DEPARTMENT OF HEALTH AND SOCIAL CARE AMR NATIONAL ACTION PLAN – CALL FOR EVIDENCE Jan 2023.

National Biofilms Innovation Centre (NBIC) response.

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From your experience, how has the scale of the threat of AMR changed since the national action plan was published in 2019? a) the threat of AMR has increased since 2019 b) the threat of AMR has stayed the same since 2019 c) the threat of AMR has reduced since 2019 d) don't know.
Answer: c

In your opinion, what are the top 3 drivers of AMR? Please give 3 short answers.

1) Biofilms are resistant to antibiotics and are difficult to diagnose and treat
2) Biofilms cause the transmission of AMR genes between bacteria and the evolution of new AMR mechanisms
3) There is a lack of industry standards or a regulatory framework to address biofilms – this is blocking innovation, new medicines and new products for biofilm control or eradication.

We call for a clear recognition of the role of biofilms as a major cause of AMR infection and transmission with a huge economic and health impact. There is a huge global burden of recurrent and chronic infections caused by biofilms forming on medical surfaces and devices (e.g. prosthetics, catheters, implants, non-healing wounds, musculoskeletal infection and recurrent UTIs) that are resistant to antibiotics and are continuing to increase within aging populations. The problem of AMR will not be resolved without considering bacteria in their predominant, naturally occurring and resistant biofilm form.

Which of these areas would you most like to see prioritised over the next 5 years?
1. reducing the need for, and unintentional exposure to, antimicrobials
2. optimising the use of antimicrobials
3. investing in innovation, supply and access
Answer: 3

Are there any actions you think are required to tackle AMR that do not fall within one of these categories?
Answer: yes **(please specify)**

In 2021, the Taskforce on Innovation, Growth and Regulatory Reform reported that the UK should take the lead on the development of global standards, which will allow the UK to benefit from knowledge transfer and de-risk innovation.

The lack of a regulatory framework and industry standards to assess new medicines or products for biofilm control or eradication in any medical, environmental or engineered setting is a huge block in addressing biofilm challenges. Industry standards developed for microbiology more broadly are not applicable to microbes in their biofilm forms.

The UK has the opportunity to take global leadership in the development of new regulatory standards and guidelines for biofilms, which will drive innovation and lead to the development and adoption of new medicines, products and services effective against biofilm-associated AMR.

Within the UK, what are the key successes we should look to maintain or build on in responding to AMR? Please include up to 3 examples in no more than 250 words.

Continue to develop and support innovative new models for evaluating and paying for new classes of antimicrobials. The aim is to give companies a better incentive to develop new strategies and to stimulate a critical mass of the adoption of similar models internationally, so that sufficient global scale is achieved that will drive and attract the necessary investment into innovation and R&D.

Continue to influence global research strategies on AMR-related topics by representing the UK on regional and global mechanisms such as the Joint Programming Initiative on Antimicrobial Resistance (JPIAMR).

Continue and expand the development and support for novel bacterial biofilm inhibiting strategies (This is in part recognised in the new commitment under 4.2 'Development of new therapeutics' in the addendum to the NAP, but should become a mainstream strategy for addressing AMR).

Within the UK, what are the areas that require more focus or development to address AMR? Please include up to 3 examples using no more than 250 words in total.

The market access and challenges that exist for new antibiotics has led to the situation that academic discovery science is still the primary source of new antimicrobials and antibiofilm agents, and not companies. *Therefore, we suggest that there remains a huge opportunity for the Government to develop and expand models that catalyse efficient and interdisciplinary knowledge transfer between the UK academic research base and industry.*

Part of the economic challenge is that very few recognised industry standards are available to assess new medicines or products for biofilm control or eradication in any medical environmental or engineered setting; those developed for microbiology more broadly are not applicable to microbes in their biofilm forms. *The UK has the opportunity to take global leadership in the development of new regulatory standards and guidelines for biofilms,*

which will drive innovation and lead to the development and adoption of new medicines, products and services.

Biofilm infections are difficult to diagnose and treat - It is not possible to detect the presence of a biofilm with conventional microbiological or molecular diagnostic approaches. Identification of biofilm-associated AMR requires advanced analyses that are time-intensive and require specialized training – causing delays and costing lives. *We recommend that the Government supports the development of new and rapid biofilm evaluation platforms and that the UK becomes the first country to embed biofilm clinical care within its national health provision.*

Within your sector, do you think the UK has sufficient capacity and capability to tackle AMR?
No **(please specify)**

Our network of >150 industry partners have consistently identified a key skills gap and requirement for scientists, thought leaders and entrepreneurs capable of working across disciplinary boundaries. This is a particular problem for biofilm associated AMR where combined physical, chemical and biological strategies and approaches are required. A focus on AI, machine learning and computational approaches to modelling and predicting biofilm AMR outcomes is also needed. NBIC is working to deliver a programme of training, co-created with our industry partners, that addresses these interdisciplinary skills gaps.

What additional capacity and capability is needed in your sector to effectively tackle AMR? Please give up to 3 examples using no more than 250 words in total.

There is a requirement for a nationally accessible infrastructure and capability to rapidly evaluate and diagnose biofilms, their associated AMR, and evaluate the efficacy of new interventions targeted at biofilms. This will require precision (integrated 'omic's), AI and computational approaches and allow for spatially resolved analyses for localised biofilm infections. This will enable the UK to become the first country to embed biofilm clinical care within its national health provision and to reduce biofilm-associated AMR.

NBIC's consultation with its partners and stakeholders has highlighted a critical unmet need for the creation of a biofilm biobank. Biofilms represent complex microbial communities yet microorganisms are typically stored as single type-strains, rarely as consortia, and rarely has the material been well characterised both genetically and phenotypically, such that it's function is well documented and preserved. Biobanking resource is considered a critical need for the development of new biofilm control strategies.

We lack a national capability for the real-time pathogen, biofilm and AMR surveillance within the environment e.g. new technolology for rapid wastewater analysis and surveillance infrastructure.

We lack a flexible and agile regulatory and standards framework for biofilm technologies – this will stimulate innovation and catalyse the development of new medicines and

interventions. We recommend to identify new ways to catalyse efficient knowledge transfer between scientists, industry, standards bodies and regulators, in the field of biofilms.

What, if anything, do you think we can learn from other countries' responses to AMR? Please be specific about which countries you are referring to in your answer. Please give up to 3 examples using a maximum of 250 words in total.

The UK has led the world in highlighting the global problem and challenge and has been at the forefront of responses to AMR. The UK is also distinctive in recognizing the challenges caused by biofilms across a range of sectors, as evidenced by the establishment of the National Biofilms Innovation Centre. The US and Singapore have also invested substantially in biofilm research and development capability. We should ensure that the UK continues to provide world leadership and remains at the forefront in biofilms and AMR.

In your opinion, which of these tools should be prioritised for adapting to use in tackling AMR?

1. **diagnostics**
2. **surveillance**
3. **therapeutics**
4. **vaccines**

All of the above are critical and need to be brought forward in parallel.

In your opinion, are there any other tools that should be adapted from use during the COVID-19 pandemic for tackling AMR?

Yes **(please specify)**

We learned during the pandemic that rapid, bedside, molecular diagnostic technologies can be used and we believe that similar approaches can now be developed for the evaluation and diagnosis of biofilm-associated AMR. As one example, rapid covid diagnostics at the bedside (1) were developed at the NIHR Antimicrobial Resistance Laboratory awarded to University Hospital Southampton and NBIC, and we and other groups are working on new molecular technologies that will similarly provide rapid diagnoses of biofilms and biofilm-associated AMR.

The pandemic also led to the development of technologies for mass Covid surveillance within the population (for example NHS Saliva Testing Program), and for assessing epidemiology within the environment through the monitoring of covid incidence in wastewater. We believe that both of these approaches could be adapted for monitoring AMR and associated pathogen incidence.

Routine molecular point-of-care testing for SARS-CoV-2 reduces hospital-acquired COVID-19. Livingstone R, Lin H, Brendish NJ, Poole S, Tanner AR, Borca F, Smith T, Stammers M, Clark TW.J Infect. 2022 Apr;84(4):558-565. https://doi.org/10.1016/j.jinf.2022.01.034

Do you believe the changes in ways of working within your organisation due to the COVID-19 pandemic have affected efforts to respond to AMR, such as delivery of the current national action plan (NAP)?
Yes

To address the challenges of Covid we have developed high throughput molecular diagnostic approaches as identified above, and we have also shown that we can work jointly and effectively across networks – both of these changes will be critical to address AMR. The negative impact of the pandemic for AMR outcomes was that clinical colleagues working and collaborating in biofilm and antimicrobial research were diverted for 2 years therefore access to patient samples, translational clinical research infrastructure and collaboration in AMR research all stopped during the pandemic, however these activities and collaborations are now restarting.

In what way have they affected the response to AMR or delivery of the NAP? Please give up to 3 examples using no more than 250 words in total.
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Are there other ways in which the COVID-19 pandemic has altered the AMR risk landscape?
Please give up to 3 examples in no more than 250 words in total.

NBIC does not have sufficient evidence / data to support that COVID 19 has altered the AMR risk landscape either positively or negatively.

Are there other global events, such as supply chain disruption or the conflict in Ukraine, that have changed the UK's ability to respond to AMR?
yes
If yes, how have other global events changed the UK's ability to respond to AMR? Please specify which global event you're referring to.

Lack of agreement on participation in Horizon Europe will impact on the UK's ability to collaborate with colleagues in major international R&D programmes in AMR.

In your opinion, what are the best measures of success in tackling AMR? Please give up to 3 suggestions.

Global surveillance of AMR, including the evaluation and incidence of biofilm-associated resistant infections in humans and animals, and global monitoring of AMR within the environment.

Reduced resistant infections globally, including those caused by chronic and recurrent biofilm-associated disease.

New diagnostics and therapeutics effective for biofilms, embedded within a regulatory framework and environment that supports innovation and rapid translation into the NHS.