Innovate UK
Global Expert Mission

Antimicrobial Resistance Germany 2019

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Innovate UK
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Abbreviations

AMR	Antimicrobial Resistance
ARDIS	African and Asian Resilience in Disaster Insurance Scheme
B2B	Business to Business
BMBF	German Federal Ministry of Education and Research (Bundesministerium für Bildung und Forschung)
BMG	German Federal Ministry for Health (Bundesministerium für Gesundheit)
BSAC	British Society for Antimicrobial Chemotherapy
CARA	Conscience of AMR Accountability
CARB-X	Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator
CDC	US Centre for Disease Control and Prevention
CDx	Companion Diagnostics
DART	Deutsche Antibiotika Resistenz Strategie
DZIF	Deutschen Zentrum fur Infektionsforschung
EC	European Commission
ECDC	European Centre for Disease Prevention and Control
FAO	Food and Agriculture Organisation
GARDP	Global Antibiotic Research and Development Partnership
GDP	Gross Domestic Product
GP	General Practitioner
IBMT	Fraunhofer Institute for Biomedical Engineering
IMI	Innovative Medicines Initiative
IZI	Fraunhofer Institute for Cell Therapy and Immunology (Fraunhofer-Institut für Zelltherapie und Immunologie)
IZI-BB	Fraunhofer Institute for Cell Therapy and Immunology branch Bioanalytics and Bioprocesses (Fraunhofer-Instituts für Zelltherapie und Immunologie Bioanalytik und Bioprozesse)
JPIAMR	Joint Programming Initiative on AMR
JPIAMR VRI	JPIAMR Virtual Research Institute

KTN	Knowledge Transfer Network
LMICs	Low- and Middle-Income Countries
NOVA	Novel approaches for design and evaluation of cost-effective surveillance across the food chain
MRC	Medical Research Council
MRSA	Methicillin-resistant Staphylococcus aureus
NHS	National Health Service
OECD	Organisation for Economic Co-operation and Development
OIE	Organisation for Animal Health
PHE	Public Health England
RKI	Robert Koch Institute
SIG	Special Interest Group
SME	Small and Medium-sized Enterprise
UKRI	United Kingdom Research and Innovation
UN	United Nations
WHO	World Health Organisation
WHO GLASS	WHO - Global Antimicrobial Resistance Surveillance System

Welcome

Innovate UK global missions programme is one of its most important tools to support the UK's Industrial Strategy's ambition for the UK to be the international partner of choice for science and innovation. Global collaborations are crucial in meeting the Industrial Strategy's Grand Challenges and will be further supported by the launch of a new International Research and Innovation Strategy.

Innovate UK's Global Expert Missions, led by Innovate UK's Knowledge Transfer Network, play an important role in building strategic partnerships, providing deep insight into the opportunities for UK innovation and shaping future programmes.

In May 2019, an expert UK delegation travelled to Germany. The delegation met with German federal officials, academics and commercial entities from sixteen antimicrobial resistance (AMR) related organisations and learnt about many programmes that could directly benefit from collaboration and joint ventures with organisations involved in AMR in the UK.

This report shares information and insights gathered during the visit, considering how collaboration could help curb AMR in both countries while also exploring opportunities for increased innovation and economic development.

Executive Summary

The Global Expert Mission to Germany on antimicrobial resistance (AMR) assured the UK delegation of the commonalities the UK and Germany share as it relates to combating the escalating global threat of AMR. The countries clearly share the same concerns, pinpoint the relevance of innovation, and agree that joining forces in combating AMR is of key importance.

The UK delegation meeting with officials from the German Federal Ministry of Health, the German Federal Ministry of Education and Research, and the German Centre for Infection, at the British Embassy, Berlin.

Overall Germany has the same perception of the challenges posed by AMR; however, there are substantial differences when trying to curb AMR. The German AMR Strategy (DART 2020)[1] stresses the importance of "measure and improve treatment". In contrast, the UK's long-term strategy focuses on "contain and control" which places emphasis on "infection prevention, stewardship and innovation"[2].

Although Germany has the German Centre for Infection Research (DZIF)[3] and the National AMR Strategy, DART 2020, the execution of this strategy is complex. Germany has sixteen autonomous, federal states which differ in financial strength and innovation potential and compete for the same national funding. They may also implement the national strategy differently.

Germany is increasingly expanding its geographic scope when it comes to AMR-related activities; this contrasts from its previous German-centric focus. In comparison, the UK assumes a more international approach (and takes related responsibilities), demonstrated by its strategy of tackling AMR in many low- and middle-income countries (LMICs).

Germany and the UK have unique capabilities and technologies that could assist other nations to address AMR, including in LMICs. In essence, there are opportunities to bring organisations from both countries together that would allow greater output than could be achieved if they acted independently. This Global Expert Mission has defined a number of objectives and related follow-up actions that the UK should consider taking forward.

An Initial investment has the potential to enhance the likely success of UK and German industry in the AMR arena, by increasing wealth in both countries through products that could be commercialised and sold throughout the developed world. While at the same time helping to address the problems of AMR in the developing world, which indirectly have a knock-on effect on the German and UK health systems and economies.

In the short term, the Global Expert Mission recommends that the UK should consider the following actions:

1. UK-German collaboration in developing diagnostic tools that:
    - Create evidence for the test to improve antibiotic treatment decisions (target-product-profile) for specific conditions.
    - Evaluate and benchmark current available diagnostic tools.
    - Are ideally highly accurate and highly specific, and able to work with minimum healthcare resources (perhaps able to transmit data via mobile technology), providing information which is suitable to contribute to the WHO GLASS System.

[1] DART: Deutsche Antibioka Resistenz Strategie
[2] Contained and controlled: The UK's 20-year vision for antimicrobial resistance
[3] https://www.dzif.de/en

2. Explore UK-German challenges and opportunities in companion diagnostics such as co-developing and commercialising AMR companion diagnostics technology and further discussing areas around regulation, clinical and technological need and business models, among others.

3. Explore UK-German collaboration opportunities in alternative antimicrobials such as phage therapy, natural compounds and DNA-based CRISPR-Cas9. This is an area where Germany appears to be conducting a lot of research, and the UK could complement this by sharing its medicines manufacturing techniques. This could be an opportunity for collaboration where both the UK and Germany bring different strengths.

4. Share information on microbiome-related activities to AMR and explore the potential for bilateral cooperation. This is a new area of focus for both countries, and there was a strong appetite to share research being conducted in this area and also bring industry into this discussion.

1. Introduction to Antimicrobial Resistance

Antimicrobial resistance (AMR) develops when bacteria, fungi or viruses are exposed to antibiotics, antifungals or antivirals. As a result, the antimicrobials become ineffective and infections may persist in the body, increasing the risk of spread to others[4]. In addition, medical interventions including surgery, caesarean sections, chemotherapy and stem cell therapy may become impossible.

AMR is deemed one of the most severe threats to health and food safety. It is estimated that AMR causes at least 700,000 casualties per year[5]; however, more recent recalculations suggest substantially higher numbers. According to the 2014 Review on Antimicrobial Resistance by Jim O'Neill, the global population may face some 10,000,000 casualties per year by 2050 due to AMR, with a cumulative Gross Domestic Product (GDP) loss of USD 100 trillion[6]. Unless action is taken, it is highly likely that this will have a detrimental impact on our to ability meet the Sustainable Development Goals for 2030, including no poverty, zero hunger, good health and wellbeing, gender equality and partnerships for the goals. The impact of AMR with regard to poverty are especially worrying. "In a high AMR-impact scenario, an additional 24 million people will be forced into extreme poverty by 2030. Most of the increase in AMR will occur in LMICs"[7]. As highlighted by the Dag Hammarskjöld Foundation and ReAct, "Planet Earth faces the very real threat of having to survive in a 'post-antibiotic' era in which there are few if any, antibiotics which effectively and affordably cure infections"[8].

1.1 AMR in 10 Statements

AMR is a complex, multifaceted societal and economic challenge comparable with other global challenges like climate change. In short, AMR can be described in 10 statements:

1. AMR is a global challenge affecting all countries and potentially impacting everybody: young and old, healthy and diseased. As a result of mobility and food transportation, AMR has the potential and ability to spread quickly around the globe.
2. AMR is a hidden and likely underestimated threat as infectious diseases may not always be diagnosed, even if the causing microorganism has been identified and its antibiotic resistance profile determined. Furthermore, even if it is properly diagnosed, patient data may not always be documented and communicated to the relevant health authorities: there is no standardised system for recording the prevalence of AMR deaths.
3. Reducing antimicrobials for human and veterinary use is urgently needed and adds to the prevention of AMR. However, antimicrobials remain necessary; in countries where antibiotics are difficult to obtain and/or unaffordable, the chances of epidemics substantially increase[9].
4. AMR prevents the effective treatment of infectious diseases but also complicates medical treatments where antibiotics are used on a routine basis, such as surgery, chemotherapy and stem cell therapy.
5. AMR includes resistant bacteria and also viruses, fungi, yeasts and parasites. Antibiotic resistance in bacteria provides the biggest health and economic problems. Recent outbreaks of resistant fungi (azole-resistant Aspergillus[10] and multidrug-resistant Candida[11]) show that these microorganisms increasingly threaten public health.
6. AMR so far has developed against all commercially available antibiotics. Resistant bacteria were found within months or years after the introduction, and sometimes even before commercial introduction, of antibiotics. Second and third-generation antimicrobial products claim that they will not result in resistant microorganisms.
7. The current pipeline of novel antibiotics is rather empty, despite the constant need for novel antimicrobial products and alternative strategies. Novel antibiotics are the most underserved area within drug discovery and development pipelines. The major reasons for this are the lack of a solid business case for involved pharma

[4] https://www.who.int/en/news-room/fact-sheets/detail/antimicrobial-resistance
[5] https://www.who.int/news-room/detail/29-04-2019-new-report-calls-for-urgent-action-to-avert-antimicrobial-resistance-crisis
[6] https://amr-review.org/
[7] http://documents.worldbank.org/curated/en/455311493396671601/pdf/executive-summary.pdf
[8] https://www.daghammarskjold.se/publication/antimicrobial-resistance-and-sustainable-development-a-planetary-threat-but-a-financing-orphan/
[9] https://cddep.org/wp-content/uploads/2019/04/AccessBarrierstoAntibiotics_CDDEP_FINAL.pdf
[10] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4706635/
[11] https://www.cdc.gov/fungal/candida-auris/index.html

companies and that the low hanging fruit of promising compounds has already been picked.

8. AMR at a global scale is escalating whereby LMICs bear the harshest burdens in terms of fatalities, loss of livestock and economic losses. There are indications that climate change, especially observed in these LMICs, will further spread the impact of AMR.

9. AMR is considered a global "One Health" challenge involving both human health, animal health and the environment, together with related industries such as the agriculture and food (dairy, meat) sectors, the water sector and also the tourism sector.

10. There is no single solution to AMR. AMR can only be restrained and contained by the global implementation of key strategies, as detailed below.

1.2 Key Strategies to Curb AMR

Both international and national level action plans have been set up to fight AMR by organisations such as the World Health Organisation (WHO), the Food and Agriculture Organisation (FAO), the European Commission (EC), the US Centre for Disease Control and Prevention (CDC) and others. These plans have five underlying "key strategies" in common:

1. **Improving the prevention of infectious diseases** by raising awareness, improving hygiene and sanitation, and vaccination.

2. **Extending the implementation of antibiotics stewardship**, including the mandatory prescription of antimicrobials for human and veterinary use, refraining from using antibiotics as animal growth enhancers, and prohibiting the sale of over-the-counter antibiotics, as occurs in some LMICs.

3. **Developing and applying improved molecular microbiological diagnostics** for both microbial species identification as well as antimicrobial susceptibility testing. Hopefully resulting in better, more selective and more justified prescriptions of appropriate antimicrobial products.

4. **Developing new classes of antibiotics** and other antimicrobial products to which no resistance exists as of yet. This strategy includes the reuse of older antibiotics and the revitalisation of previously written-off antibiotics, as well as the registration of existing commercially available antibiotics for novel indications.

5. **Developing alternative antimicrobial strategies** that pave the way to entirely new therapeutic approaches to treat bacteria and other microorganisms, such as phage therapy, CRISPR-Cas9, nanomaterials and the use of natural products, as well as other strategies.[12]

AMR is increasingly gaining global attention, and at a national level, many organisations are involved in curbing the escalating threat, through the following mechanisms:

- Authorities are involved in setting guidelines for infection prevention; hospitals and healthcare centres implement the guidelines to prevent infection.

- Academia is involved in fundamental research for novel antimicrobials and big pharmaceutical companies may take forward these developments, register, produce and market the products. For the clinical development part, hospitals are also involved.

- Funding organisations provide the means for basic research at universities, which is needed for the development of novel diagnostic tools, then start-ups, small and medium-sized enterprises (SMEs) and multinational companies commercialise these innovations.

Target group	Strategy				
	Improved prevention	Improved stewardship	Improved microbial diagnostics	Novel antimicrobials	Alternative strategies
Authorities					
Healthcare centres					
Academia and research centres					
Pharmaceutical industry					
Diagnostics industry					
Funding organisations					

Table 1: Organisations involved in curbing AMR. The colours indicate: dark grey – leading role; light grey – supporting or contributing role; and white – no involvement in the activity.

[12] https://www.amr-insights.eu/antimicrobial-resistance-in-10-elementary-statements/

1.3 The UK and German National AMR Strategies

1.3.1 Contained and Controlled: The UK's 20-Year Vision for AMR

AMR is a serious threat to public health in the UK. NHS England's Chief Medical Officer, Professor Dame Sally Davies, has reported that antibiotic resistance kills 5,000 people in the UK each year. Some sources suggest at least 12,000 people in the UK are likely dying each year from drug-resistant sepsis alone[13].

According to its vision, Contained and Controlled: The UK's 20-Year Vision for Antimicrobial Resistance,[14] published in January 2019, the UK is determined to sustain its efforts in combating resistance, taking local, national and global "One-Health" approaches across humans, animals, the environment and food, in line with global ambitions and in collaboration with other nations, partners and the international community. Policy and practice are being developed and strengthened by multiple actors from different levels of governance. Knowledge and understanding continue to improve through research and surveillance, whilst effective regulation and advocacy efforts are helping to contain and control resistance.

As part of this strategy, the UK's international effort to control AMR and strengthen the associated policy and regulatory environment it places emphasis on the following three points:

1. A lower burden of infection and better treatment of resistant infections in order to effectively minimise the transmission of AMR across communities, including farming and food production communities, and the environment.
2. Optimal use of antimicrobials and good stewardship across all sectors, promoting access to safe and effective medicines that have been manufactured responsibly for all who need them. The UK government seeks to establish itself as a country of global best practice, in line with the best countries in the world, in achieving and maintaining antimicrobial usage levels by sector.
3. New diagnostics, therapies, vaccines and interventions in use and a full AMR research and development pipeline for antimicrobials, alternatives, diagnostics, vaccines and infection prevention across all sectors; with access to new and old technologies for all.

1.3.2 Tackling AMR 2019-2024: The UK's 5-Year National Action Plan

In 2019, the Department for Health and Social Care (DHSC)[15] introduced the UK's 5-year action plan for Tackling Antimicrobial Resistance 2019 to 2024[16], which will be used to complement and ensure progress towards the 20-year vision on AMR to effectively contain and control resistance. Extensive cooperation and collaboration has taken place across a number of government bodies in England, Scotland, Wales and Northern Ireland to develop both the 20-year vision and the 5-year action plan. The NHS and animal health and welfare agencies were also extensively consulted and fed into both documents.

The 5-year action plan is structured around the United Nations Interagency Framework for Action on AMR[17]. This framework emphasises the need for action in 15 distinct areas; this will be in addition to domestic and global efforts already in place. The UK will work alongside other countries to help establish this as a blueprint for their own initiatives. The action plan focuses on three key areas for tackling AMR:

1. Reducing need for, and unintentional exposure to, antimicrobials.
2. Optimising use of antimicrobials.
3. Investing in innovation, supply and access.

The previous UK 5-year AMR strategy 2013-2018 brought together 21 research funders, including the UK Research and Innovation (UKRI) Councils, government departments, devolved administrations and charities. The following outcomes were achieved:

1. Identified four key research themes to target investments:
    - o understanding resistant bacteria
    - o accelerating therapeutic and diagnostic development
    - o understanding real-world interactions
    - o behaviour within and beyond the healthcare setting.
2. A cross UKRI Councils AMR initiative was established.
3. Some 78 interdisciplinary projects were supported with a total commitment of circa £44 million.
4. In recognition of the global dimension of AMR, approximately £41 million was committed to supporting projects in partnership with members of the EU Joint Programming Initiative on AMR (JPIAMR)[18], with emerging economies and with LMICs.

Under the previous AMR strategy, Innovate UK invested

[13] https://www.thebureauinvestigates.com/stories/2016-12-11/superbugs-killing-twice-as-many-people-as-government-says
[14] https://www.gov.uk/government/publications/uk-20-year-vision-for-antimicrobial-resistance
[15] https://www.gov.uk/government/organisations/department-of-health-and-social-care
[16] https://www.gov.uk/government/publications/uk-5-year-action-plan-for-antimicrobial-resistance-2019-to-2024
[17] https://www.who.int/antimicrobial-resistance/interagency-coordination-group/20170818_AMR_FfA_v01.pdf
[18] https://www.jpiamr.eu

over £12 million in more than 60 companies to develop new antimicrobial therapies and over £9 million in more than 70 companies to develop new diagnostic capabilities.

The UK Catapult Centres[19] are also involved in research related to AMR[20] and work together with renowned organisations such as the British Society for Antimicrobial Chemotherapy (BSAC[21]) and the AMR Centre[22] in Alderley Park. These centres are working to build on, and accelerate advances, in the field of new antibiotics and diagnostics through an integrated development capability. The AMR Centre is a public-private joint initiative that offers R&D from pre-clinical stages right through to clinical proof-of-concept.

1.3.3 The German AMR Strategy | Deutsche Antibiotika Resistenz Strategie (DART)

It is estimated that an average of 400,000 to 600,000 people are infected with pathogens whilst undergoing in-patient medical treatment in Germany every year, with between 10,000-to-15,000 dying as a result of such infections.[23] According to DART, AMR has played a significant role in such alarming statistics. It has been observed that a third of the infections could have been avoided had suitable measures been taken, including the correct use of antibiotics in human and veterinary medicine, as well as appropriate hygiene measures and control of the spread of resistant pathogens in the commerce and tourism sectors[24].

The 2008 German Antimicrobial Resistance Strategy (DART), and its update in 2015 (DART 2020)[25], aimed to reduce any further development and spread of antibiotic resistance. DART contains a number of measures for recognising, averting and combatting antibiotic resistance in Germany.

DART 2020's central goal is to reduce antibiotic resistance by:

1. **Strengthening the "One Health" approach:** Recognition that the health of humans and animals is closely linked when it comes to infectious diseases will help identify future measures and activities.
2. **Recognising changes in resistance at an early stage:** Monitoring systems are being expanded in order to detect new pathogens and resistance at an early stage and to obtain representative data for the whole of Germany, which will also be available for research.
3. **Retaining and improving therapy options:** The monitoring of antibiotic consumption is being further expanded. At the national level, these data form the foundation for intervention measures. In addition, concepts for preparing and applying guidelines are being developed.
4. **Breaking chains of infection early and avoiding infections:** In both human and veterinary medicine, diagnostics are being improved, and the implementation of hygiene measures are being supported. Livestock farming methods must be optimised.
5. **Raising awareness and strengthening skills:** Gaps in knowledge, both in the general population and amongst doctors, veterinary surgeons and other health professionals, must be closed by the provision of targeted, group-specific information.
6. **Supporting research and development:** Research makes an important contribution to containing the increasing spread of antibiotic resistance. All the corresponding research areas in human and veterinary medicine are therefore being strengthened, from basic research through clinical research and research into public health matters to research in co-operation with the health, agricultural and food sectors.

[19] https://catapult.org.uk/
[20] https://md.catapult.org.uk/next-generation-antibiotics-2018-the-presentations/
[21] http://www.bsac.org.uk/
[22] https://www.amrcentre.com
[23] https://www.bundesgesundheitsministerium.de/themen/praevention/antibiotika-resistenzen/antibiotika-resistenzstrategie.html
[24] https://www.bundesgesundheitsministerium.de/fileadmin/Dateien/3_Downloads/D/DART_2020/BMG_DART_2020_Bericht_en.pdf
[25] https://www.bundesgesundheitsministerium.de/themen/praevention/antibiotika-resistenzen/antibiotika-resistenzstrategie.html

2. The AMR Mission to Germany

2.1 German Stakeholder Overview

The table below provides an overview of the key German stakeholders involved in tackling AMR. These include companies, government departments and research institutes visited during the mission, as well as other stakeholders. The visited stakeholders are involved in one or more of the five key strategies to curb AMR (see 1.2).

Visited organisation	Key strategy				
	Improved prevention	Improved stewardship	Improved microbial diagnostics	Novel antimicrobials	Alternative strategies
Authorities BMG and BMBF					
Healthcare centres Charité University Hospital, Jena University Hospital, University Hospital Frankfurt					
Academia and research centres Fraunhofer Institute IZI-BB, RKI, Leibnitz Institute for Photonic Technology					
Pharmaceutical industry Adrenomed and Aicuris					
Diagnostics industry Thermofisher Scientific BRAHMS, BLINK, Curetis, Bosch Healthcare Solutions and Qiagen					
Funding organisations Wellcome Trust – Berlin Office					
Other Global AMR R&D Hub, Biocom and Infectognostics					

Table 2; Overview of organisations visited during the mission to Germany. The colours indicate: dark grey – leading role; light grey – supporting or contributing role; and white – no involvement in the activity.

2.2 German Stakeholders in Improved Prevention

2.2.1 German Federal Ministry of Health | Bundesministerium für Gesundheit (BMG)

The German Federal Ministry of Health (Bundesministerium für Gesundheit; BMG) launched its first DART plan in 2008 to prevent AMR which was mainly focused on the community healthcare sector. Upon implementing the AMR strategy, it became clear that Germany needed to work more collaboratively with its international counterparts and support capacity building if it was to address AMR successfully. This led to an updated version of the DART in 2015. Since then, the BMG has increasingly prioritised international collaboration as well as capacity building in the international context.

In our discussions, the BMG confirmed Germany's focus on the "One Health" approach and their desire to operate with existing international institutions (like the WHO and UN) and to avoid the creation of additional governance structures. The ministry recognised that the UK has pushed the topic of AMR and has cooperated effectively with different international initiatives. Germany sees the UK as a leader of the AMR global agenda and, in particular, they (as did many other visited stakeholders) commended the work of Chief Medical Officer, Professor Dame Sally Davies, and acknowledged her value as a great spokesperson for the cause.

The BMG is responsible for policies relating to infection prevention and control and for approving the use of (novel) antibiotics.

The BMG has a small budget to fund research that will help inform their policy. It funds the Robert Koch Institute (see below), but it will not fund other types of research.

2.2.2 German Federal Ministry of Education and Research | Bundesministerium für Bildung und Forschung (BMBF)

The focus of the German Federal Ministry of Education and Research (Bundesministerium für Bildung und Forschung; BMBF) is on national measures and multilateral initiatives but there is room to change this. There is an appetite to work more closely with the UK, and collaboration with the UK on AMR is valued.

The German Federal Ministry of Education and Research considers AMR to be an important topic. They contribute financially to the German Centre for Infection Research (Deutsches Zentrum für Infektionsforschung; DZIF) (see section 2.2.5). They have been instrumental in setting up the Global AMR R&D Hub (see section 2.7.1).

The Ministry of Education and Research is the funding organisation that the UK could engage with to fund possible collaborations between the UK and Germany. Currently most of the funding is invested within Germany; however, the ministry is taking part in international funding schemes, such as the Joint Programming Initiative on AMR (JPIAMR), Global Antibiotic Research and Development Partnership (GARDP), Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator (CARB-X) and World Health Organisation (WHO). The ministry would like to see the UK invest in GARDP.

2.2.3 The Robert Koch Institute

The Robert Koch Institute (RKI)[26] in Berlin was established to initially focus on the investigation and prevention of infectious diseases. The institute now covers a range of areas including national public health monitoring. Around 1,080 people, including 450 scientists, are working at the RKI in five departments and more than 50 units, projects and junior groups. The RKI cooperates with many international partners like the European Centre for Disease Prevention and Control (ECDC) and the WHO. RKI is the WHO Collaborating Centre for Emerging Infections and Biological Threats and also partner of WHO's Global Outbreak Alert & Response Network, supporting affected countries world-wide to tackle outbreaks.

RKI has been commissioned by the German Ministry of Health to explore ideas on possible global governance mechanisms. As the German equivalent to Public Health England (PHE), the RKI is the leading German institution for surveillance and capacity building. Germany does not seem to have a federal AMR environmental surveillance programme, but projects are funded at the regional level. The RKI is collecting antibiotic resistance data from some 80 laboratories throughout Germany. In addition, it is collecting data on antibiotic use and consumption in primary care centres and at general practices.

The RKI has previously focused on Germany, but during our meeting, they highlighted that they were looking to change this and recognised the need for international collaboration.

In the area of AMR, the institute is involved in four types of international projects:

1. Capacity building and research in collaboration with the German Federal Ministry of Education and Research in Sub-Saharan Africa. Their experience of working in Africa proved that better microbiology analysis and data collection are needed and there is consequently a strong need for capacity building and standardisation within LMICs.

[26] https://www.rki.de/EN/Home/homepage_node.html

2. Surveillance and diagnosis-related activities in collaboration with the UK Aid funded Fleming Fund in Nigeria.

3. Various AMR-related activities and projects in Asia.

4. Participation in different European projects (African and Asian Resilience in Disaster Insurance Scheme (ARDIS) and Novel approaches for design and evaluation of cost-effective surveillance across the food chain (NOVA) in collaboration with the ECDC.

RKI is in the process of setting up an office for international cooperation within RKI. This office will provide the administrative link to help researchers at RKI work globally. RKI is already working with UK researchers on the surveillance and African and Asian Resilience in Disaster Insurance Scheme projects. They see an opportunity for more cooperation, particularly given that Germany and the UK face many of the same problems in tackling AMR.

2.2.4 Charité Universitätsmedizin Berlin

Charité Universitätsmedizin Berlin (Charité) is one of the largest university hospitals in Europe. Charité represents a single medical faculty, which serves both Humboldt Universtität zu Berlin and Freie Universität Berlin. It extends over four campuses and has close to one hundred different departments and institutes, which make up a total of seventeen different Charité Centres[27]. Their AMR activities relate to every aspect of infection control, teaching and research. Since 1999, Charité has been the national reference centre for nosocomial (hospital-acquired) infections. Charité is involved in large German research projects for the consumption of antibiotics, hospital infections, KISS (Krankenhaus-Infektions-Surveillance-System[28]), Surveillance AMR in Intensive Care Units (SARI[29]; 2001) and MRSA-related projects (MRSA-KISS[30]), which collects data of MRSA positive cultures from patients screened in 600 German hospitals.

Charité focuses a lot of their attention on education and stewardship, as well as on infection control programmes. They are working with design companies to create tailored interventions for different target groups. In a research project[31] they have been working on the "Infozept" (information-prescription), a paper or digital prescription which provides advice and information for the patient, fulfilling their perceived need for a prescription, without using antibiotics. It has been well-received by doctors (in three federal states so far), and they are looking to roll it out across Germany.

Another initiative they have trialled is a "tab" for doctors (a small handheld device), which they can use to track their own activity and receive direct feedback at the end of each day on how many antibiotic prescriptions they have written. This device was initially well-received but failed because it operated through the Apple iPhone system (which was too costly). Another issue raised was the difference in prescription behaviours by privately and publicly-employed doctors – it was highlighted that doctors working in the private sector are more likely to prescribe antibiotics as patients are more likely to expect antibiotics in return for their payment.

Charité expressed their desire to stay in contact with UK stakeholders and to have more formal information exchanges, whether this is through multilateral channels (e.g. JPIAMR Virtual Research Institute), or bilateral exchange. They already have some formal institutional links in place with Public Health England and Imperial College London, but there is scope for more.

2.2.5 The German Centre for Infection Research | Deutsches Zentrum für Infektionsforschung (DZIF)

The German Centre for Infection Research (Deutsches Zentrum für Infektionsforschung; DZIF[32]) works to align translational research with unmet global medical needs caused by infectious diseases. The virtual centre coordinates a funding stream for infection research in Germany to address national, as well as global, challenges with great societal impact as defined by the WHO health agenda[33]. DZIF's translational mission, therefore, includes the implementation gap as an integral part of its strategy. In addition, the development gap for antibiotics is steadily increasing. Research institutions have to rely on partners who are willing to share the economic risks with them and make their scientific contribution. This is where DZIF comes in: in recent years, DZIF has become an important stakeholder in infection research and a reliable cooperation partner for the biotechnology and pharmaceutical industry in Germany.

Over 500 doctors and scientists from 35 establishments collaborate with DZIF, jointly developing new approaches to prevent, diagnose and treat infectious diseases. Their research areas include novel antibiotics, emerging infections, tuberculosis, gastrointestinal infections, hepatitis, HIV, infections of the immunocompromised host, healthcare-

[27] https://www.charite.de/en/
[28] https://www.nrz-hygiene.de/en/surveillance/hospital-infection-surveillance-system/
[29] https://www.aerzteblatt.de/int/archive/article/195331/Surveillance-of-antibiotic-use-and-resistance-in-intensive-care-units-(SARI)-a-15-year-cohort-study
[30] https://www.nrz-hygiene.de/en/surveillance/hospital-infection-surveillance-system/mrsa-kiss/
[31] http://www.rai-projekt.de/rai/startseite/
[32] https://www.dzif.de/en
[33] https://www.who.int/about/vision/global_health_agenda/en/

associated and antibiotic-resistant bacterial infections, malaria and the microbiome.

They have their own funding already assigned to specific projects which are between 2-4 years, but they also have a small pot of funding named the "Flex-Fund" for new projects. This was highlighted as a potential opportunity and worth exploring the potential to establish a joint UK-German partnership with both jointly-funded collaborative projects from their respective budgets (e.g. the Flex-Fund from DZIF and an equivalent fund from the UK).

This synergistic alliance of universities, hospitals and research institutions has resulted in a national infrastructure aiming to translate research results from bench to bedside effectively and vice-versa, applying the insights gained from clinical practice to research.

Since its inception, DZIF has been strengthening collaborations with partner institutions in Africa to investigate diseases like malaria, tuberculosis and HIV. DZIF is one of nine founding organisations of CARA (Conscience of AMR Accountability): an international alliance that aims to ensure that effective antibiotics will also be globally available in future. DZIF's head office is located in Braunschweig[34].

2.3 German Stakeholders in Improved Stewardship

Charité and DZIF are the key stakeholders in Germany when it comes to improving the stewardship of antimicrobials. Charité mentioned the RESIST[35] project funded by insurers. The project aims to enhance doctor-patient communication to reduce antibiotic use in respiratory tract infections.

2.4 German stakeholders in Improved Diagnostics

2.4.1 Fraunhofer Institute for Cell Therapy and Immunology | Fraunhofer-Institut für Zelltherapie und Immunologie (IZI)

The Fraunhofer Society for the Advancement of Applied Research[36] was created in 1949 and it is Europe's largest application-oriented research organisation. It has 72 institutes and research units across Germany and has affiliated research centres across the world, each focusing on a specific field of applied science. The Fraunhofer Society employs more than 26,600 staff who work with an annual research budget of EURO2.6 billion. Of this sum, EURO2.2 billion is generated through contract research. Around 70 per cent of the Fraunhofer Society's contract research revenue is derived from contracts with industry and from publicly-financed research projects.

The Fraunhofer Society is considered to be an international leader in applied science. It does not market or sell any of its products but instead depends on clinical development, commercialisation and marketing partners.

The Fraunhofer Institute for Cell Therapy and Immunology (Fraunhofer-Institut für Zelltherapie und Immunologie; IZI) in Potsdam investigates and develops solutions to specific problems at the interface of medicine, life sciences and engineering. One of the institute's main tasks is to conduct contract research for companies, hospitals, diagnostic laboratories and research institutes operating in the field of biotechnology, pharmaceuticals and medical engineering.[37] The Bioanalytics and Bioprocesses branch in Potsdam-Golm (IZI-BB) was affiliated with the Fraunhofer Institute for Cell Therapy and Immunology on July 1, 2014. The site was initially founded in 2005 as a branch of the Fraunhofer Institute for Biomedical Engineering (Fraunhofer-Institut für Biomedizinische Technik; IBMT) and has since worked on technological solutions for biomedicine and diagnostics as well as on biotechnology and bioproduction.

AMR is an important theme at the IZI-BB and a considerable amount of research is undertaken in this space into areas such as: diagnostics, analytics (e.g. characterisation of the microbiome), biofilms and alternative therapeutic modalities (e.g. aptamers). One of the focal areas is rapid testing systems/ point-of-care-testing (30-60 minutes) and AMR across a range of indications e.g. from MRSA in humans to mastitis in cattle. Thanks to the production system they have onsite, they are able to take an idea to a packaged product. In Germany, the IZI-BB is a preferred partner for AMR diagnostics collaborations.

2.4.2 InfectoGnostics Campus

The InfectoGnostics[38] research campus in Jena is a public-private partnership (with funding from the German Ministry of Education and Research) whose aim is to bring industry and academia together and to bridge the value-chain gap. The InfectoGnostics campus brings together partners from research, medicine and industry to develop rapid, cost-effective and marketable point-of-care diagnostics for infectious diseases that can be applied to human and animal health as well as for the detection of pathogens in food production.

The InfectoGnostic programme has a unique public-private partnership model which links hospitals, researchers and industry. The research campus is interested in international collaboration and there exists the possibility to include

[34] https://www.dzif.de/en
[35] https://www.kbv.de/html/resist.php
[36] https://www.fraunhofer.de/en.html
[37] https://www.izi.fraunhofer.de/en.html

Electronics and engineering at Fraunhofer Institute in Potsdam (left); Group picture of UK delegation with colleagues from the Fraunhofer Institute in Potsdam (right).

new partners in its programme. The Centre for Excellence in Sepsis is based at Jena Hospital and it plays a significant role in the clinical validation of technology and access to samples. The hospital also has a pathogen biobank. There might be substantial interest from UK academics and companies to collaborate in order to gain access to the large amount of patient samples, as well as to big data and to bring in their expertise and services (specifically in the area of bioinformatics).

The InfectoGnostics campus is most interested in collaborations on an individual project basis, where sharing expertise makes sense. Currently, the barriers to international collaboration include the requirement for sufficient co-funding and differences in regulatory pathways.

The ultimate goal of InfectoGnostics is to be a European Centre for Infection Research. To this end, they are constantly seeking new partnerships and also would like to engage in more formal international relationships. The UK NHS and Medical Research Council are seen as the UK strengths, and closer ties with the research council would be welcomed.

Although the region has some pharmaceutical companies (17-20 small biotechs), the widely-recognised strength of the InfectoGnostics Campus and surrounding areas is instrumentation for diagnostics, particularly optics and photonics. The partners at InfectoGnostics mentioned further organisations of relevance to AMR, such as the Hans Knoell Institut in Jena, the Leibniz Institute on Aging–Fritz Lipmann Institute and Friedrich Loeffler Institut in Greifswald.

2.4.3 BLINK DX

BLINK DX[39] is a partner of the InfectoGnostics Research Campus. BLINK was founded in 2015 by Eugen Ermantraut, Torsten Schulz and Thomas Ellinger, who have a wealth of experience in designing and commercialising point-of-care diagnostics. Their assay development model is designed to enable the in vitro diagnostics community to quickly develop and deploy point-of-care tests on a shared development and product platform. BLINK is building a customised diagnostic toolset that enables developers, both large and small, to create a diverse and meaningful menu of tests to meet the many and varied needs of healthcare professionals, researchers and patients. The platform provides ample opportunities to UK academics and SMEs for (co-) development of novel diagnostic tests.

2.4.4 QIAGEN

QIAGEN[40] located in Hilden, consolidated under the Dutch holding QIAGEN NV, is a provider of sample preparation and assay technologies for molecular diagnostics, applied testing, academic and pharmaceutical research and has 35 offices across 25 countries.

QIAGEN define themselves as the world's biggest bioinformatics company with 600 employees in this field. The company presented a strong interest in the microbiome and could well be linked to the UK Microbiome SIG (special interest group). So far, all QIAGEN products for microbiome applications are for research use only.

According to QIAGEN, the future of AMR research will focus on personalised medicine. It is mentioned that the concept of companion diagnostics might be useful in curbing global AMR.

2.4.5 Curetis

Located in Holzgerlingen, Curetis[41] is a molecular microbiology diagnostics company addressing the challenge of detecting infectious diseases and identifying antibiotic

[38] https://www.infectognostics.de/en/campus/infektionsdiagnostik.html
[39] https://www.blink-dx.com/
[40] https://www.qiagen.com/nl/

resistances in hospitalised patients. Their Unyvero A50 System is a molecular diagnostics platform used for the diagnosis of severe infectious diseases. The system uses multiplex polymerase chain reaction (PCR) technology to detect a wide variety of microorganisms, antibiotic resistance markers, or toxins from sample-to-answer within 4-5 hours. So far, the market acceptance of the Unyvero System has been limited, but Curetis health economic studies have demonstrated that the technology is viable. The reason that it has not been picked up may be because of the slow nature of behavioural change. Curetis claims to have placements in the UK and partners are keen, but they find that the reimbursement issue continues to be problematic. In addition, wide adoption of AMR and infectious disease point-of-care diagnostic tools require complex implementation packages which slow down market implementation.

2.4.6 Bosch Healthcare Solutions

Bosch Healthcare Solutions[42] in Waiblingen is a spin-off initiative of Bosch. Its products and solutions build on the core competencies of the Bosch Group. These include sensor and microsystem technology, miniaturisation and smart networking.

With Vivalytic, Bosch Healthcare is presenting a universal platform for molecular diagnostics which analyses a wide variety of sample materials in an automated way. The Vivalytic platform combines different analysis methods in one device and is open to providers for further tests. Bosch Healthcare has partnered with UK-based Randox and Germany-based R-Biopharm and is looking for more distributors. Bosch Healthcare would also be interested in gaining access to clinical networks and diagnostics-related expertise in the UK.

The existing partnership with Randox has developed through delivering a molecular diagnostics solution for a number of conditions including respiratory infectious diseases and sexually transmitted diseases. Bosch Healthcare provides the diagnostic system expertise, and Randox provides the molecular diagnostic assay expertise. In future, there could be opportunities for other UK/German companies to develop similar partnerships.

2.4.7 Thermo Fisher Scientific BRAHMS

Thermo Fisher Scientific BRAHMS[43] in Henningsdorf focuses on identifying novel biomarkers to develop and manufacture novel diagnostic tools to improve early diagnosis and treatment of life-threatening diseases. These

The UK delegation visiting InfectoGnostics Campus (Jena)

The UK delegation with Bosch Healthcare Solution group, Waiblingen

include immunodiagnostic tests for prenatal screening, cardiovascular, pulmonary and cancer disorders as well as sepsis. They are part of the InfectControl 2020 consortium which brings industry and researchers together to develop and commercialise new strategies for early diagnosis, control and fight infectious diseases at a national and global level. Adrenomed, a privately financed, clinical-stage biopharmaceutical company[44] and Thermo Fisher are amongst the industrial partners; Charité, University Clinic Jena and RKI are amongst the research partners.

2.5 German Stakeholders in Novel Antimicrobials

2.5.1 AiCuris

Located in Wuppertal, AiCuris (Anti-infective Cures)[45] focuses on the discovery, research and development of novel antiviral and antibacterial agents for treating infectious diseases. It was founded in 2006 as a spin-off from Bayer's virology and bacteriology research divisions. Bayer still owns a significant part of the company, and therefore AiCuris is considered a large enterprise under the EC definition. The company has an

[41] https://curetis.com
[41] https://www.bosch-healthcare.com/en/
[43] https://www.brahms.de
[44] https://adrenomed.com/

innovative pipeline of novel anti-infectives.

AiCuris has a fully differentiated R&D pipeline focused on developing novel anti-infectives for hospital-acquired infections and characterises themselves as a "clinical proof-of-concept company". AiCuris is seeking new technical solutions and new technologies. Although, like most product pharma/biotech companies they utilise a virtual model of development based on a large amount of outsourcing, they have in-house expertise in pharmacokinetics/pharmacodynamics, CMC (chemistry manufacture and controls), regulatory affairs and pharmacovigilance. AiCuris spends approximately EURO25-30 million per year on investigating new drugs.

AiCuris is constantly evaluating strategic partnerships and collaboration opportunities with biotech or pharmaceutical companies. The company is interested in the use of, and access to, big data including infection intelligence platforms, artificial intelligence and gene sequencing data.

A focus of AiCuris is on high-throughput screening from natural products (in collaboration with the Max Planck Institute[46]) as well as new approaches, e.g. macrocycles. The company has received funding for projects from the EU and the German Ministry of Education.

For their drug discovery and development activities the company collaborates with the US and Europe, including universities and service providers in the UK. They noted that their experience of working internationally has been complicated at times, and any new bilateral collaboration needs to be simple with limited restrictions.

2.6 German Stakeholders in Alternative Antimicrobial Strategies

Alternative strategies to antimicrobials is a priority of the German government. These alternatives include natural products, probiotics and microbiotics among others. The Helmholtz Centre for Infection Research and the Leibniz Institute for Natural Product Research and Infection Biology are two of Germany's key research centres for alternative antimicrobial strategies.

2.6.1 Adrenomed AG

Adrenomed AG[47] in Hennigsdorf is a private clinical-stage biopharmaceutical company with a clear mission to rescue vascular integrity in order to save the lives of critically ill patients with limited treatment options. Their treatment approach combines the therapeutic antibody with a specific diagnostic, which uses Adrenomedullin as the biomarker to identify patients. The most important target indications are sepsis and septic shock, as well as acute heart failure. Adrenomed is also a member of the InfectControl 2020[48] consortium.

2.7 Other Relevant German Stakeholders

2.7.1 The Global AMR R&D Hub

In 2017, the G20 heads of state and government took the decision to intensify global collaboration in the fight against AMR. The German Federal Ministry of Education and Research then proposed plans for a Global AMR Research and Development Hub[49], an investment from the German government that demonstrates its commitment to tackling AMR.

The Hub was launched in May 2018 coinciding with the World Health Assembly in Geneva. The Hub aims to improve the coordination of international efforts and initiatives to tackle AMR while further increasing investments into R&D for AMR. Since then, the Wellcome Trust and the Bill & Melinda Gates Foundation have joined the Hub. The WHO, FAO, World Organisation for Animal Health (OIE) and Organisation for Economic Co-operation and Development (OECD) are observers.

Internationally, Germany supports global governance efforts such as those from the UN and the WHO. The Hub is expected to launch the first version of its global "Dynamic Dashboard" at the end of 2019, which builds on existing mapping research carried out by JPIAMR and others. The Dynamic Dashboard will provide easy-to-read and up-to-date global information and incentives on AMR-related research and development on diagnostics, therapeutics, vaccines and alternative therapies like phage therapy. Resistance data is not included. The data on the dashboard is intended to be used to formulate national recommendations and suggestions for incentive schemes.

2.7.2 The Wellcome Trust German Office

The Wellcome Trust German Office[50] in Berlin is a biomedical research charity founded in the UK. It was established in 1936 with legacies from the pharmaceutical magnate Sir Henry Wellcome to fund research to improve human and animal health. As an international organisation they do not want to be seen as a UK-only or UK-focused organisation. In 2019, the Wellcome Trust opened its first overseas office in Berlin. The team is primarily focused on policy and does not have

[45] http://www.aicuris.com
[46] http://www.aicuris.com/index.php/fuseaction/download/lrn_file/190418_aicuris_pr_mpi.pdf
[47] https://adrenomed.com
[48] https://www.infectcontrol.de/de/english.html
[49] https://www.gesundheitsforschung-bmbf.de/en/GlobalAMRHub.php

the ambition to replicate the London headquarters of the Wellcome Trust. Consequently, all funding activities will stay in the UK. In the future, the Wellcome Trust Berlin will act as a vehicle to engage with other European countries.

2.7.3 Biocom

Biocom[51] in Berlin is a life sciences B2B communications company working for various target groups in business, politics, science and the general public. Biocom focuses on high-tech areas of the life sciences: biotechnology, bioeconomy and medical technology. Biocom is the organiser of an annual "AMR Conference" (the next conference is scheduled for 12-13 March 2020).

2.7.4 Evotec-Bridges Programme

Located in Hamburg, Evotec[52] is a major player in the area of discovering novel antibiotic therapeutics having acquired the Sanofi research site in Toulouse, France, in 2015. Although the delegation did not visit this company, the Evotec-Bridges Programme[53] was mentioned during the meeting with Biocom as a financial vehicle to support research and early development of therapeutics that target unmet medical needs, including infectious diseases.

2.7.5 Boehringer Ingelheim Venture Fund (Ingelheim am Rhein)

Although many large multinational pharmaceutical companies have stopped investing in anti-infectives due to the lack of market incentives, the family-owned German pharmaceutical company Boehringer Ingelheim is one of the few pharmaceutical companies that still invest in the area.

Boehringer Ingelheim has set up a corporate venture fund[54] to make strategic investments in start-ups and early-stage biotechnology companies with innovative and potentially ground-breaking technologies in the areas of regenerative medicines, anti-infectives and cancer immunomodulation, the microbiome and new therapeutic modalities such as gene therapy and cell-based therapeutics.

This venture fund welcomes co-investors and has a long-term vision to support their companies with up to EURO10 million follow up investment over the company's lifetime.

2.7.6 Additional German Initiatives Relevant to AMR

BIO-Germany[55] is the German biotechnology industry association. It supports and represents the German biotechnology industry at a national and international level. It has over 330 members including companies in the AMR space: AiCuris, Vakzine Project Management, Hyglos, Curetis, Artes, Progen and Noscendo.

Overview of German BioRegions Source: German Trade & Invest

2.7.7 German BioRegions Involved in AMR

The BioRegions[56] are regional initiatives that bring together academia, research centres and industry working on a specific thematic area. These bio-clusters have been instrumental in supporting the translation efforts in life sciences and biotechnology.

Approximately 25 bioregions with just under 600 biotech companies have been established since the late 1990s, which is a significant achievement from an international perspective. Some ten bioregions are involved in diagnostic activities, which is broader than only microbial/infection diagnostics. The following regions are involved in AMR:

[50] https://wellcome.ac.uk/about-us/german-office
[51] https://biocom.de/?lang=en
[52] https://www.evotec.com/en/invest/news--announcements/ad-hoc-releases/p/evotec-and-sanofi-sign-definitive-agreement-for-major-multi-component-strategic-alliance-5618https:/
[53] www.evotec.com/en/innovate/bridges
[54] https://www.boehringer-ingelheim.com/innovation/human-pharma/boehringer-ingelheim-venture-fund
[55] https://www.biodeutschland.org/en/home.html
[56] https://d-nb.info/971374856/34

1. BioRegioN for its vaccine research (www.bioregion.de)
2. BioRiver for its activities in infectology (www.bioriver.de)
3. IGZ-Innovation & Entrepreneur Centre Bavaria for its activities in infection biology and microbiology (www.igz.wuerzburg.de)
4. BMD Life Sciences Agency for its activities in vaccination research (www.bmdlifesciences.de)
5. Infectognostics for its activities in infection diagnostics, companion diagnostics (www.infectognostics.de).

3. Observations

Germany and the UK share the same sense of urgency and solution-oriented attitude to tackling AMR. The German organisations visited during the mission showed a clear appetite to collaborate with the UK, as it is recognised as a leader in pursuing the global AMR agenda with Professor Dame Sally Davies championing the cause.

Both countries have national AMR strategies that acknowledge the need for a "One Health" approach. However, the execution of the respective AMR national strategies differs slightly; Germany has sixteen autonomous federal states which vary in financial strength and innovation potential, and compete for the same national funding, and consequently implements the DART 2020 in different ways. Comparatively, the UK has only four countries (England, Scotland, Wales and Northern Ireland) and although the implementation of the previous strategy (2013-2018)[57] varied across the UK, the new action plan (2019-2024)[15] was developed in partnership with UK-wide representatives.

Germany has been supporting large international efforts, including CARB-X, the WHO and the UN. It has also demonstrated its commitment to tackling AMR through the Global AMR R&D Hub.

In addition to supporting these international investments and governance structures, the UK has been very active in fostering bilateral collaborations and has well-established AMR related networks and laboratories in many countries, including several LMICs. Germany is in the process of expanding its AMR-related capacity building activities in the LMICs. Therefore, the UK is well-positioned to act as a natural partner for Germany in this endeavour.

The delegation found that the academic approach taken to tackling AMR differs between the UK and Germany. The German academic system encourages research and publications within a particular research discipline, whilst in the UK a more multidisciplinary approach is taken, particularly in relation to social sciences.

Both countries have an excellent research base, but the translation still remains a challenge. In Germany, the Bio-regions initiative and Fraunhofer Institutes, and in the UK, the Catapult centres have been instrumental in supporting translation efforts.

During the mission, the lack of funding for AMR start-ups was highlighted, and it was flagged that this was leading to a shortage of German entrepreneurs in the AMR area. In comparison, the UK is perceived as a better environment to foster AMR entrepreneurship.

Reimbursement for novel diagnostics and novel antimicrobial therapeutics is a shared challenge in both countries. The UK is leading a pilot reimbursement programme for the use of novel antibiotics which is of interest to Germany and could be an area for future collaboration.

Companion diagnostics is another potential opportunity for both countries which can guide appropriate treatment and delay the progression of AMR. The UK has a robust medicines manufacturing industry and Germany has strong expertise in photonics and high-tech instrumentation design and engineering. This was particularly visible during the delegates' visit to the Fraunhofer IZI-BB, InfectoGnostics, Curetis and Bosh Healthcare.

The table overleaf provides a brief SWOT analysis for UK-German cooperation and collaboration in AMR:

[57] https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/244058/20130902_UK_5_year_AMR_strategy.pdf

Strengths	Weaknesses
• Both countries have an excellent research base and complementary technology and innovation centres to support the translation of technology. • Both countries have national AMR strategies. • Both countries have national and regional funding for research and innovation. • German Bio-regions are excellent initiatives to support the development and translation of technologies. • Both countries have strong microbiome research bases. • There is a demonstrable commitment from the German government to tackle AMR through their investment in the Global AMR R&D Hub. • Germany has expertise and a well-established high-tech instrumentation industry. • The UK is recognised as a global AMR leader with vast experience of collaborating with LMICs. • The UK has a world-renowned champion who is spearheading the AMR cause. • The UK has the Knowledge Transfer Network, which can connect cross-sectoral actors across the country. • The UK has a multidisciplinary approach to AMR. • The UK has medicines manufacturing capabilities and good support for clinical trials. • Germany has strong investment and expertise in alternative therapeutic approaches.	• Translating research is a challenge for both countries. • Lack of funding for AMR related start-ups is a common challenge. • Lack of sufficient market pull incentives for diagnostics and therapeutics is a shared challenge. • Germany has limited bilateral collaborations in AMR. • Currently there is no dedicated bilateral funding for the UK and Germany to collaborate. • Germany does not have a dedicated national cross-sectoral network that links all AMR actors across the country. • Engaging in clinical trials in Germany could be a very bureaucratic process. • Implementation of some digital health technologies to support AMR stewardship in primary care is challenging.
Opportunities	**Threats**
• There is an appetite from both countries to collaborate in the AMR space. • Germany is interested in expanding its AMR capacity building activities in LMICs. The UK could be an ideal partner due to its large and well-established collaborations with LMICs. • German institutions recognise the need and are actively engaging in AMR international collaborations. The UK could be a good partner as it is seen as a global leader in the area. • The development of companion diagnostics is an opportunity for both countries. Germany could be an excellent partner due to its well-established high-tech engineering instrumentation industry. • Taking an effective One-Health approach to AMR. • Multilateral funding initiatives including H2020/Horizon Europe, IMI, EUREKA, JPIAMR could be used to fund some AMR collaborations.	• Shift in policy priorities.

4. Conclusions

4.1 Diagnostics

Germany has strengths in design and engineering of high-tech instrumentation, which could complement UK expertise in sensing. The delegation learnt that German diagnostics companies, like BLINK and Bosch Healthcare Solutions, have diagnostics platforms which offer co-development opportunities for UK companies.

Our German counterparts' impressions of the NHS were that it was easier to conduct clinical trials in the UK and consequently, the technology adoption process is more straightforward.

The UK and Germany have a strong pharmaceutical and diagnostic industry. Consequently, companion diagnostics could be a potential opportunity for both countries.

4.2 Therapeutics

Some German companies were interested in working with UK Contact Research Organisations (CRO) and clinical partners.

There are opportunities for UK start-ups and early-stage companies to obtain equity funding from Boehringer Ingelheim Venture Fund if their technology aligns with Boehringer Ingelheim's corporate strategy.

Germany is investing in alternative antimicrobials such as natural products, phage therapy and DNA based CRISPR-Cas9 technologies. The UK strengths in medicines manufacturing could complement this work.

4.3 Capacity Building in LMICs and Surveillance

The UK plays a leading role in capacity building in LMICs and has supported many reference centres within these countries. During the mission, some of our German counterparts expressed an interest in collaborating with the UK.

During the mission, the delegation learnt that RKI and Charité have collected vast amounts of AMR-related data from German healthcare centres at a national scale. This complements ongoing work being conducted by UK organisations such as the Oxford University Big Data Institute and Edinburgh University.

4.4 Multidisciplinary Approaches

Both the UK and Germany understand the importance of a multidisciplinary approach to AMR. Germany recognised that the UK is leading the way in working across disciplines to fight AMR.

4.5 Stewardship

Charité is working on a number of stewardship projects in collaboration with German hospitals and highlighted challenges associated with the implementation of digital health technologies. This is a challenge that the UK also faces and offers an opportunity to work together.

Training and education are of particular importance in Germany given that many of their private doctors feel the pressure to prescribe antibiotics, as patients expect to receive treatment even when not necessary.

Annex 1

List of UK Participants

AMR Insights+
British Embassy in Berlin*
Destiny Pharma
Department for International Trade*
Innovate UK
Knowledge Transfer Network
Science and Innovation Network*
Summit Therapeutics
The British In Vitro Diagnostic Association
The University of Oxford
The University of Edinburgh

*Supporting organisations
+ Technical writer, based in Netherlands

List of German Participants

Adrenomed
Aicuris
Biocom
BLINK DX
Bosch Healthcare Solutions
Charité University Hospital
Curetis
Federal Ministry for Health
Federal Ministry of Education and Research
Fraunhofer Institute fort Cell Therapy and Immunology: Bioanalytics and Bioprocesses branch
Global AMR Hub
Infectognostics
Leibnitz Institute of Photonic Technology
Qiagen
Robert Koch Institute
Thermofisher Scientific
University Hospital Frankfurt
University Hospital Jena
Welcome Trust – Berlin Office

Innovate UK
Knowledge Transfer Network