sites fully met the CAMF requirements, 40% (n=8) reported some of their manufacturing sites fully met CAMF requirements (13–93% at the company level), and 10% companies (n=2) reported that none of their sites fully met CAMF. Of the surveyed companies that had assessed at least one site (80%), there were 16 whose sites all either fully or partially met CAMF requirements. Three companies (15%) had some assessed sites that did not meet CAMF requirements.

We asked Alliance members about the activities they undertook to ensure that their own manufacturing sites meet CAMF requirements. The two most common actions reported by members that assessed their own sites were implementing operating procedures and providing training to support improvement practices in their sites to meet framework expectations (75%, n=15) and developing and implementing improvement plans (65%, n=13).

TO WHAT EXTENT DO ALLIANCE MEMBERS ASSESS PRODUCTS MANUFACTURED AT THEIR OWN SITES AGAINST PNEC TARGETS, AND DO THE PRODUCTS MEET PNEC TARGETS?

The Alliance's PNEC targets (Tell et al. 2019) are science-driven risk-based values for risk-assessing antibiotic discharge in receiving water. These values aim to protect ecological species and minimise selective pressure on bacteria in receiving water bodies to mutate. They are typically extremely low concentrations of antibiotics (e.g. microgram per litre, parts per billion).

Alliance members are committed to assessing products manufactured at their own sites against the PNEC targets. During the survey timeframe, surveyed companies reported a total

of 800 antibiotic products manufactured at their own sites, with a range of 11–118 products per site (median = 22; mean = 38). Overall, 88% of these products (700 of 800) were assessed against PNEC targets.⁴ The assessment rate in the R&D pharmaceutical sector was 91% (247 of 271) and 86% within the generics sector (453 of 529).

Of the 21 surveyed Alliance members with their own manufacturing sites, 76% (16 of 21) assessed all of their products against PNEC targets. A further 14% (n=3) assessed some of their products against PNEC targets, evaluating between 46% and 82% of their products and 10% (n=2) did not assess any of their products against PNEC targets.⁵

Overall, 84% (487 of 582) of products assessed against PNEC targets and for which assessment results could be provided met PNEC criteria.⁶ At the sector level, this translates to 88% (398 of 453) of generics products and 69% (89 of 129) of R&D pharmaceutical products meeting PNEC criteria.⁷

Over half (56%; 10 of 18) of surveyed Alliance members who assessed products from their own manufacturing sites against PNEC targets had all their products meet PNEC. The remaining eight companies had some of their products meet PNEC targets, ranging from 38% to 95% of products.

Alliance members who undertook PNEC assessments were asked about actions taken to ensure that their own manufacturing sites met PNEC targets. Nearly three-fourths of the 19 companies (74%, n=14) reported dry/vacuumed cleaning of product areas, and 68% (n=13) companies reported collecting equipment rinses and treating them separately. Overall, 63% of companies reported performing Mass Balance for all compounds, and 53% reported sampling and analysis for some compounds (n=12 and n=10, respectively). Fewer than half of respondents reported 'Other' activities.

TABLE 1. COMPARISON OF KEY MEASURES FOR MEMBER-OWNED MANUFACTURING SITES AND DIRECT SUPPLIER SITES ACROSS THE 2021 AND 2023 SURVEY PERIODS

Survey year	For own manufacturing sites		For direct supplier sites	
	2021	2023	2021	2023
Per cent of sites to which CAMF requirements were conveyed	--	--	86% of sites	73% of sites ↓
Per cent of sites assessed against CAMF requirements	85% of sites	95% of sites ↑	44% of sites	50% of sites ↑
Per cent of members with all sites meeting CAMF requirements fully or partially	95% of members	90% of members ↓	46% of members	56% of members ↑
Per cent of products assessed against PNEC targets	88% of products	88% of products —	42% of products	53% of products ↑
Per cent of products that met PNEC targets	87% of products	84% of products —	73% of products	76% of products —



Assessment of direct supplier sites and products against CAMF criteria and PNEC targets

BOX 2. SUMMARY OF THE ASSESSMENT OF DIRECT SUPPLIER ANTIBIOTIC MANUFACTURING SITES AND PRODUCTS AGAINST CAMF CRITERIA AND PNEC TARGETS



Overall, 73% of the 809 direct supplier sites reported in the survey had CAMF requirements conveyed to them by an Alliance member.



Over three-quarters (76%) of surveyed companies with direct supplier sites assessed some or all of their supplier sites by audit against CAMF requirements. Of these companies, over half (56%) reported that all of their sites either fully or partially met CAMF requirements, with 25% of these meeting them fully.



Surveyed Alliance members provided data on assessment against PNEC targets for 698 antibiotic products manufactured at direct supplier sites. Over half (53%) of these products were assessed against the PNEC targets, and 76% of the assessed products met PNEC targets.

As introduced earlier, in addition to their own antibiotic manufacturing sites, Alliance members also have antibiotic manufacturing suppliers. Across the Alliance, 22 surveyed members reported 809 direct antibiotic manufacturing supplier sites. This ranged from 0–140 direct supplier sites per company, with a median of 22 and a mean of 37. One R&D pharmaceutical company reported that they had no direct supplier sites.⁸

TO WHAT EXTENT ARE ALLIANCE MEMBERS' DIRECT SUPPLIER SITES ASSESSED AGAINST CAMF CRITERIA, AND DO THEY MEET THEM?

Nearly three-quarters (73%) of the direct supplier sites (593 of 809) had CAMF requirements conveyed to them by Alliance members.⁹ Over half of the 21 surveyed Alliance members with direct supplier sites (52%; n=11; four generics and seven R&D pharmaceutical companies) conveyed CAMF expectations to all of their antibiotic manufacturing supplier sites, 38% (n=8; five generics and three R&D pharmaceutical companies) conveyed these expectations to some of their supplier sites, and 10% (n=2; one generics and one R&D pharmaceutical company) did not convey CAMF expectations to any their supplier sites. For Alliance members that had conveyed expectations to some but not all of their suppliers, the percentage of supplier sites who had CAMF expectations conveyed to them varied widely from 27–90%.¹⁰

Half of the direct supplier sites had been assessed by audit against the CAMF criteria during the survey reporting timeframe (50%; 405 of 809).¹¹ By sector, the assessment rate of direct supplier sites against CAMF criteria was substantially higher for R&D pharmaceutical company supplier sites (90%; 281 of 312) than those of generics sector supplier sites (25%; 124 of 497).

Most Alliance members reported assessing some but not all of their direct supplier sites. Approximately a quarter (24%; n=5; two generics and three R&D pharmaceuticals) of surveyed members with supplier sites assessed all of their sites against CAMF, 52% (n=11; six generics and five R&D pharmaceuticals) assessed some but not all direct supplier sites (1–97% of sites), and 24% (n=5; two generics and three R&D pharmaceuticals) did not assess any of their direct supplier sites against CAMF criteria.¹²

Of the 16 members who assessed some or all of their supplier sites by audit against CAMF, nine companies (56%) reported that all their sites either fully or partially met CAMF requirements during the current survey timeframe. More specifically, a quarter of the 16 surveyed companies that assessed at least one site against CAMF requirements (25%; n=4; three generics and one R&D pharmaceutical company) had all of the assessed sites fully meeting the requirements, and 63% (n=10; three generics and seven R&D pharmaceuticals) had some but not all of their assessed sites fully meeting CAMF requirements (from 25–98% at the company level), and 13% (n=2; two generics companies) had none of their sites fully met CAMF requirements. Six members with at least one assessed direct supplier site (38%) reported that some of their assessed sites do not meet CAMF requirements. Of the 16 companies that assessed one or more sites against CAMF, 11 intended to have all their sites meet CAMF requirements within the next five years (for further details, see Annex A1).

TO WHAT EXTENT DO ALLIANCE MEMBERS ASSESS PRODUCTS MANUFACTURED AT DIRECT SUPPLIER SITES AGAINST PNEC TARGETS, AND DO THE PRODUCTS MEET PNEC TARGETS?

Across the 21 surveyed Alliance members who reported having at least one direct manufacturing supplier site, a total of 816 products were manufactured during the survey timeframe, with a range of 0 to 138 products per site (median = 15; mean = 39). One company did not have any direct supplier sites that manufactured products for them during the survey period, and another could not report on assessment against PNEC targets as it did not have the data available.



Overall, 19 companies could report results for the PNEC target assessment for 698 products.¹³ Over half (53%, n=368) of these products were assessed against PNEC targets.¹⁴ By sector, this translates to 43% (193 of 445) of supplier-site products within the generics sector and 69% (175 of 253) of supplier-site products within the R&D pharmaceutical sector.

Of the 19 surveyed Alliance members with direct supplier sites able to provide product data by site, approximately a fifth (21%, n=4) assessed all of their direct supplier products against PNEC targets. Nearly two-thirds (63%, n=12) assessed some of their direct supplier products against PNEC targets (7–95% of products) and just under a fifth (16%, n=3) did not assess any.

Of the products manufactured at direct supplier sites assessed against PNEC targets and for which assessment data was made available, 76% (281 of 368 products) met PNEC criteria.¹⁵ At the sector level, this translates to 67% (130 of 193) of assessed generics products manufactured at supplier sites and 86% (151 of 175) of R&D pharmaceutical products manufactured at suppliers' sites.

Of the 16 surveyed Alliance members who assessed all or some of the products from their direct suppliers and could provide assessment data, nearly two-thirds of the companies (63%, n=10) reported all of their supplier site products meet PNEC targets (n=10) and 38% (n=6) reported some of their supplier site products meet these targets (ranging from 28– 98% of products at the company level). No members had direct supplier sites where no products met PNEC targets. The mean percentage of products from supplier sites that were assessed and met PNEC targets was 88%, ranging widely from 28–100%.

Alliance members took diverse actions to ensure that direct antibiotic manufacturing suppliers meet the PNEC targets. No single distinct action was taken by more than half of the companies responding. However, notable actions taken by a third or more of the companies include providing technical guidance/toolkits to suppliers for performing mass balance, reviewing/checking that their suppliers took corrective actions post-audit if such actions were needed, and reviewing supplier Mass Balance for some (but not all) compounds.



In reflection: AMRIA's progress in commitments to responsible manufacturing

The results of the Alliance member survey highlight notable progress made by Alliance members in terms of their own manufacturing site delivery against commitments to responsible antibiotic manufacturing, including assessment against both CAMF criteria and PNEC targets.

Reflecting on the comparative performance data between the current and prior survey rounds shows an increase of ten percentage points for Alliance members' own manufacturing sites that were assessed against CAMF criteria (95% in the current versus 85% in the prior survey round).

Data on the assessment of products manufactured at own sites against PNEC targets shows sustained commitments to monitoring performance on this front, with 88% of products manufactured at Alliance members' own manufacturing sites assessed against PNEC targets in both the current and prior survey rounds (Marjanovic et al. 2022). In addition, in the current reporting period, 76% of surveyed Alliance members with their own manufacturing sites had assessed 100% of the products manufactured at these sites against PNEC targets,

compared to 65% of surveyed members doing so in the prior AMRIA survey and progress report, suggesting an increased commitment to assessment of products manufactured at many of the Alliance members' own sites (Marjanovic et al. 2022). Overall, 84% of products assessed in this survey round met PNEC criteria, a little lower than the prior reporting period, where 87% of assessed products met PNEC targets (Marjanovic et al. 2022).

Substantial progress has also been made on some fronts for products manufactured at direct supplier sites, but there are also areas where future collective efforts of Alliance members could further support responsible manufacturing activity at supplier sites.

Alliance members have shown progress in ensuring direct supplier sites are assessed against CAMF relative to the prior survey round. However, there are opportunities for the generics sector, in particular, to enhance activity in this regard. Overall, a greater percentage of direct supplier sites to surveyed Alliance members have been assessed by audit against CAMF criteria (50% in the current versus 44% in the prior survey round) (Marjanovic et al. 2022). However, assessment rates of direct supplier sites against CAMF criteria were much higher for R&D pharmaceutical company supplier sites than for those of antibiotic manufacturing suppliers to generics sector members (90% and 25%, respectively).

Going forward, there is scope to ensure progress is sustained or reinforced in terms of maintaining focus on conveying CAMF requirements to direct supplier sites and assessing as many direct supplier sites against CAMF as possible. However, it is important to recognise that Alliance membership has changed over time and that some newer members need time to engage with diverse direct supplier sites about CAMF expectations. Although a majority of Alliance members' direct supplier sites had CAMF requirements conveyed to them (73%), the percentage was lower than in the prior survey round (86%)(Marjanovic et al. 2022). Most Alliance members (76%) had also assessed some or all of their supplier sites against CAMF criteria, but nearly a quarter had not. Reassuringly, among companies that assessed some or all of their supplier sites against CAMF, over half (56%) reported that all of their sites either fully or partially met CAMF requirements. However, only a quarter (25%) had all assessed sites fully meeting the requirements, a substantial decrease from the prior round, where half of the assessed sites were reported as fully meeting CAMF requirements (50%)(Marjanovic et al. 2022).

Efforts to ensure supplier sites are monitored for compliance with PNEC targets have translated into improvements over time. Alliance members with direct supplier sites should continue to support these sites' efforts to assess their products against PNEC criteria. In the current survey round, a substantially higher percentage of products manufactured at direct supplier sites were assessed against PNEC targets than in the prior survey round (53% compared to 42%, respectively) (Marjanovic et al. 2022). Over three-quarters (76%) of the assessed supplier site products met the PNEC targets, a slight increase from the results reported in this regard in the prior survey (73%)(Marjanovic et al. 2022).



A forward look: supporting good practice in the context of global collaboration

As introduced earlier in this report, Alliance members are seeking to further evolve industry practices in support of reducing emissions from antibiotic manufacturing into the environment, with recent developments including the June 2022 publication of the AMR Industry Alliance Antibiotic Manufacturing Standard 2022 (AMR Industry Alliance 2022) with the process of developing the standard facilitated by the British Standards Institution (BSI). This standard seeks to provide clear guidance to industry manufacturers in support of efforts to ensure that antibiotics across global supply chains are manufactured responsibly and minimise detrimental impacts on the environment and antimicrobial resistance. In June 2023, BSI launched a certification program intended to provide independent verification that an antibiotic is made in accordance with the requirements of the industry standard (which combines the prior AMRIA CAMF and the PNEC values)(The British Standards Institution 2023).

These steps taken by the AMRIA, working with the BSI, reflect the Alliance's leadership in setting industry standards and committing to their implementation. Although implementing the standard at scale will take time, the development of the standard signals AMRIA's efforts to raise awareness of the importance of responsible antibiotic manufacturing globally and to expand the reach of AMRIA's foundation work beyond the supply chain footprint of its members. As an industry-led standard developed for industry, there are likely to be opportunities for AMRIA to exchange insights and share learning with others who may work to advance regulation (e.g. at the European Union level) or guidelines on responsible antibiotic manufacturing in the future, including the efforts of supranational bodies such as the World Health Organisation. Sustained global collaboration across industry, public and not-for-profit sectors will be central to supporting shared endeavours to curb the rise of antimicrobial resistance for the benefit of populations worldwide.

Endnotes

- 1 Membership numbers are based on membership at the time of the survey.
- 2 In the the prior Alliance progress report, 20 surveyed Alliance members reported manufacturing antibiotics at a total of 211 of their own manufacturing sites.
- 3 In the prior Alliance progress report, the overall assessment rate was 85% (179 out of 211 antibiotic manufacturing sites).
- 4 This is the same overall assessment rate as in the prior Alliance member survey.
- 5 In the prior Alliance progress report, 65% (n=13) of Alliance members reported assessing all products against PNEC targets, 20% (n=4) reported assessing some but not all of their products, and 15% (n=3) reported assessing none of their products against PNEC targets.
- 6 One company could not provide data on how many of their assessed products met PNEC targets.
- 7 In the prior Alliance progress report, 87% of the 1226 assessed products met PNEC targets.
- 8 Compared to the last survey round's progress report, Alliance members reported a relatively similar number of direct supplier sites (821 in total in the prior progress report).
- 9 The percentage of direct supplier sites having CAMF requirements conveyed them was 86% in the last survey round.
- 10 Compared to the prior Alliance member survey and progress report, 59% of Alliance members with at least one direct supplier site reported conveying CAMF to all of their direct supplier sites, while 29% and 12% reported conveying the framework to some and none of their sites, respectively.
- 11 In the prior Alliance progress report, 44% of direct supplier sites had been assessed against CAMF requirements (359 of 821 members that had assessed at least one site and had assessment information available).
- 12 In the prior Alliance progress report, 31% of the 13 surveyed Alliance members reported assessing all and 69% reported assessing some of their supplier sites.
- 13 Surveyed companies had data on PNEC assessment for 698 of the 809 products manufactured at direct supplier sites.
- 14 Compared to 42% (345 of 831) products manufactured at direct supplier sites assessed against PNEC targets in the prior survey period.
- 15 In comparison, 73% (252 of 245) of assessed supplier sites products met PNEC criteria in the prior survey period.

Bibliography

- AMR Industry Alliance. 2018a. *Tracking progress to address AMR*. As of 7 November 2023: [AMR_Industry_Alliance_Progress_Report_January2018.pdf](https://www.amrindustryalliance.org/Progress_Report_January2018.pdf) ([amrindustryalliance.org](https://www.amrindustryalliance.org))
- AMR Industry Alliance. 2018b. Common Antibiotic Manufacturing Framework (CAMF). As of 7 November 2023: https://www.amrindustryalliance.org/wp-content/uploads/2018/02/AMR_Industry_Alliance_Manufacturing_Framework.pdf
- AMR Industry Alliance. 2022. 'Antibiotic Manufacturing Standard 2022'. As of 7 November 2023: <https://www.amrindustryalliance.org/antibiotic-manufacturing-standard/>
- AMR Industry Alliance. 2023a. *AMR Industry Alliance 2022 Year in Review*. As of 7 November 2023: <https://www.amrindustryalliance.org/mediaroom/amr-industry-alliance-releases-2022-annual-report/>
- AMR Industry Alliance. 2023b. 'Predicted No-Effect Concentrations (PNEC) Targets list'. As of 7 November 2023: https://www.amrindustryalliance.org/wp-content/uploads/2023/02/AMR-Table-1-Update-20230222_corrected.pdf
- Dadgostar P. 2019. 'Antimicrobial Resistance: Implications and Costs'. *Infection and Drug Resistance*, 12, 3903–3910. As of 7 November 2023: <https://doi.org/10.2147/IDR.S234610>
- European Commission. 2022. 'Health Union: HERA delivers list of top-3 health threats to prepare against'. As of 7 November 2023: https://ec.europa.eu/commission/presscorner/detail/en/IP_22_4474
- Marjanovic, S., Parkinson, S., Francombe, J., Romanelli, R.J., Rodriguez-Rincon, D and Manville C. 2022. Progress Report: AMR Industry Alliance 2021 Survey. As of 7 November 2023: https://www.rand.org/pubs/external_publications/EP68833.html
- Murray, C. J., Ikuta, K. S., Sharara, F., et al. 2022. 'Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis'. *The Lancet*, 399(10325), 629–655. As of 7 November 2023: [https://doi.org/10.1016/S0140-6736\(21\)02724-0](https://doi.org/10.1016/S0140-6736(21)02724-0)
- Tell, J., Caldwell, D.J., Häner, A., Hellstern, J., Hoeger, B., Journal, R., Mastrocco, F., et al. 2019. 'Science-Based Targets for Antibiotics in Receiving Waters from Pharmaceutical Manufacturing Operations.' *Integrated Environmental Assessment and Management* 15 (3): 312–19.
- The British Standards Institution. 2023. *New certification aims to mitigate antimicrobial resistance risk in antibiotic manufacturing*. As of 6 November 2023: <https://www.bsigroup.com/en-US/about-bsi/Media-Center/Press-Releases/2023/june/new-certification-aims-to-mitigate-antimicrobial-resistance-risk-in-antibiotic-manufacturing/>



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.

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