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Global AMR Innovation Fund (GAMRIF) Interim Evaluation

December 2021

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Abbreviations

AMR	Antimicrobial Resistance
ARS	Argentine peso
BARDA	US Biomedical Advanced Research and Development Authority
BBSRC	UK Biotechnology and Biological Sciences Research Council
BE	British Embassy
BMBF	German Federal Ministry of Education and Research
BMGF	Bill and Melinda Gates Foundation
CA	Contribution Analysis
CAD	Canadian Dollar
CARB-X	Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator
CHAI	Clinton Health Access Initiative
CoI	Conflict of Interest
CONICET	Argentina's National Scientific and Technical Research Council
CSTEC	China Science and Technology Exchange Centre
DAC	OECD's Development Assistance Committee
DHIS2	District Health Information Software
DHSC	UK Department for Health and Social Care
DNDi	Drugs for Neglected Diseases initiative
EAB	Expert Advisory Board
EQs	Evaluation Questions
FAO	Food and Agriculture Organization
FCDO	UK Foreign, Commonwealth and Development Office
FGD	Focus Group Discussion
FIND	Foundation for Innovative New Diagnostics
GAMRIF	Global Antimicrobial Resistance Innovation Fund
GAN	Global Accelerator Network
GAP	Global Action Plan on AMR
GARDP	Global Antibiotic Research and Development Partnership
GDPR	General Data Protection Regulation
GHIT	Global Health Innovation Technology Fund
GHR	Global Health Research (DHSC)
GHS	Global Health Security (DHSC)
GSC	Governance Steering Committee
HIC	Higher Income Country
HMG	Her Majesty's Government (UK Government)
IDDO	Infectious Diseases Data Observatory
IDRC	International Development Research Centre
ILRI	International Livestock Research Institute
IMPAM	Institute of Microbiology and Parasitology
INIE	National Institute of Infectious Diseases, Argentina
InnoVet-AMR	Innovative Vaccines for AMR Prevention Research Program
INTA	National Institute of Agricultural Technology
JOC	Joint Oversight Committee
JPIAMR	Joint Programming Initiative on Antimicrobial Resistance
KI	Key Informant
KII	Key Informant Interview
KTN	Knowledge Transfer Network
LMIC	Low and Middle-Income Country
LVIF	Livestock Vaccine Innovation Fund
M&E	Monitoring and Evaluation
MoST	Chinese Ministry of Science and Technology
NERC	UK Natural Environment Research Council
NESTA	National Endowment for Science, Technology and the Arts
NIH/NIAID	US National Institute of Health/National Institute of Allergy and Infectious Disease
NIHR	National Institute for Health Research
OIE	World Organisation for Animal Health
ODA	Official Development Assistance
OECD	Organisation for Economic Cooperation and Development
PI	Principal Investigator
PD	Product Developer
PDP	Product Development Partnership
PM	Project Manager
POC	Point of Care
POCT	Point of Care Technology
QA	Quality Assurance
R&D	Research and Development
RDTs	Rapid Diagnostic Tests

RFP	Request for Proposal
RMB	Chinese Yuan
S&A	Stewardship and Access
SAB	Scientific Advisory Board
SAC	Science Advisory Committee
SENASA	National Service for Agrifood Health and Quality
SMEs	Small and Medium Sized Enterprises
STAR-IDAZ	International Research Consortium on Animal Health
STI	Sexually transmitted infection
TA	Technical Advisor
TCM	Traditional Chinese Medicine
TL	Team Leader
ToC	Theory of Change
ToR	Terms of Reference
TPP	Target Product Profile
TRL	Technology Readiness Level
UKRI	UK Research and Innovation
VfM	Value for Money
WHO	World Health Organization
WP	Work Package
ZNPHI	Zambia National Public Health Institute

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Disclaimer

This report has been prepared by Ecorys for DHSC, for services specified in the Terms of Reference and contract of engagement. The closure point for new information for this evaluation (including key informant interview data, focus group data and regular GAMRIF programme reporting) was September 2021.

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There are no conflicts of interest.

1.0 Executive summary

The Global Antimicrobial Resistance Innovation Fund (GAMRIF) was established by the UK Department for Health and Social Care (DHSC) in 2016. GAMRIF was originally conceived as a GBP 50 million Research and Development (R&D) programme designed to tackle drug resistance in Low and Middle-Income Countries (LMICs). It achieves this through targeting neglected areas of Antimicrobial Resistance (AMR) research, building partnerships with industry, governments, and global organisations and leveraging additional funding. In July 2021, Ecorys was commissioned to undertake the Interim Evaluation of GAMRIF, with a focus on its relevance, efficiency, and effectiveness.

Summary of Main Findings

The evaluation finds that the GAMRIF portfolio supports work which is highly relevant to AMR priority needs, as identified by expert analyses in global AMR strategy documents. The portfolio is also unique amongst large-scale R&D AMR funds in that it directs support to product development tailored to the needs of people living in LMICs, where the burden of drug-resistant infections and AMR is highest. Further added value is provided by GAMRIF's ability to fund transnational groups leveraging the best solutions globally; fund industry partnerships focused on delivering tangible innovations; and tackle AMR across multiple One Health dimensions – humans, animals, and the shared environment[1]. GAMRIF has also placed the UK in an active leadership role in supporting transnational AMR R&D efforts, fulfilling political commitments and relevant aims within the UK's global health security strategy. GAMRIF has achieved such complementarity through initial mapping of other funders' activities, and ongoing strong coordination mechanisms.

The management of GAMRIF has been efficient and within budget, despite the diverse portfolio and geographical coverage. GAMRIF selected delivery partners with relevant relationships, expertise, and systems for conducting rigorous project selection processes, facilitating the progression of grantees through R&D, and for facilitating dissemination and policy impact. The GAMRIF delivery team has learned useful lessons about the ability of delivery partners to spend according to forecasts, account for expenditure, and demonstrate results. Challenges that have arisen, particularly due to COVID-19 (resulting in notable delivery delays and inability to conduct fieldwork as planned), have been well-handled, with a high level of responsiveness from DHSC staff and major delivery partners.

The evaluation finds that GAMRIF is effective and is fulfilling its objectives. Funding from other governments and foundations has been directly and indirectly leveraged, through multi-donor working and influencing a greater focus on addressing the needs of LMICs. GAMRIF funding - of which GBP 63.5 million has been programmed, and GBP 56.5 million has been leveraged overall - has influenced existing product development organisations, such as the Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator (CARB-X), Global Antibiotic Research and Development Partnership (GARDP), and Foundation for Innovative New Diagnostics (FIND), towards stronger LMIC collaborations and/or increased focus on LMIC-specific needs. Key vaccines, antibiotics, alternatives to antibiotics and diagnostics have been advanced along the product development pipeline.

The longer-term impact of GAMRIF funding will depend on how projects are sustained, and the mitigation of potential barriers to implementation (e.g inefficient regulatory environments) and the risks of market failure inherent in the introduction of innovative technologies into low-resourced markets. However, by funding multiple areas through its 7 Work Packages (WPs), some of which would otherwise be poorly addressed, GAMRIF has enriched a sparse product development pipeline and set a precedent for further funding support from other agencies. Below we summarise evaluation findings at the WP level.

Work Package (WP)-level findings

Work Package 1 (WP 1) has successfully been facilitating testing, focusing on research and business partnerships in industry. This has helped to avoid common pitfalls between early-stage research and commercialisation. Projects are

[1] https://www.cdc.gov/onehealth/basics/index.html

generally making good progress despite set-up delays and are yielding positive results, although there is a need to identify clear pathways to accessing additional funding, to enable projects to continue development down the R&D pipeline.

Work Package 2 (WP 2) has sought to leverage investments and expertise to stimulate the development of alternatives to antibiotics, including preventatives and non-traditional therapeutics of relevance to LMICs. CARB-X is proven to have effective and efficient mechanisms in place to identify lead candidates with the best potential, facilitate their transition to clinical evaluation, and support stewardship and access. GAMRIF funding has been effective in increasing a focus on LMICs within the CARB-X portfolio, and through the development of strategic partnerships, including in India and with the Fleming Fund's in-country work. The geographical scope and service offering of the accelerator network has been improved, widening the applicant pool, and improving movement through pipeline and commercialisation potential.

In supporting new vaccines and alternatives to antimicrobials (specifically to reduce their use in livestock and aquaculture), Work Package 3 (WP 3) enriches the product development pipeline for LMICs through funding 11 multi-partner projects in swine and poultry farming and aquaculture, with a wrap-around component supporting work towards market readiness. IDRC was effective and efficient in providing timely and flexible support to grantees, covering diverse research topics and geographies that would otherwise go unsupported. Achieving longer-term impact will require successful transfer to commercialisation and/or broad knowledge dissemination.

Relatedly, by supporting research in agricultural and environmental AMR, Work Package 4 (WP 4) has operated an effective competitive project selection process and positive progress against outputs is being made which included a joint policy translation proposal and ODA statement, prepared collaboratively by the research teams. Such activities have included informing policymaking by generating and disseminating evidence and bringing an additional social science perspective within all funded projects.

GAMRIF's funding to Work Package 5 (WP 5) supported two drug-resistant gonorrhoea diagnostic candidates; one failed to achieve performance milestones and funding was ceased while the other (an antigen test detecting pathogen presence) is currently planned for trial against clinical samples. Target Product Profiles (TPP) and market landscapes developed should support eventual market entry. While the digital projects need to find support to ensure sustainability, the Zambia One Health data project is a model for others to follow and clearly addresses the requirements for downstream surveillance funders, such as the Fleming Fund (also operational in Zambia). This has high potential for expansion. The other digital projects must demonstrate greater effectiveness and efficiency than their competitor products.

GAMRIF's support to Work Package 6 (WP 6) is credited as a catalyst to GARDP taking a more integrated (diagnostic and treatment) approach to sexually transmitted infections (STIs), to supporting commercialisation and uptake potential, and to strengthening the GARDP partnership overall. Working further downstream in product development than CARB-X, the GARDP investment also has the potential to complement WP 2 investment. It has further complementarity with WP 5, where GAMRIF is funding a new diagnostic for drug-resistant gonorrhoea. GARDP has demonstrated efficiency and value for money (VfM) through the utilisation of pre-existing networks and its model of performing high-quality clinical trials in LMICs, building the capacity of those trial networks, ensuring relevance to local populations, and lowering trial costs. GARDP has also established relationships with regulators in India and South Africa to encourage product entry. Interim results are promising, with two antibiotic products in Phase 3 clinical trials, and a licence granted to expand LMIC access to a new important antibiotic. However, there is still a need to secure manufacturing and market authorisation holder partners, determine the timing of a complementary diagnostic strategy, and secure further funding to complete its development and market launch.

GAMRIF funding further supplements existing research competitions and projects under Work Package 7 (WP 7) that aim to develop new vaccines to bacterial pathogens in order to accelerate developments relevant to LMICs as well as AMR. WP 7 has leveraged GBP 600,000 during implementation and GBP 5.6 million in follow-on funding which directly responds to gaps identified during the establishment of the CARB-X and InnoVet-AMR programmes. These include the limited size and diversity of the pipeline of vaccine projects to tackle AMR and the limited number of existing, tested collaborations between LMIC and UK researchers. BactiVac has been effectively and efficiently managed, demonstrating flexibility in funding decisions, as well as being supportive at all levels of the application process. GAMRIF's funding to WP 7 has created unique

opportunities for researchers in LMICs to advance early-stage research that facilitates progression of bacterial vaccines along the pipeline to licensure, which may not have been funded by other donors or industry.

Lessons and Recommendations

A number of key lessons and recommendations were identified during the evaluation period. Some projects require further support to sustain and broaden their reach, while engagement with international stakeholders will be important to facilitate expansion across borders. A strategic decision was also made in the business case that GAMRIF should engage with early-stage development, to help enrich the product development pipeline, rather than concentrating on reducing downstream barriers and market readiness. The current approach, while addressing major gaps, represents a high risk/potentially high reward strategy. Going forward, it will be important to ensure that downstream issues are being addressed by partners, driving products to completion through addressing, for example, regulatory hurdles, barriers to uptake and other causes of market failure. DHSC appears well placed to contribute to all of this work, through its convening power and reach, and its ability to work with all the major sectors involved.

The evaluation recommends that DHSC continues to fund the GAMRIF programme. However, there is potential to increase programme effectiveness in a potential GAMRIF 2.0. Some key recommendations are outlined below:

- For successful projects, a focus should be placed on leveraging other funding support and industry partners, and/or further direct GAMRIF support to help projects achieve commercialisation and uptake.
- GAMRIF should also look at ways to increase collaborations through strengthening and communicating linkages across Work Packages in areas such as complementary diagnostic and therapeutic development, and between earlier and later stage platforms (e.g BactiVac and CARB-X), as well as with external actors globally (e.g in animal health AMR, to help share knowledge of what works) and nationally (to help broaden the applicant pool in LMICs).
- In relation to GAMRIF's bilateral partnerships, it is recommended that the suitability of partners is reviewed, and lesson learning occurs from differing research contexts and capacities. Such actions can help secure greater longer-term value from the GAMRIF investment.
- Generally, all refinements should be embedded within a refreshed Theory of Change (ToC)

Conclusions

GAMRIF is filling important investment gaps in AMR-relevant R&D. Based upon the evaluation's Contribution Analysis (CA) the plausibility of GAMRIF's investments impacting on the first three outcomes in its ToC is high. These include i) international focus and funding in tackling AMR in LMIC research increased; ii) innovative solutions tested and moved up the Technology Readiness Level (TRL) through the R&D pipeline; and iii) improved supply of appropriate and affordable products and tools for combatting AMR available to LMICs. Contribution to the fourth portfolio-level outcome behaviour change in industry and clinical practice on LMICs was graded slightly lower. This is because human health-focused work is at too early a stage to expect changes in LMIC policy or clinical practice. GAMRIF animal and environmental health-focused projects require additional investment and partnering (including with industry) to achieve this outcome. As with other investments in early-stage R&D, the full value for money of GAMRIF is difficult to assess, given its ultimate objectives take time to realise and will be fulfilled beyond the end of GAMRIF's current funding period. However, to date, the value of enhanced diplomatic ties, UK visibility internationally, and leveraging of wider and future funding through GAMRIF's work is likely to be significant.

2.0 Introduction

2.1 GAMRIF

GAMRIF invests in innovative R&D that will help prevent, detect, and/or treat drug-resistant infections in LMICs. The programme was established by DHSC with GBP 50 million of Official Development Assistance (ODA) following the UK Government's 2015 Comprehensive Spending Review (CSR). It supports under-funded and neglected areas of early-stage research in resource-poor countries, and, by engaging industry, aims to advance research ideas through to product development. By funding research across human, animal, and environmental health, it also takes a One Health multi-disciplinary and multi-sector approach to tackling Antimicrobial Resistance (AMR). GAMRIF supports the broader goal of DHSC's Global Health Security (GHS) programme to sustainably prevent and reduce the future burden of AMR in LMICs.

GAMRIF's specific aims are to:

- Establish international research partnerships and support research competitions that fund innovation and development of new technologies and interventions to tackle AMR;
- Leverage investment from other partners and donors to support sustainable financing in AMR R&D;
- Establish research partnerships using a One Health approach;
- Fund projects that will develop solutions specifically for LMICs, where the burden of AMR is greatest.

In 2016, DHSC convened an independent GAMRIF Expert Advisory Board (EAB)[2] to advise on the scientific scope and direction of the GAMRIF funds. The EAB defined the parameters for GAMRIF's focus: drug-resistant bacteria; the WHO priority pathogen list (excluding tuberculosis); specific solutions to resistance rather than infection control; a portfolio of Work Packages, rather than a single mechanism; and the leveraging of existing portfolios and delivery mechanisms wherever possible. Guided by these parameters and the Strategic Research Agenda set by the Joint Programming Initiative on Antimicrobial Resistance (JPIAMR)[3], the EAB recommended thematic areas of importance and priority topics as the basis for 5 Work Packages, and defined outcomes for and allocated funding to each WP.

2.2 Purpose and scope of evaluation

In July 2021, Ecorys were procured by DHSC following a competitive tender to conduct an interim evaluation of GAMRIF. The evaluation reviewed the programme's processes and performance in order to:

- Assess whether GAMRIF has been designed and delivered in a way to maximise its impacts and meet its objectives as an R&D portfolio fund;
- Assess GAMRIF performance so far and whether the programme is on track to achieve its outcomes and impact;
- Identify lessons learned from implementation to date to inform programme improvement and a potential successor R&D programme.

The evaluation covers all 7 Work Packages of the programme, as well as assessing overall performance at the portfolio level.

During the inception phase, in consultation with DHSC, the GAMRIF delivery team altered the framing of the overarching Evaluation Questions (EQs) from the original Terms of Reference (ToR) to align these more closely with the Organisation for Economic Cooperation and Development's (OECD) Development Assistant Committee (DAC)[4] evaluation criteria. New sub-EQs were added and repositioned within the three overarching EQs. This became the framework for synthesising

[2] www.gov.uk/government/news/expert-advisory-board-to-support-the-global-amr-innovation-fund
[3] www.jpiamr.eu/document-library/strategicresearchagenda/
[4] https://www.oecd.org/dac/evaluation/daccriteriaforevaluatingdevelopmentassistance.htm

evaluation data and triangulating across data sources. More detailed WP-specific questions are covered in the interview Topic Guides (Annex 5, p.75).

Table 1 Evaluation questions

Question 1: Relevance and coherence
Has GAMRIF allocated resources strategically towards potentially high impact activities aligned with global priorities, taking into consideration needs and gaps not already well filled by others, and considering GAMRIF's comparative advantages and goals? Sub-EQs are as follows: ▶ To what extent have GAMRIF investments been aligned and are coherent with AMR needs outlined in the Global Action Plan (GAP) and considering gaps not filled by other funders/partners, representing a clear value-add? ▶ How is GAMRIF different to other AMR research programmes? ▶ What are its unique selling points? ▶ To what extent have GAMRIF's comparative advantages influenced choice of investments? ▶ What other/alternative things should GAMRIF be doing to achieve its goal and objectives?
Question 2: Effectiveness (intermediate results) and efficiency
Does the current design and management of GAMRIF's portfolio (and the delivery partners' efficiency and effectiveness) allow it to effectively maximise its impact and objectives? Are there opportunities to improve ways of working towards better efficiency/effectiveness? Sub-EQs are as follows: ▶ How effective is GAMRIF's multiple delivery mechanism at achieving its objective? Are there any other delivery mechanisms that could be explored? ▶ How efficient and effective is DHSC in managing GAMRIF? ▶ Are there any constraints to effective management of any of the Work Packages? ▶ To what extent do delivery partners' services (admin, technical oversight, financial reporting running competitions etc.) provide good VfM? ▶ Does reporting from each delivery partner provide DHSC with sufficient information to manage the programme efficiently? ▶ Are there any changes required to the programme and Work Packages' design in order to improve its VfM (economy, efficiency, effectiveness and equity)?
Question 3: Impact and Sustainability
Are there indications that the GAMRIF programme has produced positive change likely to contribute to sustainable impact? Sub-EQs are as follows: ▶ To what extent have programme outputs and outcomes been achieved / are likely to be achieved? ▶ What factors have provided: i) most support; and ii) the primary challenges to GAMRIF staying on track to achieve its desired objectives? ▶ What evidence is there that demonstrates the potential for LMIC access and uptake of products when they are developed in years to come? What more could be done to ensure access and uptake? ▶ How could GAMRIF maximise R&D outputs that will lead to successful product development? ▶ How can GAMRIF and/or a potential successor R&D programme adapt in line with learning from the ToC and its assumptions?

The full evaluation framework, including EQs and associated data collection methods, can be found in Annex 1 (p.57).

The findings of this evaluation will be used by DHSC to better manage the GAMRIF programme and inform the design of a possible successor programme. In addition, the findings will be communicated by DHSC, to the wider AMR research community, and other funders of research in this field to share lessons learned. Ecorys and DHSC agreed that an executive summary would be shared with relevant stakeholders prior to publication, should findings and recommendations be useful to share earlier.

2.3 Data collection, stakeholder engagement and risks

The evaluation commenced with a Desk Review of available secondary evidence sources for GAMRIF, including the business case, annual reviews, Monitoring & Evaluation (M&E) data, research outputs, and relevant external literature (see document list at Annex 7, p.83). Documents were analysed against the EQs, and at the WP level, using a tailored Project Assessment Framework.

During the study inception phase, the delivery team worked with DHSC to finalise a comprehensive stakeholder list as the basis for setting up Key Informant Interviews (KIIs) and subsequent Focus Group Discussions (FGDs) to explore the EQs in more detail. An initial list of stakeholders was provided by DHSC to Ecorys, which was refined, and then expanded, where necessary, through snowball sampling. In order to gain a balanced perspective, Ecorys took the final decision on which individuals to interview, ensuring breadth of key stakeholders involved and relevant sectors (industry, academia, government, international organisations, etc.) at the WP and portfolio levels. When using a snowball approach, good practice would be to continue identifying new KIs until the point where no new data, categories or relationships are emerging. Unfortunately, time and resources meant that we were not able to fully reach this stage, and this must be acknowledged as a limitation.

FGDs were selected through consultation with GAMRIF delivery partners, and in some cases based on their recommendations to engage specific research projects. While this was an opportunistic sample (some grantees' late responses or non-responses and a limited timeline for the analysis phase resulted in them not being selected), we ensured that the selected research projects covered the full breadth of the following criteria (as agreed with DHSC):

- Projects at differing stages of completion: Mid-stage and complete;
- Projects with LMIC region of impact: LMIC multi-country, Sub Saharan Africa, South America, South and Southeast Asia;
- Projects with differing interventions reflecting a One Health focus: Human, animal, and environmental

The delivery team further proposed FGDs with the GAMRIF delivery team at DHSC (hereafter referred to as 'the GAMRIF delivery team') to better understand the relevance of GAMRIF's design, the specific value-add of GAMRIF as a delivery model and funding mechanism, how GAMRIF is monitored and data is used, and the longer-term impacts and sustainability of GAMRIF. In total, the delivery team consulted with 75 key stakeholders through in-depth interviews, and 21 project partners through the FGDs. Annex 4 (p.73) provides a full list of the organisations engaged and consulted.

To analyse the evaluation data, we used Contribution Analysis, a theory-based approach designed to increase clarity about the contribution of a programme by building understanding of why observed changes have occurred, and the role played by an intervention and any other internal or external factors creating this change. Contribution Analysis uses a programme's ToC to gather and triangulate evidence about whether and how an intervention has contributed to observed results, whether these are in line with anticipated results, and the key factors influencing this. To support a consistent and objective preliminary assessment of evidence, the delivery team followed a set of judgement criteria to identify the strength of evidence that demonstrates whether GAMRIF is contributing to outcomes and meeting its objectives. A guide to how contribution was classified and assessed is included in Annex 6.

Below we set out some of the evaluation methodology key limitations and mitigation strategies.

Limitation / risk	Mitigation strategy
Short evaluation timescale and limited financial resource: Limits ability to adopt truly participatory approach to contribution analysis	The delivery team prioritised close collaboration from inception and established regular meetings with DHSC. This included fortnightly meetings as well as additional contact through emails and sharing logistical documents and early drafts of findings and deliverables. The kick-off meeting and September workshop were valuable forums for receiving feedback from DHSC early in the evaluation design phase.
Late timing of evaluation relative to implementation: The evaluation started over four years after programming began and relied on secondary data sources (alongside stakeholder reflections of past events). It can be challenging to access all required documentation, particularly when it is coming from multiple teams and the evaluation is operating on a tight delivery plan.	The delivery team obtained access to required documents as early as possible, working with DHSC to identify and prioritise key sources, and maintaining clear communication regarding remaining gaps in documentation. The delivery team were able to obtain as much documentation as was reasonably possible in the evaluation timeframe via documents uploaded in real time to a share drive/workspace.
Response rate for KIIs: Although the response rate to our request for interviews was very positive, there were some Key Informants (KIs) who were not interviewed due to unavailability or feeling ill placed to participate in KIIs. Some grantees' late responses or non-responses and a limited timeline for the analysis phase resulted in them not being selected.	To mitigate the challenges posed by low response rates, the delivery team sent approximately 85 interview requests at the beginning of the fieldwork period. They implemented a process for chasing response, including follow up emails and requesting alternative suitable informants. Where stakeholders decided not to participate, the delivery team ensured interviews took place across a wide enough breadth of to cover similar level of expertise and seniority.
Reliance on individual data sources: With a qualitative-led study, individual data sources may not be as robust or representative.	Triangulation across data sources which inform the same EQs and sub-EQs was prioritised throughout the evaluation to ensure that key learnings were robust and well-evidenced.
Positivity bias: It is possible informants were more inclined to share success stories, particularly if they are fund recipients, feel there are existing sensitivities or that anonymity may be compromised if discussing a specific WP	The delivery team included KII sub-questions and tailored probes on challenges and barriers in topic guides. This provided a consistent opportunity for informants to reflect on examples of failure or inefficiency. Interviews were held with different individuals on the same topic.

2.4 GAMRIF Theory of Change

As background to our implementation of a theory-based evaluation, we sought to understand the work the programme had already undertaken to define its results chain. DHSC has developed an overarching ToC for GAMRIF (Figure 1), to help articulate the theories and assumptions underpinning the anticipated change process for the programme. The evaluation team have adapted the presentation of the ToC to show more clearly how assumptions articulated in the ToC are mapped against the activities, outputs, and outcomes.

Although the GAMRIF ToC was helpful to understand the direction of the GAMRIF portfolio overall, it was insufficient to enable us to interrogate programme impact or to answer our EQs. Consequently, we drafted 'nested' ToCs for each of the

Work Packages (or groups of Work Packages, where they are similar). This was based on: i) initial discussions with GAMRIF staff and a review of programme documents; and ii) the delivery team's understanding and experience of the sector, and what additional activities and partner efforts would be required to ensure GAMRIF-funded activities translated into longer-term outcomes and impact. The nested ToCs were validated with the GAMRIF delivery team during the inception phase. This ToC approach also helped us to generate the more detailed EQs for each WP.

We then used each WP ToC to test programme assumptions and causal links, focusing on how and why each activity is expected to lead to the planned outputs and outcomes, what assumptions are being made, and what role others are expected to play (including as part of the Contribution Analysis). See Figure 2 for an illustrative nested WP ToC.

Figure 1 GAMRIF ToC and assumptions

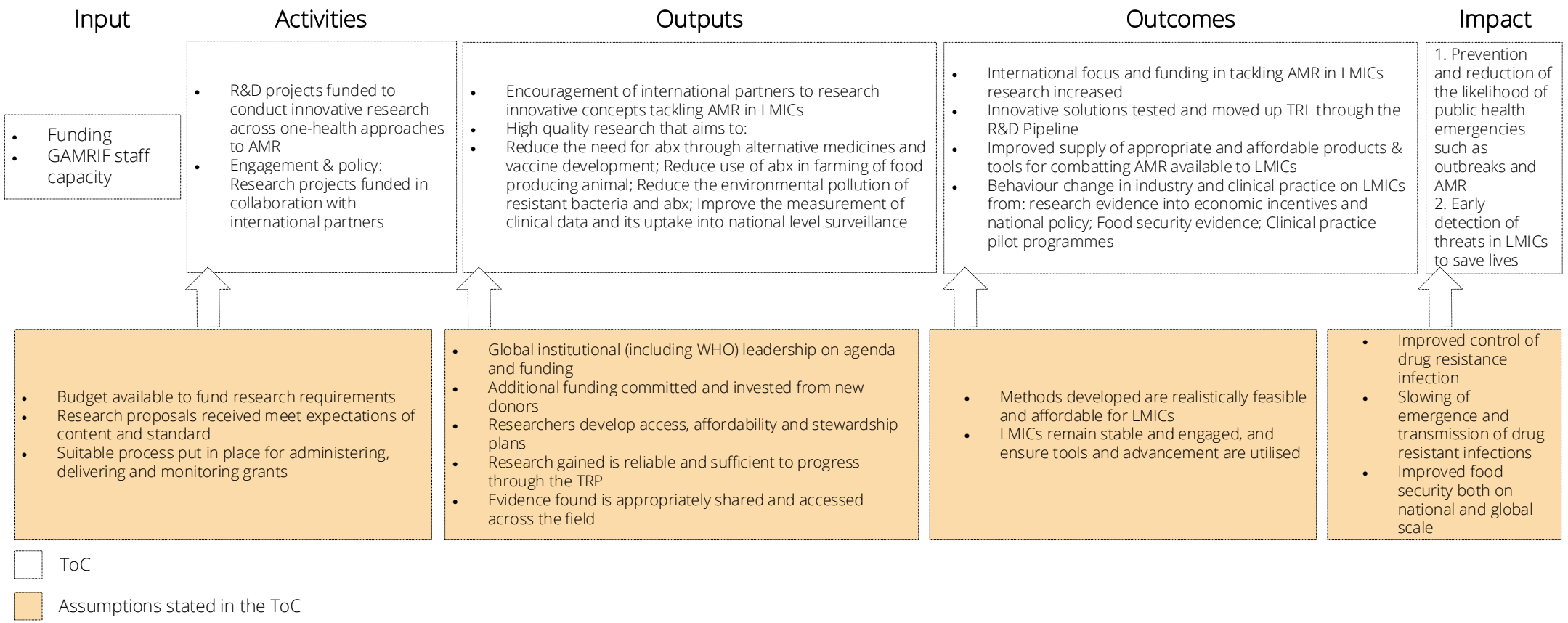
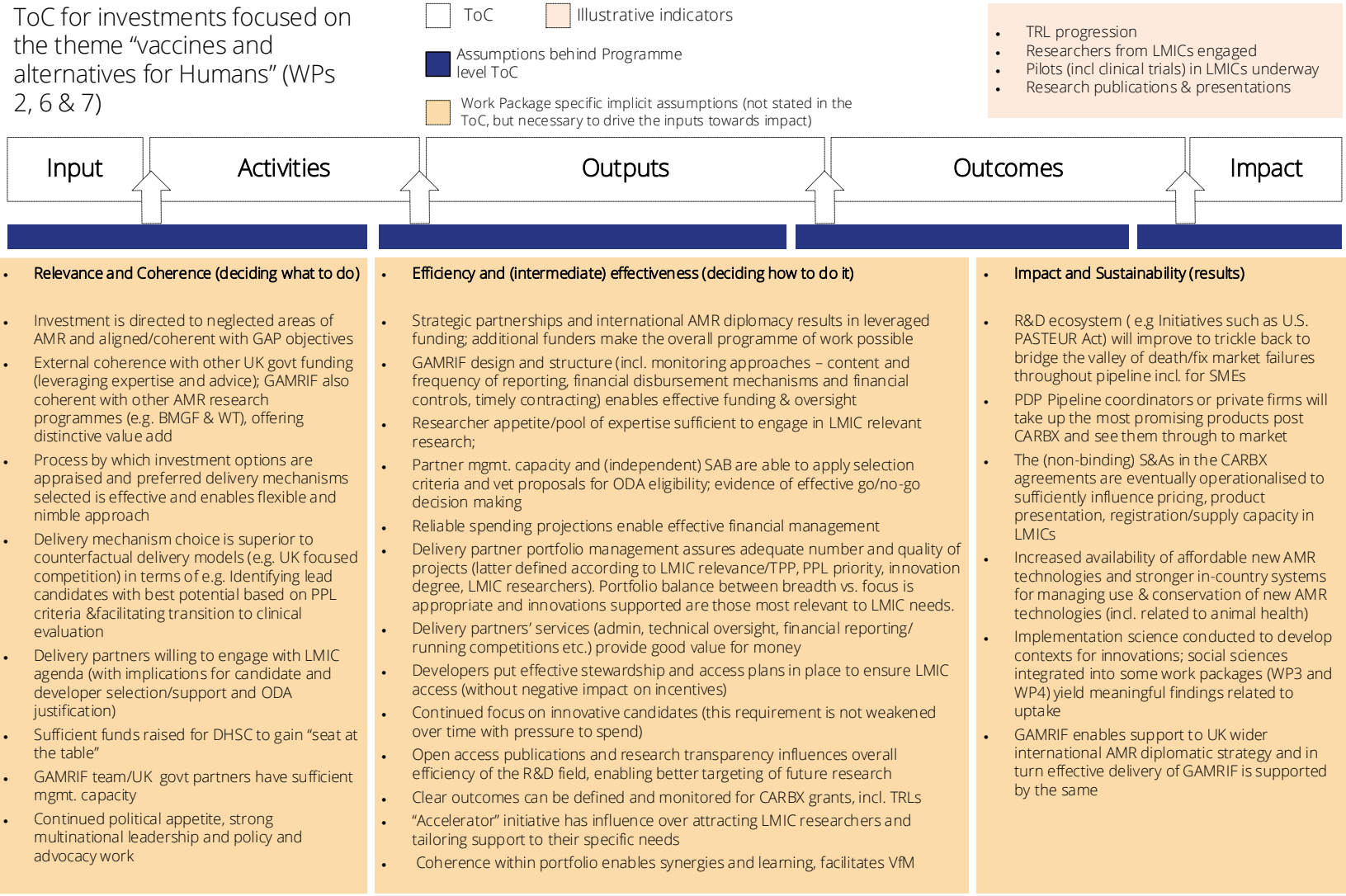


Figure 2 Illustrative nested WP ToC



3.0 Findings

Below we discuss the findings from each of the 7 GAMRIF Work Packages, reported against the three EQs relating to relevance and coherence, effectiveness and efficiency, and impact and sustainability. This is followed by a cross-portfolio analysis of findings and lessons learned, including our GAMRIF programme Contribution Analysis (with further detail by WP in Annex 3, p.63).

3.1 Work Package 1: UK-China

Summary details

Type: Bilateral Partnership between UK (DHSC) and China (MoST)

Aim: Address the challenges of AMR in China and other LMICs for humans and animals through the development of vaccines, diagnostics, and alternatives to antibiotics and animal feed

Duration: January 2019 - September 2022*

GAMRIF funding: GBP 10 million

Leverage: RMB 60 million (approximately GBP 7 million) from China

Number of projects: 14

Implementing partners: Innovate UK (UK side), China Science and Technology Exchange Centre – CSTEC (China Side)

Other partners: KTN - UK-based information and partnering roadshows and a five-day visit to China in 2017; Medical Research Council (MRC) – shared costs for the 2019 launch event

** Project 104983 has received an extension until December 2022 to account for delays.*

3.1.1 Relevance and coherence

Under Question 1, our theory is that WP 1 allocated resources strategically towards potentially high-impact activities aligned to priority AMR issues, taking into consideration complementarity with other funding as well as considering the WP's comparative advantages and goals.

Global AMR will not be managed successfully without the involvement of China, given its large antibiotic consumption and role in pharmaceutical manufacturing. WP 1 has provided an opportunity to leverage the life science R&D expertise of Chinese and UK-based small and medium enterprises (SMEs) to support research that seeks to address AMR challenges relevant to China and wider LMIC contexts. Antibiotic consumption in China is expected to double by 2030, given increased purchasing power and a shift to large-scale farming. Increased travel to and from the region is associated with an increasing influx of drug-resistant pathogens, as travellers to areas with high AMR prevalence are likely to be exposed to resistant bacteria and return to their home countries colonised. Furthermore, weak antibiotic stewardship for animal health and wastewater management also contributes to the spread of AMR.[5] WP 1 also followed the success of the UK–China scientific partnerships that led to the discovery of the *mcr-1* gene, and ultimately to changes in Chinese use of colistin in pig farming[6], so there were good reasons to think that bilateral UK–China scientific partnerships could lead to change. Some stakeholders considered that WP 1 projects are more focused on business/commercialisation opportunities than on the needs of LMICs. However, addressing LMIC needs and cultivating commercialisation opportunities are not mutually exclusive; this is especially true in the case of AMR, where market failure stymies products from reaching target populations.

There were political and economic, as well as scientific reasons, to work with China. China was an original partner in the conceptualisation of GAMRIF – the establishment of a Global Antimicrobial Resistance Research Innovation Fund was announced during an October 2015 state visit to the UK by Chinese President Xi Jinping.[7] A proportion of the Fund (GBP

[5] Yam et al, Antimicrobial Resistance in the Asia Pacific region: a meeting report. Antimicrobial Resistance and Infection Control (2019) 8:202. Also see: Frost I, Van Boeckel TP, Pires J, Craig J, Laximinarayan R. Global geographic trends in antimicorbial resistance: the role of international travel. J Travel Med. 2019 and https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6777638/

[6] Wang et al, 'Changes in colistin resistance and mcr-1 abundance in Escherichia coli of animal and human origins following the ban of colistin-positive additives in China: an epidemiological comparative study', Lancet Infectious Diseases, Volume 20, Issue 10, October 2020. Pages 1161-1171, https://doi.org/10.1016/S1473-3099(20)30149-3

[7] Following the O'Neill Review on AMR, GAMRIF was initially thought of as a seed funding grant that would go on to become a global fund for innovation in AMR R&D, with the UK, China and BMGF, as the 3 initial donors, leveraging other donors across the G20. With the change in UK and US governments, and recognition of little G20 appetite for a new global health fund, the conceptualisation of GAMRIF evolved into its current form.

10 million) was subsequently allocated to work with China (with the remainder being used to leverage funding from others through the six other Work Packages). It was hoped that working with China would help crowd in other donors, as well as influence a change in practices in China and the wider region. WP 1 also provides an opportunity for UK businesses. However, stakeholders pointed out that there are opportunities and challenges in relation to commercialisation. China is generally not a preferred market for SMEs, as it can be a challenging country to establish a foothold in without local partners, and Chinese intellectual property (IP) rules can be difficult to navigate.

The projects that resulted from this bilateral partnership are relevant to AMR needs in China and have the potential to be of global benefit. Project scope was set by a joint panel of UK and Chinese experts, and project selection was negotiated based on those shortlisted by MoST, as well as those shortlisted by an expert panel chaired in the UK. Projects have focused on R&D for alternatives to antibiotics for humans and animals, diagnostics (e.g detecting bovine disease in cows) and addressing the use of antibiotics in animal feed. ODA compliance was reviewed at application stage and monitored during implementation by the WP 1 delivery partner, Innovate UK.

3.1.1.1 Complementarity and value-add with other HMG funding

The available evidence suggests that WP 1 is complementary to adding value to work being done by UK Research and Innovation (UKRI)[8] and the British Embassy (BE) in China. Stakeholders at UKRI and the BE reported that WP 1's focus on bringing together academic and industry representatives is a unique selling point as compared to other UKRI work in China. This is seen as being particularly valuable because it has been challenging to effectively link academic and industry work in this area. Furthermore, WP 1 is more output-driven, focused on product development, whereas other programming UKRI is leading in China has a surveillance and primary health focus (prescription practices, etc.). As such, WP 1 is adding value to what UKRI is already doing in China rather than overlapping with it. However, one stakeholder noted that they felt more could be done by GAMRIF to ensure there is coherent messaging about Her Majesty's Government (HMG) strategies and policies related to AMR between colleagues in London and China, especially because AMR stretches across several departments, making coordination particularly complex.

3.1.2 Effectiveness (intermediate results) and efficiency

Under Question 2, our theory is that the current design and management of WP 1 – including the delivery partners' efficiency and effectiveness – allows it to effectively maximise its impact and objectives.

3.1.2.1 Work Package design

One of the key advantages of WP 1's design is the linkage of academic research with businesses for product development. WP 1 specifically focuses on turning research into products that can make a difference and enter the market to meet a recognised need, since academic projects on their own typically are unable to efficiently produce a commercial product. To be eligible for funding under this WP bidding project consortia needed to be business-led on the UK side and include at least:

1. One UK-based business of any size.
2. One UK academic or research organisation
3. One Chinese business of any size.
4. One Chinese academic or research organisation.

The addition of industry partners can help make sure that academic research is using the standard necessary for commercialisation, making the process faster and more efficient.

[8] UKRI is a non-departmental public body of the UK government – funded through the Department for Business, Energy, and Industrial Strategy's science budget – that directs research and innovation funding. Both Innovate UK (WP1 delivery partner) and Biotechnology and Biological Sciences Research Council (BBSRC – WP4 delivery partner) are part of UKRI.

WP 1's bilateral partnership model offered a viable means of engaging with China, although with some challenges. China has historically hesitated to engage in multilateral or global partnerships. The bilateral model has provided a viable platform for building high-level relationships with relevant stakeholders and agencies in the Chinese government, helping to bring together the UK's well-developed research and China's growing strength. Furthermore, a bilateral partnership model is also seen as being comparatively low risk, as ODA money only funds the UK researchers, and no ODA money leaves the UK.

However, slow processes on the Chinese side with administration by MoST has created issues throughout the programme, particularly during set-up. WP 1-funded projects started considerably later on the Chinese side due to delays with the approval process. There is still some concern that initial delays and ongoing issues with late delivery on the Chinese side – largely due to uncertainty with COVID-19 – could create challenges for reporting at the end of GAMRIF. Secondly, stakeholders involved in implementation on the UK side have experienced ongoing issues with communication, including communication around different approaches. For example, the criteria for MoST's project short-listing were not clear to stakeholders on the UK side, which created difficulties in understanding why some of the projects scored most highly by the UK-chaired Expert Committee were not shortlisted by MoST.

3.1.2.2 Work Package management

DHSC's role in managing WP 1 and GAMRIF more generally was viewed positively. Stakeholders at the UKRI and the BE felt that GAMRIF has good potential to be influential on the policy front because of DHSC's reputation as a department. There was also a positive perception of the GAMRIF delivery team specifically, particularly in relation to their relevant technical background and expertise.

Perceptions of Innovate UK's performance as a delivery partner for WP 1 were also positive. Innovate UK is experienced in managing research and innovation projects in the sector for the UK Government, which is thought to have made the project set-up and management process smoother and more efficient. Innovate UK also had an established process with MoST from previous projects, which seems to have made the commissioning process easier than it might have been with another delivery partner. Stakeholders were also very positive about Innovate UK's GAMRIF Project Manager (PM), reporting that they have been diligent and worked closely with UKRI China and other UK Government actors in China. They were also generally positive about the fact that Innovate UK had a designated PM looking after GAMRIF throughout the programme cycle, as it promotes continuity and effective monitoring.

Knowledge Transfer Network (KTN) were considered a good choice for managing partnership-building activities, as they have good health sector connections in the UK, but it is unclear whether the specific activities that KTN ran represented good VfM. They also have connections and experience not only in human, but also animal health. Some interviewees remarked, however, that they were not sure that the in-person activities KTN ran for WP 1 – namely, three one-day UK-based roadshows and a five-day visit to China with a UK delegation of researchers – were the most efficient way to build new bilateral partnerships. However, it could alternatively be argued that face-to-face conversations and meetings facilitated by the roadshows and China visit in particular are important for establishing relationships and supporting the longevity of partnerships. Moreover, Meeting Mojo, a web-based partnering tool, provided an online alternative to the in-person events offered.

3.1.3 Impact and sustainability

Under Question 3, we are testing the theory that funded projects will produce outputs that have the potential to result in commercialised products and/or influence policy and practice in LMICs, and that investment will result in sustainable research partnerships, stimulate wider investment in AMR focused work, and enable support for the wider UK AMR diplomatic strategy.

Given the long timescales associated with AMR research, particularly early-stage projects like those funded by WP 1, it is difficult to comment on the potential impact and sustainability of WP 1. However, several stakeholders expressed that **it will be challenging for projects to produce commercialised products and/or influence policy in LMICs without clear next steps for funding**. One research team spoke about how they were going to run out of funding just as their prototype will

be ready to be transferred into a product. Investing in small projects without planning for what follows the end of the programme could be a waste of money unless a business or government is ready to fund it moving forward. However, the projects that have been funded under WP 1 are progressing well, and the nature of this kind of AMR research is that even if one project out of the 14 funded is able to successfully commercialise products and/or influence policy, the impact could be substantial. Relatedly, **it is not clear if GAMRIF's investment in partnership building will result in sustainable research partnerships, as these can be challenging to maintain without a financial incentive in place**.

Although stakeholders reported that **GAMRIF had been useful for keeping China involved in the conversation around AMR, it is also not clear what level of ongoing commitment the Chinese government are able to provide in terms of investing and engaging in AMR research and innovation beyond GAMRIF**. This is beyond the UK Government's control but is salient to whether WP 1 will stimulate wider investment in AMR focused work in China.

There are likely to be intangible benefits from the political goodwill and relationships forged between individuals and organisations, however. GAMRIF includes high-level government-to-government interactions, and stakeholders at both UKRI and the BE noted that these were important for building relationships between the UK and China, especially with MoST. WP 1 engaged with the right actors and agencies in China for technology and innovation, especially since MoST also formulates policy. However, MoST cannot influence the national health system. Future GAMRIF programming might therefore have more of a public health focus, facilitating opportunities to promote links with the Chinese National Health Commission (NHC) and fill the gap between MoST and NHC, which could help increase GAMRIF's policy influence in public health specifically. However, the NHC does not have a research budget, and MoST is the CCP's ministry responsible for R&D partnerships. As such, the likelihood or feasibility of this partnership option GAMRIF may be limited or beyond what is possible for the portfolio.

3.2 Work Package 2: Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator (CARB-X)

Summary details

CARB-X

Type: Global initiative

Aim: To support the best scientific research around the world towards innovation that can be used to prevent and treat drug-resistant bacterial infections in humans

Duration: 2018- 2022

GAMRIF funding: GBP 20 million

Leverage: $18 million (reported in GAMRIF's Annual Report 2019/2020, when 8 projects were supported)*

Number of projects: 14 R&D projects, plus cross-project work (e.g Global Accelerator Network and stewardship and access activities)

Implementing partners: CARB-X, led out of Boston University

Other partners: Biomedical Advanced Research and Development Authority (BARDA – US government); The UK Wellcome Trust; BMGF); The German Federal Ministry of Education and Research (BMBF); in-kind support from NIAID, as well as from industry partners

* *"As stated in the Annual Review, it is difficult to quantify the exact proportion of these leveraged funds that will directly benefit LMICs as GAMRIF projects do.....This is in addition to the $25 million leveraged from the BMGF at the beginning of GAMRIF negotiations to join as a CARB-X funder"*

3.2.1 Relevance and coherence

Under Question 1, our theory is that CARB-X is targeting priority AMR needs (relevance), filling gaps in the activity of other funders involved in existing therapeutic, preventative or diagnostic-focused AMR R&D efforts (coherence), and that GAMRIF offers distinctive added value as a funder.

CARB-X's focus is aligned with priority AMR needs as identified in global consensus documents and with market bottlenecks identified in the 2016 O'Neill Review on AMR. [9] As stated in CARB-X's vision: CARB-X supports the world's largest, most scientifically diverse antibacterial portfolio and selects projects aligned with an integrated strategy focused on the most serious bacterial threats. It provides non-dilutive R&D funding to product developers (PDs) for antibiotics in novel classes, non-traditional therapeutics, vaccines, preventatives (phage, microbiome, antibody), and rapid diagnostics. Requests for proposals and candidate selection are based on the WHO and Centers for Disease Control and Prevention (CDC) priority pathogen lists, ensuring alignment with priority needs globally. Innovation is a key focus – over 90% of the CARB-X therapeutic portfolio can be classified as novel[10], and CARB-X investments have addressed areas previously under-represented by investment in the global clinical pipeline. Cross-project activities are also supported, addressing R&D challenges that are common across technology and pathogen types.

GAMRIF funds only a portion of the entire CARB-X portfolio, however there are arguments against imposing such a limitation. In alignment with the steer set initially by the GAMRIF EAB and its guidance on the most ODA-relevant and significantly under-funded areas, GAMRIF only funds preventatives and non-traditional therapeutics in the CARB-X portfolio, not diagnostics or small-molecule therapeutics. The 14 projects supported[11] include: seven in the prevention category (six vaccines and one monoclonal antibody) and seven in the treatment category (two protein-based products, one direct-acting peptide, one peptide acting as a potentiator, one engineered-phage product, and two anti-virulence products). GAMRIF also supports CARB-X's cross-project work, including the Global Accelerator Network (GAN) and stewardship and access activities.

The EAB-guided focus of GAMRIF's technology scope to non-traditional and preventatives, excluding small molecules and diagnostics, has resulted in GAMRIF funding only 16/92 CARB-X projects, these being relatively more risky candidates.[12]

[9] O'Neill Review on AMR 2016, DRIVE-AB Report.
[10] Criteria: New class of drugs, new molecular target, new mode of action, or no cross-resistance to other antibiotic classes.
[11] Originally 16 projects were supported; two have been terminated for technical reasons
[12] Vaccines are relatively more expensive to develop and the clinical and regulatory pathway for non-traditionals is riskier than for small-molecule antibiotics.

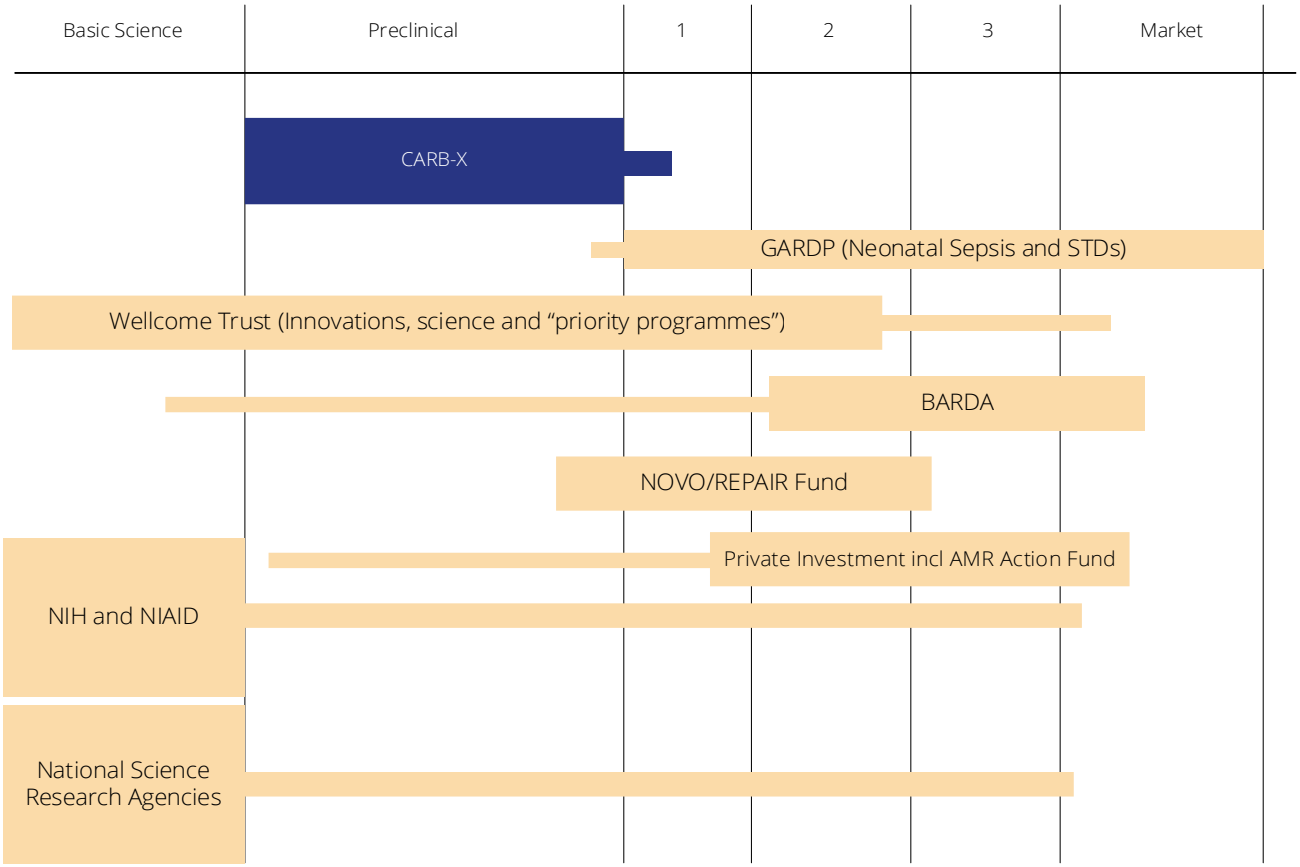
However, the rationale for this limitation may require further consideration. AMR has a disproportionate impact in LMICs[13], it can well be argued that most of the candidates in the CARB-X portfolio – excluding those which can only be delivered in very advanced, wealthy health systems – should be eligible for GAMRIF funding. Also, direct-acting small molecules. especially if in tablet form, are readily deployable in LMICs, so on that basis it is arguably more appropriate to widen the GAMRIF/ODA eligibility to small-molecule antibiotics. Vaccines, improved sanitation, or better stewardship all reduce dependence on antibiotic agents, but only new therapeutics actually treat existing resistant infections. By excluding direct-acting small molecules and diagnostics, GAMRIF also misses an opportunity to influence those PDs whose focus might otherwise be exclusively on developing products for HIC markets and meeting FDA requirements. The potential to apply for ODA funding could influence a wider range of PDs to shape candidates to meet global needs (e.g investing in chemistry and formulation work to improve shelf stability or lower cost of goods. There is also a practical consideration in terms of predictability of UK fund utilisation (meeting fiscal year targets), as inevitably a smaller portfolio means that GAMRIF will face a higher risk of being unable to disperse the full CARB-X budget envelope, should one or several GAMRIF-backed candidates not advance.

CARB-X is filling important gaps in the investment activity currently directed towards therapeutic and preventative R&D of AMR relevance. The stage of the R&D pipeline supported by CARB-X has filled a recognised funding gap – early development stages from hit to lead until Phase 1 clinical trials (Figure 3). Complementarity with upstream and downstream work and other pre-clinical research outside of CARB-X is facilitated through the review processes and composition of people involved in portfolio decision-making – the scientific advisory board, CARB-X management, and the Joint Oversight Committee (JOC). The other major funders in this area – Wellcome Trust, BARDA, and the US National Institute of Health/National Institute of Allergy and Infectious Disease (NIH/NIAID) – are represented on the JOC and CARB-X communicates with the closest comparator also funding pre-clinical work, the Novo-Nordisk REPAIR fund.[14]

[13] See for example Alessia Savoldi, Elena Carrara, Beryl Primrose Gladstone, Anna Maria Azzini, Siri Göpel, Evelina Tacconelli, 'Gross national income and antibiotic resistance in invasive isolates: Analysis of the top-ranked antibiotic-resistant bacteria on the 2017 WHO priority list', Journal of Antimicrobial Chemotherapy, Volume 74, Issue 12, December 2019, Pages 3619–3625, https://doi.org/10.1093/jac/dkz381

[14] REPAIR's funding is dilutive equity investment, not grant funding. Established in 2018 with a budget of USD 145 million, it is much smaller than CARB-X. REPAIR and CARB-X management are both based in Boston and communicate frequently to ensure a degree of co-ordination and avoid 'double-dipping' when the same developer is supported for different projects.

Figure 3 Funding for AMR Therapeutics[15]



GAMRIF has added value to the pre-clinical R&D effort by shaping the CARB-X investment towards LMIC needs and brokering relationships with other funders and complementary organisations. GAMRIF has been widely credited by KIs in and outside of CARB-X as influencing CARB-X's strategic direction, its portfolio, and its decision-making and grant management processes to prioritise work that is LMIC-relevant and to support the incorporation of principles of stewardship and access. GAMRIF brings the credibility of the UK Government, which according to CARB-X management has been helpful in discussions with other G7 funders, and GAMRIF brought along the like-minded Bill and Melinda Gates Foundation (BMGF) as a co-funder. Prior to GAMRIF, CARB-X was not funding alternatives (e.g vaccines) and its willingness to expand its portfolio into preventatives encouraged BMGF to join GAMRIF in becoming a funder. GAMRIF has influenced the discussions around the table – opening CARB-X up to thinking as a global entity and strengthening the Wellcome Trust's message that CARB-X needs to develop technologies with relevance to AMR globally. Practically speaking, GAMRIF brought ODA Work Packages, including technical assistance for developers, and practical tools for assessing ODA relevance. This has led to PDs thinking with a global focus (e.g altering chemistry to reduce the cost of goods and/or lengthen their shelf life), which they would otherwise not necessarily have done. GAMRIF has brokered relationships between CARB-X and other groups like the Fleming Fund, opened doors with the Indian-based global accelerator C-CAMP, and facilitated relationships for a cross-project initiative to test portfolio candidates against a global panel of isolates. Without this project, the PDs would have been restricted to the use of CDC/commercial panels, whereas this project allowed testing of their technology candidates against current pathogens circulating in South Africa and India, which are likely to be circulating in HIC in a few years. This assures effectiveness against what is to come, not what is in HIC hospitals now, and therefore serves the interests of both HICs and LMICs.

[15] Figure Source: Based on KIIs, adapted from DRIVE-AB Report Figure 7, page 42 (NB: for discussion only – may not be comprehensive)

3.2.2 Effectiveness (intermediate results) and efficiency

Under Question 2, our theory is that CARB-X is effectively and efficiently able to identify lead candidates with the best potential, facilitate their transition to clinical evaluation, and broker access and stewardship terms. Strategic partnerships would result in leveraged funding and these additional funders would make the overall programme of work possible.

CARB-X has effective and efficient mechanisms in place to identify lead candidates with the best potential, facilitate their transition to clinical evaluation, and support eventual stewardship and access. Historically, pre-clinical candidates have been funded by governments, which fund domestic projects on a project-by-project, reactive grant funding approach, and only 2–3% of candidates will make it to market. CARB-X tries to improve these chances by selecting portfolio candidates from any geography on a competitive basis – using criteria for potential health impact (priority pathogens, diversity of approaches), scientific/technical merit, and organisational capacity. The transition from academic research to drug development – i.e. translational science – is another historic challenge in the pre-clinical space, which CARB-X addresses by providing wrap-around services. Through its R&D team, services made available by NIAID and the Global Accelerator Networks (GAN), which also help expand the applicant pool, and through contracted specialists, CARB-X helps PDs with technical and business issues. This ensures that the best product candidates are identified and research work is accelerated. Another accomplishment supported by GAMRIF was the development of CARB-X's Stewardship and Access Guidance (more on this under EQ 3 below).

The application and review process of CARB-X has continually improved during the term of GAMRIF funding. Initial funding calls in 2018 were very open, resulting in over 1,000 diverse applications, creating challenges for CARB-X in dealing with such large and diverse demand. As of 2019, CARB-X started segmenting the funding rounds according to the four product categories previously mentioned. This allowed for better tailoring of expert review panel composition, as well as targeting for ODA-supported calls. The review process has also evolved, in particular the ODA eligibility review process has evolved as CARB-X has become more skilled in understanding ODA-specific R&D funding. The capacity of CARB-X's R&D team has been strengthened, and they now layer on a portfolio view as part of the review process. The LMIC-relevance of the scientific expert committee has been strengthened as well. The review process staging ensures that the work required of applicants progresses as their likelihood of funding increases, and applicants that make it to the last stage engage in technical exchange/Q&A with the review panel. Proposals can also be modified or stage gated, as necessary.

With regard to management of the ongoing portfolio, there are improved project management tools to better predict pipeline progression and corresponding funding needs over time. The M&E indicators initially developed by BARDA were too broad and easily achievable; they have now been made more ambitious and nuanced to allow for comparison against industry benchmarks (and CARB-X performs well comparatively). Recognising prevailing challenges in the overall R&D ecosystem for AMR-relevant products, CARB-X has changed some of its policies to further support struggling PDs with promising candidates. It has reduced the PD-contributed cost-share requirement for the first 3 stages of development from 30% to 10%; CARB-X can also now advance funds prior to work; and CARB-X has the ability to fund discrete pieces of work further into Phase 1, if this will help the PD build a better dossier to secure follow-on funding.

The geographical scope and service offering of the GAN has been improved as well. This is credited with widening the applicant pool (especially in India) and improving movement through pipeline and commercialisation potential. Although inclusion of an Indian-based GAN has resulted in new applicants from India, there is scope to further widen the geographical base of applicants, e.g from Japan and South Africa. This might even be facilitated by other GAMRIF grantees (e.g BactiVac) who have links to LMIC-based researchers and could sensitise researchers to the funding and services offered by CARB-X.

CARB-X's interim results look very promising in terms of attracting high quality applicants and progressing the best candidates through to clinical evaluation. Between July 2016–July 2021, 1,163 applications were received, and 92 projects have been funded in 12 countries. There are 60 active projects currently in the portfolio: 19 antibiotics – all in novel classes, 16 non-traditional therapeutics, 8 vaccines, 4 preventatives (phage, microbiome, antibody), and 12 rapid diagnostics. CARB-X has 9 graduates (7 still going) and has halted 23 programmes for technical or business reasons. CARB-X has met/surpassed all GAMRIF KPIs (e.g portfolio diversity, support delivered to PDs). For ODA-specific projects, four are

expected to commence first-in-human studies in 2022. However, according to Pew Trust research[16], it is too early to know whether this increased activity at the pre-clinical stage will ultimately lead to a fuller and richer pipeline of candidates in subsequent phases, though KIs perceive that it is likely.

CARB-X partners working together make the overall programme of work possible, achieving more than would be possible as individual funders. Since its start in 2016, over USD 500 million has gone into pre-clinical work through CARB-X, of which GBP 20 million comes from GAMRIF/DHSC, USD 400 million from public/foundation funds, and USD 100 million comes from industry in-kind support. GAMRIF's GBP 20 million is able to achieve more by leveraging the CARB-X infrastructure largely paid for by other donors, and in turn, GAMRIF brings value to CARB-X, as explained under EQ 1 above. CARB-X is an example of the UK having a significant voice with key players, such as the US Government, the Wellcome Trust, and industry.

3.2.3 Impact and sustainability

Under Question 3, our theory is that the market entry, use, and health impacts of GAMRIF investments in CARB-X will be supported by an improved R&D ecosystem and operationalisation of provisions in Stewardship and Access (S&A) agreements, enabling access and conservation of new AMR technologies.

The plausibility that CARB-X's interim results will result in longer term outcomes and impact is influenced by remaining challenges in the R&D ecosystem. Although clearly CARB-X is successfully filling the pre-clinical pipeline and helping PDs develop stronger packages to secure follow-on funding, the translation of this innovation into market-ready-products will require pharma, SMEs, and other providers of public and private finance, as well as Product Development Partnerships. Since 2016 there have been continued exits of major pharma companies from the antibiotics space, a decrease in venture capital funding, and some high-profile bankruptcies – e.g Achaogen in 2019, and Melinta in 2020 – which show that the ecosystem remains challenging, even for candidates that make it further along the development pathway. CARB-X investment has been necessary, but will not be sufficient on its own, to deliver AMR related technologies and ultimately health impact.

The ecosystem supporting development of other technologies is similarly challenged: reimbursement plans would need to change in order to promote use of diagnostics and incentivise development, and the diagnostics would need to be rapid, accurate, cheap and easy to use if they are to deter unnecessary antibiotic consumption. Non-traditionals (phages, microbiome) face an uncertain regulatory and clinical pathway, and vaccines are costly to develop, and challenged by lack of incentives for investment, and numerous barriers to uptake.

There have, however, been several promising changes within the ecosystem as well, which improve the chances of CARB-X investments resulting in product development, access, and health impact. A new industry-funded mechanism started in December 2020 – the AMR Action Fund – which has the potential to pick-up promising CARB-X graduates, and the advent and strengthening of the AMR work of follow-on portfolio managers FIND and GARDP, which are focused on more mature technology candidates and have similar ways of working to CARB-X, could potentially smooth the path to market for the most LMIC-relevant product candidates.[17] On the UK side, the GAMRIF delivery team has also been involved in wider bilateral and multilateral influencing work, to make market systems for antibiotics more sustainable and including the first UK 'subscription-type' payment model (2020), widely lauded as the first potentially powerful 'pull' mechanism providing incentives to developers.[18]

The CARB-X S&A provisions also have the potential to promote achievement of outcomes and impact. GAMRIF influenced CARB-X's S&A provisions, advocating for inclusion of a wider group of experts in their development. CARB-X's S&A provisions are contractually binding, non-negotiable terms which require all CARB-X funding recipients to produce a S&A

[16] https://www.pewtrusts.org/en/research-and-analysis/issue-briefs/2021/03/tracking-the-global-pipeline-of-antibiotics-in-development
[17] There have been positive developments in the diagnostic R&D ecosystem as well. The Wellcome Trust is funding Value Dx, which is providing a comprehensive public health assessment of the value of diagnostics; WHO and FIND have developed TPPs for AMR diagnostics; and there have been multiple competitions, such as the Longitude Prize of Nesta, to promote innovation of rapid, point-of-care diagnostics Longitude Prize (Nesta), Antimicrobial Resistance Diagnostics Challenge (NIH&BARDA).Note that GAMRIF's funding to CARB-X does not include funding to diagnostics, although this could be considered going forward.
[18] https://www.england.nhs.uk/blog/how-the-nhs-model-to-tackle-antimicrobial-resistance-amr-can-set-a-global-standard/

plan once the candidate enters pivotal human studies. S&A contractual conditions apply to IP inventions created during the term of CARB-X's funding, and they are followed until patent expiry (even if a company is sold or merges). The CARB-X S&A provisions were developed with wide consultation, and have been agreed by industry, public health stakeholders, as well as publicly backed by the US and UK Governments. The S&A guidance was published in 2021 to support PDs in drafting their plans.

Company specific S&A plans must be placed in the public domain once a product has been approved; such transparency increases the likelihood that partners will design public-health centred provisions and that they can be held accountable for implementing their S&A commitments. A commercialisation plan will also be developed and kept confidential between the Wellcome Trust and the company. If the Wellcome Trust is not satisfied with the S&A or commercialisation plans, they have march-in rights for the targeted territories. Due to the maturity of the current CARB-X pipeline relative to the stage at which the plans must be developed, only one diagnostic company (Proteus) has been actively working on their S&A plan so far.

3.3 Work Package 3: Innovative Veterinary Solutions for AMR Prevention Research Programme (InnoVet-AMR)

Summary details

Type: Global initiative
Aims:

- Support research that will identify innovative veterinary solutions, including vaccines and other alternatives to antibiotics, to reduce antibiotic microbial use in livestock and aquaculture operations in LMICs
- Build effective partnerships to better coordinate discovery, development, and sustainable delivery of affordable veterinary solutions, including vaccines, to reduce the use of antibiotics in livestock and aquaculture operations in LMICs.

Duration: Mid 2018 - end 2023
GAMRIF funding: GBP 10 million, plus GBP 960,000 extension
Leverage: CAD 10 million (GBP 5.6 million), plus further for extension
Number of projects: 11
Implementing partners: International Development Research Centre (IDRC), also acting as co-funder.

3.3.1 Relevance and coherence

Under Question 1, our theory is that InnoVet-AMR is targeting priority AMR needs (relevance), filling gaps in the activity of other funders involved in existing AMR research in farming and One Health (coherence), and that GAMRIF offers distinctive value-add as a funder. This includes developing and supporting the uptake of innovative farming alternatives to antibiotics, including vaccines.

Underlying the ToC is the fundamental assumption that reduction in, and/or modification of, antibiotic use in animal health and farming practices will result in reduced pressure toward AMR in human health, whilst protecting animal health. There are two postulated mechanisms for this:

Direct impact: A small number of pathogens directly affect both animals and humans – among them, Campylobacter, Shigella, and Salmonella species, for which the link is clear. There is also the potential for antibiotic residues in meat and wastewater and other effluent to promote AMR, both within human hosts and in the environment.

Indirect impact: Promotion of more efficient farming and higher productivity will have positive implications for food supply, and therefore overall human health.

Relevance: The GAMRIF investments in WP 3 are focused on testing these assumptions, and they also align well with the Strategic Objectives of the Global Action Plan and priorities of the World Organisation for Animal Health (OIE). WP 3 investments touch on all five areas: improved awareness; strengthened evidence base; improved sanitation, hygiene, and prevention; optimised antibiotic use; and investment in new vaccines and other interventions. The project focus aligns with the OIE priorities for AMR intervention in animal health identified as swine, poultry, and fish diseases.[19] This focus, and predominance of non-vaccine alternatives to antibiotics, complements the IDRC Livestock Vaccine Innovation Fund programme, a CAD 57 million partnership of IDRC and partners, whilst filling the pipeline for more down-stream programmes such as those of the Tripartite Collaboration (WHO, OIE, FAO)[20].

In choosing an upstream product development focus, GAMRIF has supported interventions through InnoVet-AMR that would not otherwise have received support and enriched the global product pipeline. Within the InnoVet-AMR programme, GAMRIF was faced with a choice of addressing broad downstream issues of implementation and supply lines for non-antibiotic interventions, and animal stewardship (such as environmental exposure, feed quality, zoning) and human behaviour change, or concentrating on more upstream projects. A meeting at Wilton Park brought together a range of international experts who prioritised, in addition to development of new and improved vaccines, a number of these downstream broad-focus areas. These priorities included farm management practices and biosecurity, surveillance,

[19] USDA Alternatives to Antibiotics, Symposium 2016
[20] https://www.oie.int/fileadmin/Home/eng/Media_Center/docs/pdf/Tripartite_2017.pdf

human behaviour and communication, and mechanisms for broader strategy development, to guide the investment. The InnoVet-AMR funding announcement was made during this meeting, with the intention of funding upstream development to complement other mechanisms, such as the Tripartite Collaboration, that are more involved with implementation policy and country-level delivery. However, the eventual relevance of the funded projects to AMR mitigation will depend on downstream challenges being addressed in the future.

The selection of projects has been strategic, complementing existing vaccine pipelines by expanding into other approaches including bacteriophages, probiotics and feed improvement, and environment modification in aquaculture. Projects were selected through an open call mechanism, requesting interest from multi-national research partnerships on "the development of vaccines, vaccine administration/delivery methods; or the development of alternatives to antibiotics, including but not limited to pro- and pre-biotics, immunomodulators, and bacteriophages". KIs considered these alternative areas highly relevant to reduction in antibiotic use, but poorly supported by other funding sources. However, vaccine development was widely perceived as a less appropriate target for GAMRIF due to greater time and financing requirements and regulatory barriers (also noted for bacteriophage development). The call focused specifically on product development candidates which had early proofs of concept, but were not yet ready for demonstration. The 11 projects eventually selected fit well with the criteria of the 2018 call for proposals.

GAMRIF's added value: GAMRIF has clearly addressed a gap. In bringing innovative products further down the development pipeline across a range of intervention areas, it is providing new technical innovations for downstream interventions to work with. If successful, this investment may stimulate further investment in this area.

The partnership with IDRC leveraged additional IDRC funding, demonstrating direct relevance to the intended outcomes of GAMRIF in stimulating broader support for this sector. There is potential to leverage other funding as products proceed down the development pipeline – this will be important to InnoVet-AMR achieving intended outcomes and translating product development into change of practice.

GAMRIF has filled its purpose of stimulating LMIC-based innovation and LMIC–HIC partnerships. Some KIs raised concern that only two projects have UK-based involvement (though both as lead researchers). This level of involvement may reflect the quality of applications involving UK participants, but also GAMRIF's aim to ensure a level playing field for global applicants. GAMRIF located the InnoVet-AMR launch meeting at Wilton Park in the UK, and promoted local, as well as international, interest. A related concern raised by KIs was a lack of projects transferring existing best-practice innovations from HICs (such as the UK) to LMICs, but this also reflects the stipulation for GAMRIF to support products with early proof of concept.

3.3.2 Effectiveness (intermediate results) and efficiency

The ToC for WP 3 requires GAMRIF to effectively select projects with a high chance of success leading to desired outcomes, and efficiently manage these projects, including through a process for effective transfer of technology and/or knowledge leading to scaling and sustainable use.

The project selection process was well managed, and IDRC was perceived by informants as highly responsive and engaged with grantees. The Wilton Park strategy meeting included a broad range of stakeholders. Projects were then selected after an open call for interest by a jointly convened SAC, with final selection approved by the GSC. After a meeting of grantees in late 2019 in Thailand, no in-person visits by GAMRIF or IDRC have been possible due to restrictions arising from the COVID-19 response. Although the response to the COVID-19 pandemic has considerably hindered progress on projects, grantees have praised IDRC for flexibility and responsiveness, and have indicated that remote support has been prompt and appropriate.

'Wrap-around' support included specialist intellectual property support to address limited market experience of most grantees. The impact of these services is, as yet, unclear, with some KIs raising concerns regarding a continuing lack of preparation for commercialisation of products and/or dissemination of information. Other KIs considered that support was not relevant to early-stage projects, but such criticism could illustrate lack of appreciation among academics of the importance of market readiness, further underlining the need for the wrap-around programme. Support had to be

provided remotely, and reduced familiarity with project readiness will have presented challenges. A review of the wrap-around programme impact and outputs (e.g by IDRC) will help further enhance the programme's effectiveness.

The GSC reports demonstrate good progress within most projects and close monitoring by IDRC. There is a clear description of achievements to date within the plans, current status, and activities yet to be commenced or completed. IDRC administrative management appears to have been effective. Based on the June 2021 GSC report, several projects appear likely to complete planned activities within the extended project timeline, or have final studies well underway. A minority appear unlikely to reach final milestones. This assessment is based on limited data, but reflects good progress for product development in view of the difficult circumstances of the past 18 months.

Additional funding and experience brought to the WP by IDRC has considerably expanded the scope, adding significant value to GAMRIF. IDRC matched the UK sterling contribution in Canadian dollars. The experience of IDRC in managing the LVIF programme and existing connection with countries in the animal health sector brought further efficiencies through internal knowledge, and avoided the need to contract such expertise through GAMRIF. The potential impact on efficiency due to COVID-19 restrictions was effectively reduced through IDRC maintaining close and responsive remote support.

3.3.3 Impact and sustainability

The ToC for the InnoVet-AMR programme relies on an increase in products within the development pipeline stimulating downstream interest in resolving deficiencies in regulatory and market-entry processes and in users and national authorities supporting market expansion. This in turn will result in improved practices in antibiotic use, and also stimulate broader interest in investment in further product development. The strengthening of the concept of One Health in activities to address AMR should lead to improved human population health.

Several projects are highly likely to achieve intended milestones, but barriers to market access and scaling will need to be addressed. IDRC considers projects in early stages of the pipeline, based on a developmental staging common for pharmaceutical development in the animal health space. As noted in some KIIs, certain projects could be considered closer to market than this model suggests, as they are adaptations of existing technologies (e.g nanobubbles in aquaculture) or have lower risk profile (e.g feed additives/neutraceuticals, phages). Barriers to success include a lack of clear market plans or commercial partnerships, and the need to overcome regulatory hurdles that are designed for pharmaceuticals. The wrap-around support is intended to mitigate these challenges and increase industry interaction. Demonstration that interventions are beneficial to farm incomes through efficiencies, cost-reduction, or increased yield will be important in achieving impact.

GAMRIF, with the convening power of DHSC, may be well placed to facilitate knowledge-sharing and the broader external interactions necessary to achieve market success. Although IDRC has embarked on some activities (e.g podcasts) to disseminate knowledge, the diverse nature of the portfolio of projects under InnoVet-AMR and their geographical spread limited opportunity for sharing of learning, or deeper collaboration or synchronisation between grantees. A consistent theme in KIIs was a lack of strong mechanisms for knowledge-sharing in the animal health/One Health/AMR area, and resulting poor dissemination of ideas and knowledge. This constitutes both a threat to project success, and an opportunity for GAMRIF, as IDRC has greater flexibility than multilateral agencies in working with industry. On a broader level, KIs saw opportunities for GAMRIF or a similar mechanism to play a convening role in bringing experts and stakeholders together internationally. Such a mechanism could address knowledge gaps on animal health AMR mechanisms and their influence on human health whilst evidence of successful programmes could serve as templates for others. It could address regulatory and supply line barriers and drive the development of evidence-based strategies that could stimulate investment by other funders.

3.4 Work Package 4: UK–Argentina

Summary details

Type: Bilateral partnership (UK and Argentina)

Aims:

- Develop and implement low-cost, sustainable, culturally and geographically appropriate interventions to reduce the spread of AMR in agriculture, aquaculture, and the environment
- Inform policymaking by generating and disseminating new evidence.

Duration: April 2018 - May 2023

GAMRIF funding: GBP 5 million

Leverage: ARS 2 million per year (from Argentina)*

Number of projects: 5

Lead UK partner(s): Biotechnology and Biological Sciences Research Council (BBSRC); Natural Environment Research Council (NERC)

Lead Argentina partner(s): National Scientific and Technical Research Council (Consejo Nacional de Investigaciones Científicas y Técnicas, 'CONICET')

**When expenditure was first incurred by projects, ARS 2 million was equivalent to more than £37k. However, currently it is equivalent to approximately £15k. The ARS 2 million does not include any staff or estates costs, which are not funded through grants; thus, the leveraged amount is far greater.*

3.4.1 Relevance and coherence

Under Question 1, our theory is that WP 4 activities are aligned with priority AMR needs (relevance), complementary with funding by others (coherence), and building on GAMRIF comparative advantage. Furthermore, there is continued political appetite and fulfilment of resource commitments on both sides of the bilateral partnership.

There is strong evidence to suggest that GAMRIF's aims and activities under WP 4 are relevant and well-aligned with global needs, priorities, and goals. WP 4 aims and relevant activities are aligned with the WHO Global Action Plan on AMR (2015), facilitating better understanding and awareness around AMR by strengthening the evidence base and aiming to reduce AMR incidence with the use of new and innovative measures. Current projects have a focus on: developing a conceptual framework to improve understanding of AMR in livestock systems for translation into policy and practice; AMR in Argentine broiler poultry systems: risks and mitigation; environmental and economic impacts of improved antibiotic stewardship in poultry systems; and mapping the patterns and drivers of antibiotic use and environmental resistance in the Argentine beef industry.[21]

Working with Argentina made sense, given its strong scientific community, its role as a large meat exporter, its interest in reducing antibiotic use in agriculture, and the relevance of lessons to other LMICs. The WP 4 partnership was the result of several mutual interests in AMR between the UK and Argentina, specifically around agriculture, animal health, and food security, which were highlighted during Argentina's G20 presidency in 2018. One of the key common interests/priorities between the two nations is the reduction of antibiotic usage in human and animal health, as well as the use of alternative solutions to reduce the spread of AMR. Over-prescription of antibiotics, as well as the preventative use of antibiotics in livestock, are common issues in Argentina[22]. The latter is particularly relevant to Argentina, as one of the largest producers and exporters of beef (as well as poultry and pork) in the world.

The scientific community in Argentina is strong, particularly in agriculture and animal health. Combined with technical support and significant funding from the UK, collaboration between the two countries was deemed beneficial in terms of combining the resources available to achieve a 'sum greater than its parts'. It is worth noting here that the initial aim for this WP 4 was to fund research in environmental AMR and plants (additional to agriculture and aquaculture), however the focus shifted towards agriculture and animal-transmitted AMR, as this was more relevant to the Argentinian context and could be more beneficial to Argentina, as well as other Latin American countries and LMICs.

One of the key strengths and comparative advantages highlighted by stakeholders was the environmental and agricultural focus of WP 4, which is an under-funded research area. The One Health approach was seen as a big advantage of GAMRIF as it combines a focus on human health with animal health and environmental AMR. While the One Health approach was

[21] https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/886146/projects-funded-by-GAMRIF.pdf.
[22] https://apua.org/argentina

widely considered positively, it was suggested that the phrase 'One Health' can be somewhat abstract. Caution was advised when using this as an umbrella term, as it can virtually encompass any topic in AMR. The connections between human health, animal health and the environment need to be more clearly defined, not only at the microbiological level, but at the economic and socioeconomic level.

Another particularly strong component of AMR research under WP 4 was the social science element, which is strongly emphasised in all five awarded research projects. Stakeholders emphasised that AMR research and development should not only focus on reducing antimicrobial usage (AMU), but also on understanding the main socioeconomic drivers behind AMU. The current literature is limited on this, hence the five projects funded through WP 4 will produce useful new evidence as they consider the social and economic angle of AMR. KIIs showed that this is the right way forward and that further funding in this type of research could prove beneficial.

Lastly, this package provided an opportunity for the UK and Argentina to come together in a research partnership, and to build a stronger diplomatic relationship. Each project has a UK-based, as well as an Argentinian, principal investigator (PI). However, there was consensus among stakeholders from both sides that this goes beyond AMR and research collaboration, and that it has been a significant and positive step forward for the relationship between the UK and Argentina. Stakeholders also highlighted that the partnership-building activities of GAMRIF were particularly advantageous; two workshops were held in Argentina which were met with very positive feedback from all partners, while grant holders benefited greatly, especially from the first one, as it provided the appropriate context for them to shape their research, as well as to meet fellow researchers and potential collaborators. Some of the researchers even mentioned that they changed their topic of interest after the workshop, as it provided them with a better understanding of the country context and AMR research relevant to LMICs.

3.4.2 Effectiveness (intermediate results) and efficiency

Under Question 2, there is evidence to suggest that WP 4 has resulted in the selection of ODA-eligible projects which have the most potential for AMR impact. The bilateral partnership and delivery model chosen is able to support the progress of those projects efficiently and effectively.

There is strong evidence to suggest that the competitive project selection process worked efficiently and effectively. Stakeholders thought that the organisation and management of the process was efficient, and that the quality of the applications was high. The funding criteria and awarding mechanisms of BBSRC and CONICET were quite similar, which facilitated the process, as the two partners easily reached an agreement. The applications were assessed based on two key criteria – ODA relevance and policy potential, in alignment with the GAMRIF focus on LMIC-relevance and translation to useful outputs. Efforts were also made to avoid duplication and create a diverse portfolio covering all of the animal subgroups. Nine applications were submitted and the top five were selected.

Evidence suggests that the 'Pan-Programme Integration Project (PPIP)' and the intended alignment of projects was delivered effectively, but met with some challenges and mixed feedback One of the unique components of WP 4 when compared to other GAMRIF Work Packages is the PPIP. This was a standalone project which aimed to integrate and learn across the 5 grants, to convey the bigger picture and ultimately influence policymaking. One of the most positive aspects of the PPIP was that it allowed researchers to come together, exchange knowledge through a face-to-face workshop, and coordinate into developing outputs that could translate into policy. However, the integration process started post-call, and researchers thought that the integration requirement was not very clear, and the timeframe to put together a proposal was short. Some of the projects could not be 'forced' to align after they had already been designed – more time was needed to share project ideas in advance. Stakeholders argued that it would have been more efficient if the budget, aims, and tasks were set and clear from the beginning (i.e before and during the call for proposals). Ideally, this would have allowed for more organic cross-project learning and would have reduced the burden on researchers; however, one stakeholder acknowledged that academics are naturally in competition with one another for grant funding, so expectations about incentives to collaborate and share need to be managed.

The bilateral partnership model was viewed by the partners as mutually beneficial and generally working efficiently, although there is evidence to suggest there were some constraints. The BBSRC and CONICET are similar organisations in

terms of their aims and ways of working, which facilitated collaboration and agreement in certain processes, as mentioned above. UK partners specifically highlighted that there was a good level of transparency in the collaboration with Argentina, and that this has opened doors for future research partnerships between the two countries.

However, the partnership between BBSRC and DHSC (GAMRIF delivery team) experienced some constraints to efficiency. The two partners were less aligned (as opposed to BBSRC–CONICET), as government departments and research councils work in different ways and with different priorities. One of the examples of inefficiencies raised was a long and complicated process to develop, review, and agree on the BBSRC–DHSC MoU, which caused some initial delays and misunderstandings. A concern was also that some of these processes may have been duplicated, and that this could have been avoided by sharing some of the staff workload across the two partners. Some of the delays and challenges due to the different ways of working were also visible in handling budgets and estimating expenditure between the two partners. BBSRC apply a flat yearly budget for each grant, which does not take into account the exact spending profile a project might have, as it is assumed that this will change depending on the nature of each project. Although this allows for a certain degree of flexibility for both grant holders and BBSRC, it creates a challenge for DHSC to accurately estimate spend for the financial year, and thus set an appropriate budget for the next year. BBSRC also does not require grantees to report on progress and interim outputs to the degree that DHSC is accustomed[23], and this created some challenges as well. It is worth noting that despite differences in ways of working, it was acknowledged by both delivery partners and grant holders that a certain lack of flexibility in a budget is understandable when coming from a government department, which must ensure financial probity.

Evidence collected from grant holders highlighted a lack of understanding of research cultures, as well as flexibility to reallocate resources. Argentina has been experiencing very unstable economic conditions, with high inflation, which makes the value of the Argentine Peso (ARS) unpredictable. CONICET had very limited capacity due to these economic problems, which was not clear during initial discussions with partners. Argentine researchers are responsible for some of the more 'expensive' tasks, such as fieldwork and sample/data collection in Argentina. Consultation with UK-based researchers showed that they are aware of Argentinian partners' concerns around a lack of resources to carry out the research and achieve the intended objectives, but they are not allowed to transfer funds from the UK to Argentina to provide further support, based on the current agreement.

There is also a concern about the efficiency of the resource allocation approach. UK-based Principal Investigators (PIs) are frequently hiring UK-based post-doctoral researchers to travel and conduct fieldwork. One of the research teams highlighted that hiring local researchers in Argentina could be less costly, as well as more effective, as they could develop a much better relationship with the farmers from whom they are collecting samples throughout the lifetime of the project. Stakeholders mentioned that if all this was clear at the beginning of the projects, the UK budget could have re-allocated some of those costs to cover some of the more expensive consumables (equipment such as cryovials, sampling tools, DNA kits, etc.). Buying this equipment in the UK would be preferable, as Argentine research teams now have to spend a big part of their budget on this due to high inflation. Researchers are, however, finding ways to work around these challenges, and are confident that they can deliver the objectives of their projects as intended.

3.4.3 Impact and sustainability

Under Question 3, we are testing the theory that funded projects will produce outputs that have the potential to result in commercialised products and/or influence policy and practice in LMICs; and that the investment will result in sustainable research partnerships, stimulate wider investment in AMR- focused work in the livestock and aquaculture fields, and enable support to the wider UK AMR diplomatic strategy.

There is strong evidence to suggest that progress against outputs is being made, as all five funded projects have been contracted, launched, and are on track to deliver their intended objectives. There have been some obvious delays due to COVID-19, for example restricting travel to and within Argentina for fieldwork and data collection, but a no-cost extension was approved for all projects.

[23] It is worth noting that DHSC is subject to central government ODA reporting and budget forecasting rules which are not as strict on research councils as they operate within a much larger and multi-year budget envelope.

One of the key outputs so far has been the joint policy translation proposal and ODA statement, which was prepared collaboratively by research teams through the integration project. Separate project-level outputs in terms of policy translation and LMIC uptake are yet to be produced, but all projects have planned specific outputs (policy briefs, for example) for the near future (most are planned for 2022). At this early stage of the GAMRIF programme and projects under WP 4, signs of impact are not expected, as projects need to first come to an end, and policy outputs need to be produced and disseminated, ultimately with the intention of influencing policy or practice.

Intangible benefits are likely to arise from sustained relationships between the two countries, especially at the academic level, as new connections are made, and academic institutions are likely to want to collaborate again in the future.

The research topics of the funded projects are highly relevant to animal health and to AMR in Argentina and beyond and will produce evidence which can be usable in many different settings. An example of this can be seen in one of the grants, 'AMR in Argentine Broiler Poultry Systems: Risks and Mitigation', where researchers are exploring whether reusing poultry litters[24] might lead to an increase in AMR. High use of antibiotics in broiler farms and using the same litter for up to six times (feeding and slaughtering a number of chickens) are common practices in many farms, not only in Argentina, but globally. However, there is not sufficient evidence to determine whether AMR can be spread through the environment using this system. This research aims to understand the risks to animal and human health caused by such practices and recommend mitigation measures to address this issue.

One of the key causes of uncertainty regarding intervention uptake is the significantly different levels of resources and contexts across LMICs, even within Latin America. Evidence produced through GAMRIF-funded research can be beneficial for LMICs, but it should not be expected that translation to policy and practice will happen solely based on the relevance of this evidence. LMICs will need to adapt research outputs into policies which are appropriate for their own country context. A few stakeholders recommended that including LMIC representatives in specific parts of GAMRIF programming could be beneficial in terms of ensuring the relevance and applicability of research outputs in LMICs.

A key broader recommendation for the future of AMR research and a sustainable impact is to frame the problem as a socioeconomic issue, as opposed to maintaining sole focus on the microbiological linkages of humans, animals, and the environment. The social science component of the research under this WP has therefore been recognised as very beneficial and is widely seen as the key to translate evidence into policy.

[24] A poultry litter refers to the floor bedding used in the production of poultry, usually made out of organic materials such as wood shavings, sawdust, shredded sugar cane or straw, etc.

3.5 Work Package 5: Foundation for Innovative New Diagnostics (FIND)

Summary details

Type: Product development Partnership

Aim:

- Establish connectivity for AMR diagnostics, extending to hospital and community level
- Develop new STI diagnostics to enable stewardship of new antibiotics and combat drug-resistant Neisseria gonorrhoea

Duration: May 2018 - April 2022

GAMRIF funding: GBP 10.1 million, plus GBP 600k extension

Leverage: Leverage not quantified, but builds on previous UK Government funding to FIND

Number of projects: 6

Implementing partners: FIND

Other partners:

- Two commercial developers were selected for funding for product development
- Digital health products were developed with Dimagi, Terres Des Hommes, and the Zambia National Public Health Institute (ZNPHI)
- FIND developed a partnership with Global Antibiotic Research and Development Partnership (GARDP) and WHO to oversee the STI diagnostic test strategy
- Scanwell was funded to develop the mobile phone reader application

3.5.1 Relevance and coherence

Under Question 1, our theory is that improved data flows on diagnostic results will produce knowledge that will be used to improve treatment practices, and that the availability of improved diagnostics for sexually-transmitted diseases (STIs) that drive AMR will improve stewardship of antibiotics.

GAMRIF funding for WP 5 targets improved connectivity for AMR diagnostics and more accessible diagnostics for drug-resistant gonorrhoea both of relevance to LMIC needs. The first is intended to support the development of end-to-end data transfer and apps for reporting from Point of Care (POC) tools to health surveillance tools already in place for AMR linking to District Health Information Software 2 (DHIS2). Development of a target product profile describing ideal connectivity attributes will guide further expansion. These AMR connectivity activities were divided into four projects; a pilot project to develop middleware to link AMR data from both human and animal health laboratories, a mobile-phone app to interpret Rapid Diagnostic Test (RDT) results; and two mobile-phone clinical decision aids for febrile children (based on the World Health Organization's Integrated Management of Childhood Illness (IMCI) protocol) The second set of activities involves the development and feasibility assessment of new STI diagnostics and clinical algorithms to support the roll-out and stewardship of a new drug, Zoliflodacin, being developed by GARDP with support from GAMRIF funds. These activities included development of a TPP for STI diagnostics, market assessments in South Africa, Kenya, Thailand and Vietnam, and modelling of acquisition of resistance.

The GAMRIF investment with FIND is aligned with the GAP objectives, touching on improvement of the knowledge base, improved use (targeting) of antibiotic medicines, and investing in better diagnostics, while building a sustainable economic case. The support for diagnostic connectivity within the GAMRIF portfolio is relevant to improving antibiotic stewardship through improved data transfer and surveillance. The STI diagnostics activities will improve accessibility to good quality diagnosis. These have the potential to provide benefits in healthcare well beyond AMR mitigation. The WP also addresses the GAMRIF objective to establish international partnerships in AMR (including stimulating the three-way MOU between FIND, GARDP, and WHO). All activities are focused on LMICs. One Health, an important area for AMR mitigation, is addressed through AMR connectivity activities with the Zambia One Health middleware project. While this project is focussed only on Zambia at present, it sets a precedent for other countries to follow.

AMR Connectivity

The AMR connectivity projects are focused on improving surveillance and data quality and timeliness to support good health policy and clinical decision-making. However, at a practical level, the projects face challenges due to their localised nature. The activities focused on individual country-specific projects will need further support to adapt across borders.

The potential for improved connectivity and diagnostic tests to change antibiotic use depends on behavioural, supply chain, and health infrastructure issues. Implementation did not involve high-profile AMR countries such as South Africa, Nigeria, and Kenya, and this restricts immediate impact. These activities cover a range of applications and are, for the most part, duplicative of projects elsewhere. The RDT reader app was developed for malaria RDTs, necessitated by the lack of other relevant tests that would change anti-microbial therapy. The software could be adaptable to other rapid tests, such as the *N. gonorrhoea* test also funded by GAMRIF, but a direct line to such adaptation and use is unclear. The intent to market as freeware will be important for uptake and adaption to other disease management.

The One Health middleware project with the ZNPHI is considered unique in its ability to bring animal and human AMR data together. It is also consistent with Fleming Fund country investments and sets an important model to drive similar innovation in other countries. The clinical algorithm projects are well-targeted to childhood fever, where inappropriate antibiotic use is well documented. However, similar algorithms are being developed elsewhere.

There is a significant AMR issue with drug-resistant gonorrhoea in LMICs that impacts HIC populations through travel, and support for diagnostic development for this disease is relevant to both LMIC and HIC contexts. Improving diagnostics to better detect pathogens is an important step in supporting a move from syndromic to diagnostic-based management and aligned with WHO policy. It could deliver STI interventions through relatively well-supported reproductive and sexual health/HIV programmes, with high potential for investment and sustainability. While the original intent had been a diagnostic test that detected pathogens and their antibiotic sensitivity, this aim was reduced on expert advice to a simple diagnostic test to detect pathogen presence. This change is consistent with recommendations that antibiotic regimes be based on regional sensitivity patterns rather than case-specificity. FIND also considered, reasonably, that technological barriers were too great to develop a test that could distinguish antibiotic sensitivities at an affordable cost for LMICs.

There is potential for synergy between and within GAMRIF Work Packages, although some challenges remain to realising that potential. Combining the work of FIND and GARDP (WP 6) in *N. gonorrhoea* detection provides coherence between Work Packages with potential to add value to both. The connectivity and diagnostic development projects potentially complement each other, as the value of diagnostic data obtained from the new product will be enhanced by improved data capture and transfer. However, activities were conducted in different countries and do not have a clear relationship with each other.

GAMRIF's added value

GAMRIF is unique in its exclusive concentration on AMR mitigation in LMICs and One Health focus. Other agencies are funding diagnostic development of the type included here (i.e., pathogen-specific), while CARB-X and the Nesta Longitude Prize prioritise AMR, but with less LMIC-specific emphasis. The inclusion of both animal and human health data in the middleware component of the AMR connectivity activities was also considered unique and important by KIs, as there is a lack of One Health AMR funding in LMICs.

GAMRIF has concentrated on product development for connectivity and diagnosis, which should complement downstream Fleming Fund investments in surveillance and lab strengthening. However, some KIs felt that the convening power and reputation of DHSC may have been more effective in addressing downstream barriers to implementation and policy advocacy. Advocacy concerning the long-term funding priorities of national governments, could have led to greater implementation and regulatory efficiency. It is noted that DHSC already has other avenues for such engagement.

3.5.2 Effectiveness (intermediate results) and efficiency

The ToC requires FIND, on behalf of GAMRIF, to effectively select projects with a high chance of success, and manage these efficiently. It then requires a high likelihood of transfer of technology and/or knowledge leading to scaling and sustainable use.

A considerable amount of work was achieved within budget across a diverse portfolio and geography, despite the interruptions of the COVID-19 response. Good dialogue appears to have been maintained between DHSC and FIND, and sub-recipients in turn reported a high level of responsiveness from FIND. KIIs credited FIND with having relevant expertise

in the field, providing good technical support, and demonstrating flexibility in navigating delays due to the COVID-19 response. FIND reporting to DHSC was comprehensive and timely, with a smooth flow of funds. At this stage, all the AMR connectivity projects have been handed off to recipients, and TPPs for the RDT reader and the clinical algorithms completed and published. Market assessments have also been published. STI diagnostic development continues with the drug-resistant gonorrhoea antigen test. **The contracted STI diagnostic test developers were chosen by FIND through a competitive process appropriate for this activity.** The original plan (Annex 1 of the Grant Agreement) was to fund early support of four to five STI diagnostic projects. The reduction in scope to two projects instead may reflect a paucity of candidates, but also improves efficiency in view of the costs of development involved. The subsequent decision to continue with a single development project based on the lateral flow antigen test, terminating funding to the molecular test development, was consistent with the expected risks in diagnostic development. The antigen test will require further support to take through clinical trials and regulatory passage, should performance evaluations indicate that this is warranted. **Other activities supporting STI diagnostic development were completed.** FIND has completed market assessments in four countries with WHO and GARDP. These should aid in planning of market approaches when the product from DCN will be ready, though this will occur beyond the life of current GAMRIF funding. The sample bank being developed to support STI diagnostic development and now located in South Africa, together with the published TPPs, should add long-term value. **Achieving VfM will ultimately depend on these products being successfully adopted and sustained, but reasonable steps have been taken thus far to support this.** The development of the market assessment and TPPs also form a basis for further funders to justify involvement in this area. The AMR connectivity and STI diagnostic development products have broader application than AMR, and so may leverage implementation funding from other areas. The WHO relationship ensured the relevance of TPPs, and will support dissemination of knowledge and techniques. The major partners for the AMR connectivity activities developing clinical algorithms, Dimagi and Terres Des Hommes, have strong experience in the field.

Working through FIND has allowed GAMRIF to combine funding with other partners, complement other UK support to FIND, and leverage FIND's pre-existing expertise. GAMRIF built on other UK Government funding for FIND, and will have added value in strengthening the organisation, providing some basis for future support. FIND brought expertise in diagnostic, country and multi-lateral agency contacts that GAMRIF did not have in-house, including a strong technical working relationship with WHO.

3.5.3 Impact and sustainability

The ToC for the activities of WP 5 require the projects (AMR connectivity and STI diagnostic development) to be supported, and their use or the concepts behind them expanded. The improved quality and availability of data must lead to improved stewardship of antibiotics. To achieve this, all products will have to be competitive with alternatives in the market and attractive to customers, or stimulate the development of effective alternatives.

The long-term impact of the AMR connectivity projects will be heavily dependent on future investment to sustain and scale them, and may benefit from more direct DHSC engagement. While the AMR connectivity projects are relatively country-specific, they are designed as open-source and DHIS2-compatible. Success will depend on linkage to existing and new AMR surveillance systems, such as those supported by the Fleming Fund. This will first require an appraisal of the WP outputs against potential competitor or alternative approaches in the connectivity and digital health area, to ensure that such expansion is justified and provides maximum value compared to engagement with other digital systems.

The Zambia One Health middleware project is unique and has potential to stimulate similar approaches if the current implementation can be supported and expanded. However, the limited availability of support for the Institut Pasteur Dakar and the Burkina Faso Ministry of Health, to whom the clinical algorithm projects were transferred, was of particular concern to KIs as both hardware and software need maintenance. **Data availability would have to translate into increased funding interest, or significant demonstrated savings, to stimulate diagnostic expansion. Expansion of the country-specific AMR connectivity projects is plausible, but will depend on the products having greater utility than competitors.** The utility of these products beyond AMR mitigation improves their potential for long-term support through funding for health systems strengthening. However, the assumption that developing and demonstrating these digital connectivity standards will

stimulate diagnostic markets, and therefore provide development incentives, needs to be demonstrated and will require considerable time and expansion of scope to fulfil.

As STI programmes in many countries overlap with those of sexual and reproductive health and HIV/AIDS, the potential for funding support for completing the STI diagnostic development and implementation is high. The DCN lateral flow antigen assay has yet to enter clinical trials but addresses a significant diagnostic gap that will increase in importance with the launch of Zoliflodacin. The MOU between FIND, GARDP, and WHO and the market assessments conducted with GAMRIF support increase the plausibility of successful market entry.

As the drug-resistant gonorrhoea test will not be ready for market until well after the end of this GAMRIF funding period, a decision needs to be made on whether to:

5. Continue funding of current assay development;
6. Hand off the current projects and concentrate on assays for a new AMR-relevant area (e.g. sepsis);
7. Fund downstream priorities to increase use of current relevant assays and avoid direct product development investment given the timelines and risks involved.

A review of these alternatives with stakeholders would be an important step. This should take into account the likely market entry of the product after the Zoliflodacin launch, and plan accordingly.

Other diagnostic product development priorities considered by informants relevant to AMR included neonatal and adult sepsis. This included pathogen identification and/or distinguishing bacterial infection from other pathology. Some candidates for the latter, including those competing for the Nesta Longitude prize,[25] may benefit from investment in adaption to LMICs, and are likely to require downstream support to scale.

There is an opportunity for GAMRIF to follow through with the AMR connectivity applications and demonstrate impact on metrics relevant to AMR. This could include exploration of avenues to improve sustainability through health system integration with programmes of other downstream funders, including the Global Fund and Africa CDC. An expansion of approach towards identifying and addressing policy and regulatory-level inhibitors to roll-out of AMR-relevant diagnostics was also recommended in some KIIs, based on a perception of inadequate progress in removing barriers and addressing reasons for market failure. It was considered that GAMRIF, as a government-based body with the reputation and convening power of DHSC behind it, was well-placed to address these. Reducing such barriers would improve potential for scaling and accessibility of future products.

[25] https://www.nesta.org.uk/project/longitude-prize/.

Summary details

Type: Product Development Partnership

Aim: To mobilise resources and partners to develop new and improved treatments for drug-resistant infections which pose the greatest threat to health and make those treatments sustainably and responsibly available to every person who needs them.

Duration: 2018-2022

GAMRIF funding: GBP 7 million (GBP 6 million STI programme; GBP 1 million core funding)

Leverage: Not quantified in annual reporting*

Number of projects: 4

Implementing partners: GARDP

Other partners: GARDP has also received funding from the Wellcome Trust, BMGF, MSF and several G7 governments and the UK National Institute for Health Research (NIHR)

* *Although it is noted that the multi-funder model allows GAMRIF to support Phase III*

3.6 Work Package 6: Global Antibiotic Research and Development Partnership (GARDP)

3.6.1 Relevance and coherence

Under Question 1, our theory is that GARDP is targeting priority AMR needs (relevance), filling gaps in the activity of other funders involved in existing AMR R&D efforts (coherence), and that GAMRIF offers distinctive added value as a funder to GARDP.

GARDP's R&D focus is strategic – targeting drug-resistant infections that pose the greatest threat to global health, in alignment with needs identified in global consensus documents and with market bottlenecks identified in the 2016 O'Neill Review on AMR[26]. While public funding is available in the form of 'push' incentives for early-stage research through grants and seed funding, there has been a financing gap for late-stage clinical phases and post-approval expansion of indications, which are the most expensive stages of R&D. It is even more difficult to secure financing when R&D targets LMIC-specific needs, where burden of resistance is highest but purchasing power is low. Drug-resistant gonorrhoea and neonatal sepsis provide examples where industry is least likely to be interested, as they are commercially weak areas, and hence they are the primary focus of GARDP's R&D efforts.

Created by the WHO and Drugs for Neglected Diseases initiative (DNDi), GARDP is now an independent NGO with headquarters in Geneva. GARDP's strategic plan, which it is predicted will cost USD 500 million to implement, aims to develop and deliver up to five new antibiotics by 2025 through improvement of existing drugs and development of new chemical entities. Of the USD 500 million required, only USD 100 million has so far been raised. GARDP has dealt with this pragmatically, raising the bar on the criteria for portfolio inclusion, as assessed by GARDP's scientific advisory committee, key opinion leaders, WHO, and GARDP's own team. A GARDP candidate must be especially relevant to meeting priority LMIC needs – providing good Gram-negative coverage, having the potential for paediatric/neonatal development, and with high likelihood of agreeing a suitable stewardship and access framework with the developer. Consequently, the main focus is on antibiotics for neonatal sepsis, STIs, and a Phase III late-stage asset, Cefiderocol, involving Shionogi and the Clinton Health Access Initiative (CHAI), where GARDP will contribute to securing paediatric indications as well as early access work.

Funding from GAMRIF goes towards four STI activities specific to R&D of Zoliflodacin, an antibiotic principally for patients in LMICs, where the burden of drug-resistant gonorrhoea is highest, underpinned by access strategies for LMICs. The activities focus on optimising Zoliflodacin formulation and decreasing the cost of goods; supporting registration and commercialisation of Zoliflodacin in target countries; investigating the possibility of combining Zoliflodacin with other existing antibiotics; and informing policy change and ensuring sustainable access. Under core funding to GARDP, GAMRIF also funds cross-cutting activities, and through this, GAMRIF is supporting GARDP's work on serious bacterial infections and neonatal sepsis.

The stage of the pipeline GARDP addresses and the LMIC focus also addresses a priority gap and is synergistic with other initiatives. GARDP's R&D pipeline scope covers clinical trials to licensure as well as commercialisation, access, and post-licensure studies. GARDP therefore has the potential to complement CARB-X, providing a path to market for promising

[26] O'Neill Review on AMR 2016, DRIVE-AB Report

CARB-X graduates that are appropriate for LMIC markets (see Figure 3). GARDP is already positioning to support two CARB-X candidates once they're ready for clinical trials, having signed MOUs and being in the process of conducting further due diligence. GARDP is also collaborating with BARDA. GARDP is funding certain elements and collaborating on design of the trials, while CARB-X is funding BARDA-focused elements. GARDP aims to work in concert with the AMR Action Fund in the same way – bringing the network of LMIC trial sites, working with regulators including the Indian Council of Medical Research and South African Medical Research Council, working on post-regulatory additional indications, and ensuring stewardship and access through the market entry and commercialisation strategy.

Similarly, GARDP has a diagnostic-focused strategic partnership with FIND and WHO, starting with STIs, based on a shared philosophy to determine which shared approaches and data are needed to develop AMR interventions and have them used appropriately. GAMRIF has been instrumental in spurring on GARDP and FIND's collaboration in drug-resistant gonorrhoea, funding FIND to work on diagnostics to identify the presence of drug-resistant gonorrhoea in synergy with GARDP's therapeutic work. Plans to leverage that collaboration further are already beginning, with surveillance programmes being conducted in South Africa to understand not only incidence of gonorrhoea, but also the level of resistance to standard of care antibiotics.

In its strategy, GARDP also includes expansion into earlier discovery, as well as downstream policy-influencing work. Although GARDP KIs state that the emphasis and funding required for these areas is minimal (5% of the total budget), the relevance, coherence, and comparative advantage for such expansion would need to be further justified in the context of remaining funding needs to deliver the core clinical development portfolio.

GAMRIF's funding to GARDP could not otherwise be provided by domestic science funders, which would miss an opportunity to fund the best research in the best locations, and also would not be commercially attractive to industry funding. In the AMR space, it is common for early-stage R&D funding to come from domestic Ministries of Research, while funding for domestic institutions and late-stage R&D funding would normally come from industry, if there is a prospect of commercial returns. GAMRIF is different from domestic science funders, because funding can go to the best science, regardless of location. This is important in late-stage R&D because clinical trial sites in LMICs are needed, where patients with antibiotic-resistant infections are concentrated; it is critical for getting treatment to those who need it most, as well as accelerating trial enrolment, guideline development, and early access. AMR in LMICs must be addressed if the global AMR problem is to be effectively tackled.

GAMRIF adds value to GARDP in several ways. It has been credited as a catalyst to GARDP taking a more integrated (diagnostic and treatment) approach to STIs, and to supporting commercialisation and uptake potential. Although there were already links between GARDP and FIND, GAMRIF's funding of the gonorrhoea diagnostic and therapeutic work has influenced thinking about joint diagnostic and treatment approaches to deployment in LMICs. GAMRIF has also been credited with funding the pathway to access much more holistically – not just supporting the R&D Phases 1–3, but funding GARDP to work to secure third party manufacturing with an LMIC-based manufacturer.

GARDP is important to GAMRIF's portfolio, offering portfolio risk diversification via nearer-to-market products, providing visibility of the entire R&D pipeline opportunities and challenges for AMR therapeutics, and validation of the PDP model as part of the global solution to the market failure in antibiotic R&D. The GAMRIF EAB's initial guidance, related to the most ODA-relevant and significantly under-funded areas, steered GAMRIF towards earlier stage R&D for preventives and non-traditionals, rather than clinical trials for small-molecule antibiotics. Therefore, GARDP was not initially prioritised in the GAMRIF business case. However, due to the influence of other important AMR stakeholders, and GAMRIF's experience of working with GARDP after the initial seed funding/twelve-month project, GAMRIF's position on GARDP evolved. There are several reasons why GAMRIF's funding to GARDP makes strategic sense. GARDP offers an important test of the value of a non-profit/PDP model providing 'push' funding in the AMR R&D space, as opposed to leaving late-stage R&D entirely to industry or BARDA/US-focused funders. GARDP's work is directly LMIC/ODA relevant and, given it funds later stage R&D compared to CARB-X, it offers good diversification (higher likelihood of a near-term 'win') to the GAMRIF portfolio, as well as good synergy/coherence and learning opportunities from having visibility of the different stages of R&D for AMR-relevant products.

3.6.2 Effectiveness (intermediate results) and efficiency

With reference to the ToC and what we were testing under Question 2, our theory is that GARDP is effectively and efficiently able to identify candidates with the best potential and facilitate clinical evaluation, licensure, as well as stewardship and access, that strategic partnerships would result in leveraged funding, and that additional funders would make the overall programme of work possible.

GARDP has leveraged technical partnerships and shared resources to enable more efficient and effective working. As a spin-out from DNDi, there has been organisational and technical collaboration between DNDi and GARDP, with GARDP leveraging DNDi platforms, services, and skills for greater efficiency and effectiveness. For example, the two organisations are building a shared platform and hiring individuals to work across both organisations on chemistry manufacturing and control (CMC). Legal expertise has been shared, and GARDP has learned from DNDi on post-regulatory access challenges and the approaches beyond regulatory approval required for certain countries. GARDP has leveraged DNDi's expertise in medicinal chemistry, and has benefitted from DNDi's footprint in certain countries, as well as their regional office set up. Industry hires, expert advisors, and WHO links ensure that GARDP has the right expertise to facilitate progression through clinical evaluation, licensure, and commercialisation.

GARDP's clinical trial approach, commercialisation and regulatory strategy – running trials in high burden countries, working with regulators in South Africa, Thailand, and India – helps with efficiency and accelerated clinical trial enrolment, and working with key opinion leaders and regulators in high burden countries. This can be expected to facilitate eventual stewardship and scale up once the product is licensed. GARDP has built on pre-existing networks specialising in infectious disease and paediatric trials, and is building up their proficiency through doing studies, both diagnostic and drug development. GARDP's commercialisation strategy, which focuses on lowering cost of goods through improved synthesis pathways and third-party manufacturing, can be expected to support initial uptake and scale up.

Interim results are promising. GARDP has two products in Phase III clinical trials, and has just received a license for Cefiderocol, which – in partnership with Shionogi and CHAI – will allow it to expand access to this antibiotic in LMICs. According to the most recent reporting to GAMRIF (March 2021), project reporting results are on track, with most indicators coded as green (achieved), with a few coded yellow mostly due to COVID-19-related delays. DHSC is the only GARDP funder who requires reporting against a logframe format. However, this is not onerous for the GARDP delivery team, since all the logframe indicators are tracked within the Action Plan, so the content is already tracked within GARDP's own monitoring tool. These interim results are being achieved, even despite, as noted earlier, the budget falling far short of the finance required to fulfil the priority projects GARDP could be contributing to, if its strategy were fully funded.

GARDP's results have been made possible due to multiple funders supporting the overall programme of work and the further harnessing of strategic partnerships, which are important tests of new ways of working. As mentioned, the multi-funder PDP model allows GAMRIF to support Phase III trials that would be too costly to fund alone. Also, GARDP's FIND/WHO collaboration supported by GAMRIF has potential as a way forward for treatment and diagnostic synergy and consolidation around key syndromes. GARDP's emerging partnerships with BARDA and the AMR Action Fund have potential to be further leveraged as a hybrid financing/development model.

3.6.3 Impact and sustainability

Under Question 3, our theory is that market entry, use, and health impact of GAMRIF investments in GARDP will be supported by an improved R&D ecosystem, operationalisation of provisions in S&A agreements, and stronger in-country health systems for managing use and conservation of new AMR technologies.

The plausibility that GARDP's interim results will translate to longer term outcomes and impact is heightened by GARDP's approach to clinical trials and regulatory and commercialisation strategy which, as mentioned under EQ 2, is supportive of access and sustainability. GARDP's access strategy was developed with wide consultation, including key actors such as the Medicines Patent Pool. Its operationalisation will be tested for the first time with the drug-resistant gonorrhoea product, for which GARDP will have the license to control the pricing and manufacturing strategy in key LMIC markets, including key middle-income resistance hotspot countries.

Another issue to be addressed in order to ultimately have health impact is that of securing third-party manufacturers and market authorisation holders for small volume antibiotic markets. GARDP is working with CHAI, WHO, and UNICEF to further develop a concept called 'SECURE' – a commercial model which would enable small volumes to be manufactured and deployed. Some options being explored include 'pull' incentives, a limited access model based on a regulatory process with partial/limited reimbursement or contracting for manufacturing a portfolio of products and for multiple territories, in order to make small volumes commercially attractive.

GARDP's work has the potential to make the overall R&D ecosystem more efficient, paving the way for other development efforts. GARDP's access strategy, as well as work GARDP is doing to address commercialisation, has the potential to be leveraged for other products, as other new antibiotics face the same problems. The development of clinical trial networks has the potential to be leveraged by others, enabling faster trial enrolment, reducing development costs and time.

However, the initial health impact of Zoliflodacin may be limited by health system deficiencies and the availability of diagnostic tests to guide treatment decisions. Ideally there would be a POC test to detect resistance to ceftriaxone; at present, there are only tests to look at susceptibility once there is clinical failure, and these tests are rarely used. Zoliflodacin is therefore likely to be used only in special populations where there is known resistance issues to standard of care antibiotics, or with partners who need expedited oral treatment over intramuscular ceftriaxone. The collaboration with FIND intends to address diagnostic needs regarding POCs drug-resistant gonorrhoea detection (but not antibiotic susceptibility), but, as mentioned under WP 5, the timing may not coincide with Zoliflodacin's launch.

To complete this work and bring these products to market, further funding is needed. Clinical development is the most resource-intensive phase of product development, and GAMRIF's funding alone will be insufficient to assure the outcome is achieved.

3.7 Work Package 7: BactiVac

Summary details

Type: Global initiative

Aim: Tackle AMR in humans and animals by accelerating the development of vaccines against bacterial infections relevant to LMICs

Duration: February 2019 - ongoing

GAMRIF funding: GBP 1 million for Rounds 1 + 2; GBP 400,000 for Round 5

Leverage: GBP 554,127 ; GBP 5.6 million in follow-on funding

Number of projects: 27 (of 40) projects funded by GAMRIF

Implementing Partners: BactiVac, led out of the University of Birmingham

Other partners: GAMRIF added to existing funding from the Medical Research Council (MRC) and BBSRC

3.7.1 Relevance and coherence

Under Question 1, our theory is that BactiVac is targeting priority AMR needs that are aligned with GAMRIF's intended outcomes (relevance), filling a key gap in bacterial vaccine development and related activities of other funders involved in existing AMR R&D efforts (coherence), and that GAMRIF offers distinctive value-add as an efficient, collaborative, and flexible funder.

The intended impacts of BactiVac are aligned with GAMRIF's aims to prevent and reduce likelihood of public health emergencies and early detection of threats in LMICs, with focus on under-funded/neglected R&D areas. These impacts include reduction in disease burden in humans and animals, encouraging greater investment in bacterial vaccines in LMICs, expanding LMICs' vaccine manufacturing capacity, and building vaccine R&D capacity. The funding of BactiVac directly responds to gaps identified during the establishment of GAMRIF funding for the CARB-X and InnoVet-AMR programmes, addressing the limited pipeline of early-stage vaccine projects and paucity of collaborations between researchers in LMICs and HICs in AMR research. Cross-collaboration between academic and industrial partners, which appears to be resulting in successful knowledge transfer and exchange, aims to attract wider membership (and potential funding) from other fields. New vaccines are needed to tackle a range of diseases, but progress is hindered by technical hurdles and market failures.

The involvement of GAMRIF in BactiVac brought advantages beyond the added funding alone. Both delivery partner and grantee KIIs highlighted the benefits of GAMRIF's 'nimble' and 'non-onerous' funding, which has encouraged the BactiVac network to focus more on AMR and more specifically embedded strong ODA processes into operational ways of working. This has included direct support from DHSC to the BactiVac management. The requirement to include an ODA statement to secure GAMRIF funding was beneficial not only for smoother delivery of GAMRIF funded projects and helpful oversight by DHSC, but benefitted the projects being delivered through core funding from the Global Challenges Research Fund (GCRF) in the Vaccines Research and Development Competition (co-funded by MRC and BBSRC).

In addition to its ODA-focused delivery, GAMRIF is perceived by KIs to have a strong network, flexibility, and good governance processes already in place, which has created a 'win-win' relationship for BactiVac. It was compared favourably in KIIs to larger funders, such as Wellcome Trust or NIHR (National Institute for Health Research), due to its ability to fund projects in their infancy. BactiVac bring their own network of experts and what they call 'organisational nimbleness' and 'rapid solutions', while GAMRIF adds 'linked up thinking' (to add AMR to BactiVac grantee aims) and its delivery model covering multiple partnerships and support mechanisms for product development. Sustainable partnerships are being created between involved universities and other grantees, for example, through participation in annual meetings and links created through the research grants themselves. While funding over six months would be considered beneficial from grantees' perspective, the limits of GAMRIF's size and scope are recognised; it is structured to be a helpful 'springboard' for LMIC-based organisations that provide longer-term funding.

KI responses included recommendations for expansion of GAMRIF scope. While GAMRIF funding has been important in supplying the finance to allow industry partnerships to go forward, industry partners tend to be focused on licensing of specific products, and have limited engagement in wider AMR issues. GAMRIF could therefore work more closely with industry partners who are dealing with regulatory bodies to bridge the gap between academia and industry, ensuring early industry engagement early in the R&D pipeline. Suggestions from KIs for research foci included areas beyond vaccine

development, including immune modulators and microbial interventions to modify susceptibility to certain pathogens. It is noted that GAMRIF addresses these areas under other Work Packages.

3.7.2 Effectiveness (intermediate results) and efficiency

Referring back to the ToC and what we were testing under Question 2, our theory is that BactiVac is effectively and efficiently able to identify candidates with the best potential and undertake early product development, and that outcomes would result in leveraged funding, and additional funders would take promising product candidates onward to eventual market entry.

GAMRIF added to an already well-evolved grant management process. Prior to GAMRIF funding, BactiVac had a robust assessment process in place determining grant selection, including assessment criteria to ensure projects were ODA eligible. 21 oversight board members were involved in final project selection, and a process was in place to investigate why some research entities do not apply. GAMRIF became directly involved with BactiVac relatively late into programming, so these systems and processes that underpin the delivery of catalyst calls, and mechanisms to disseminate and promote outputs, were in place or in development at the time of the initial round of GAMRIF funding. Details of all funded catalyst projects are published on the BactiVac website, including a non-confidential project summary and project outcomes.

All 17 projects from the first rounds of catalyst funding which GAMRIF supported achieved their final milestones on schedule or within the period of agreed no-cost extensions, and reports on each were published by mid-2021. Interim progress was monitored by collecting data for each catalyst project at point of application, via interim and final reporting, and via annual follow up requests for data collected via the online database, ResearchFish[27]. BactiVac recorded 4 publications, 11 industry collaborations, and 20 other collaborations arising from the programme. A further 10 projects were mid-way at the time of this evaluation and completed in March 2022.

In terms of VfM, a relatively low level of GAMRIF funding was able to support a high number of projects. By adding funding to a pre-existing programme with grant-making structures and oversight already in place, GAMRIF was able to add a focus on AMR in LMICs without the overheads required to create a new management structure. It also promoted improved ODA-compatible reporting and awareness, enhancing the potential for further activity relevant to this sector. Funding leveraged by the 17 projects represented an additional 61% of funding compared to the original awarded value, expanding its impact.

There is potential for GAMRIF to improve cross-funding collaboration and synergies. KIIs with BactiVac grantees showed that they are not well aware of other projects and networks being funded through GAMRIF. Some opportunities have already arisen to target such collaborations, such as CARB-X presenting at BactiVac's organisational meetings (KII). However, further potential opportunities for improving collaboration/synergies are apparent, particularly where there are overlaps in R&D funding (e.g InnoVet-AMR) or where one organisation potentially would hand off development to another (BactiVac grantees might go on to apply for CARB-X funding, for example).

3.7.3 Impact and sustainability

Under Question 3, our theory is that market entry, use, and health impact of GAMRIF investments in BactiVac will be supported by an improved R&D ecosystem, operationalisation of provisions in S&A agreements, and stronger in-country health systems for managing use and conservation of new AMR technologies.

The BactiVac programme has achieved good plausibility of impact through vaccine candidates progressing further along the pipeline to commercialisation and market. The combination of GAMRIF funding and DHSC support, and support of the pre-existing programme, has successfully taken 17 projects to completion. KIs reported support for developing skills in epidemiology, disease biology, and clinical trials that will serve ODA requirements for capacity-building, with 48% of BactiVac's 1,200 members being based in LMICs. KIs noted continued support from BactiVac to address bureaucratic

[27] ResearchFish is an online database for research funders, charities, research organisations, and research centres to collect impact-related data to advocate research and inform funding strategies. https://researchfish.com/

hurdles of the product development pipeline, and GBP 5.6 million of follow-on funding has been leveraged by projects thus far from further development partners, including CARB-X.

GAMRIF's funding to WP 7 has created unique opportunities for researchers in LMICs to advance research that may not have otherwise been funded by other donors or industry. While it is too early in the research process to assess ultimate health impact, the programme has created an opportunity for research grantees to progress potential solutions that are uniquely tailored to LMIC health systems delivery contexts. Projects have included LMIC-led projects (e.g Brazil, Gambia, South Africa), projects with LMIC co-applicants (including from Brazil, Nicaragua, Mexico, India, South Africa, Gambia, Democratic Republic of Congo, Madagascar, and Vietnam) and industry co-applicants. On a practical level, both the data generated from BactiVac's research and building capacity around ODA eligibility processes may have a positive longer-term impact on expanding investment to LMIC bacterial vaccine development, through improved use of research and data-management tools, and experience in building business cases for future funding. Furthermore, the capacity building support or 'oversight' by BactiVac, including the ODA requirements required by GAMRIF, has stimulated the development of more regular feedback loops to ensure applications are ready for scientific review, as well as meeting international administrative and bureaucratic processes to achieve follow-on funding.

BactiVac's network and advocacy have a continuing important role to play in communicating the need for vaccine development for LMICs to address AMR pressure. Limited funding has been a notable barrier in the development of bacterial vaccines due to limited commercial drivers or incentives for private companies. This is exacerbated when tailoring a vaccine candidate to LMIC needs. Building on the experience with GAMRIF and bridging the gap between academia and industry will be important to translate this into action.

3.8 Portfolio level performance and lessons learned

3.8.1 Relevance and coherence

There is good evidence that GAMRIF supports work which is highly relevant to AMR priority needs as identified in global consensus documents and previous expert analyses, fulfilling the requirements set out by the EAB and the business case. A ToC was developed at the commencement of GAMRIF to inform choices about projects that would contribute to achievement of outcomes and impact. The EAB gave a clear strategic steer that the programme should focus on under-funded and otherwise neglected R&D needs, addressing AMR across human, animal, and environmental dimensions (One Health), to the benefit of LMICs. The GAMRIF business case was subsequently developed in alignment with this steer. Choice of investments was also geared towards leveraging funding from other partners.

Among the large-scale funds supporting R&D to address AMR, GAMRIF uniquely directs that support towards LMIC needs, and this has placed the UK in an active leadership role in supporting transnational AMR R&D efforts. Other government agencies and foundations have subsequently joined GAMRIF in this focus, including the governments of Denmark, Canada, Argentina, and China, and BMGF. Stronger diplomatic relationships were built, extending beyond AMR and research collaboration. Under-funded areas have been targeted, addressing the limited size and diversity of the current pipeline of vaccine projects to tackle AMR; discovery and pre-clinical research on other alternatives to antibiotics in the human and animal health space; and late-stage clinical phases and post-approval expansion of indications for therapeutics targeting LMIC needs.

GAMRIF's unique positioning within UK AMR funding bodies includes an ability to fund across One Health dimensions, in alignment with GAP priorities; an ability to fund industry partnerships focused on delivering tangible innovations; an ability to fund transnational groups who can support the best solutions globally; and prioritisation of benefits to people in LMICs. Some of the Work Packages are solely focused on LMIC needs (e.g GARDP), while others (e.g CARB-X) have benefitted from LMIC-focused portfolio steering and shaping by GAMRIF, ultimately leveraging a much larger pool of funds towards GAMRIF objectives. In the Zambia One Health Middleware Project the five projects funded through WP 4 consider the social and economic drivers of AMR, and are thus meeting the need to frame One Health issues beyond the microbiological angle. The One Health middleware development under WP 5 with the ZPHRL is unique in its ability to bring animal and human AMR data together, and sets an important model to drive similar innovation in other countries.

Complementarity with other funders has been achieved through initial mapping and ongoing mechanisms for coordination. Alignment and synergy with other AMR funders is ensured through DHSC's representation on WP oversight committees and participation in global coordination groups, such as Global AMR R&D Hub and through UK colleagues representing the UK on steering or funding committees of JPIAMR and the International Research Consortium on Animal Health (STAR-IDAZ). Additionally, the GAMRIF delivery team worked closely with the Research and Evidence Division (RED) in the UK Foreign, Commonwealth and Development Office (FCDO) to ensure synergy in PDP funding. Similarly, the Fleming Fund country-focused work was mapped to understand the gaps and safeguard against replicating work that is already funded. MRC and GAMRIF-funded activities in China were well aligned in terms of their call timelines and content complementarity. Ongoing coherence and synergy of UK-funded work (for example, alignment with National Institute for Health Research (NIHR)/Global Health research (GHR) programme and the UK Vaccine Network) is ensured, partly through cross-Government meetings. However, some stakeholders did suggest that GAMRIF needs to better communicate its unique positioning – how it links to Fleming Fund's downstream work (outside of R&D) on behaviour change and health systems; with UK science funders' upstream research funding; and with the UK R&D incentives promoted by the use of procurement as a 'pull' lever; and how GAMRIF adds value when it is a small co-funder of larger Work Packages funded by many donors. In animal health/livelihoods, GAMRIF's work through IDRC, China and Argentina has supported work that would not otherwise have received support, enriching the global knowledge base and product pipeline, and complementing other mechanisms, such as the Tripartite group (WHO, OIE, FAO), that are more involved with global policy and country-level delivery.

In terms of ensuring relevance and coherence in the choice of investments going forward, the GAMRIF management and external governance structure will no doubt be considering what criteria to apply should funding be agreed for GAMRIF

2.0. It is clear that GAMRIF have notably enriched the global pipeline, and are documented as the single largest funder of animal-focused R&D in the Global AMR R&D Hub's dynamic dashboard. However, two themes have arisen when looking across the portfolio, which are suggested as appropriate areas for further reflection and consultation – i) portfolio breadth vs. focus, and ii) risk appetite.

Considering breadth vs. focus across the portfolio, the current GAMRIF portfolio is indeed very broad, and this brings opportunities as well as challenges. The current portfolio supports work that is:

- Cutting across One Health dimensions (human, animal, environment);
- Covering a range of technology types – diagnostics, antibiotics, vaccines, non-traditional alternatives to antibiotics;
- Spanning the entire R&D ecosystem from basic science/discovery (e.g some of BactiVac's portfolio) to late-stage R&D and commercialisation (GARDP);
- Supporting innovation targeted at tangible products vs. those targeted at influencing policy, practice and behaviours.

While all projects should be designed to have applicability beyond the countries in which activities are taking place, some projects are trans-national, and others focus on science being delivered through bilateral partnerships (UK-Argentina or UK-China).

The opportunities of a broad portfolio may include:

- Portfolio diversification can mean there is statistically a better chance of backing a winner;
- Better chance for the UK Government to influence widely across One Health, technology types, stages of R&D pipeline, product vs. policy, and practice focus;
- Broad portfolio eligibility may allow projects to be added subsequently to respond to new technology, funding or political opportunities;
- Breadth across One Health enables GAMRIF to support the full spectrum of AMR research across multiple dimensions; and
- Breadth avoids reliance/risk for fewer delivery partners to achieve the programme's results and utilise the budget, to meet ODA spending targets.
- Breadth enabled a new fund to explore/test different AMR innovation challenges and work with a wide range of delivery partners. It could be argued that not narrowing down too soon and 'letting 100 flowers bloom' might be better for fostering innovation.

The challenges of a broad portfolio may include:

- Funding to individual projects may be sub-critical to produce a step-change towards results, and/or GAMRIF may have less opportunity to influence "deeply" by providing a higher percentage of the project's total funds and specialising in more focused areas. Opportunities for sharing of learning, deeper collaboration, or synchronisation, coherence and synergies between grantees may be limited by too diverse a portfolio – e.g enabling portfolio level lessons learned and 'sum greater than parts'.
- The size of the portfolio has implications for team size, skills, and managerial efficiency, requiring the team to stay abreast of a wide range of innovation content areas, develop wide networks across many government departments, other funding agencies, and One Health experts
- Managing multiple delivery partners may be challenging each with their own particularities e.g in financial systems and reporting standards.
- Opportunities for sharing of learning, deeper collaboration, or synchronisation, coherence and synergies between grantees may be limited by too diverse a portfolio – e.g enabling portfolio level lessons learned and 'sum greater than parts'.

There may be an opportunity to increase programme effectiveness in a potential GAMRIF 2.0 through further strengthening and communicating linkages and synergies between Work Packages. The GAMRIF programme was not designed at the outset to be a tightly coordinated and interconnected set of activities, other than through their culmination in two ultimate and quite broad impact level objectives (1. Prevention and reduction of the likelihood of public health emergencies such as outbreaks and AMR, and 2. Early detection of threats in LMICs to save lives). The GAMRIF delivery team has however taken opportunities where possible to identify linkages within and between portfolios, e.g FIND and GARDP's work on drug-resistant gonorrhoea and BactiVac/CARB-X's S&A guidance for CARB-X and eliciting expertise from GARDP. As the GAMRIF programme matures, there may be an opportunity to leverage further synergies and linkages (meaning its contribution is greater than the sum of its parts) and to communicate the programme's strategic narrative and fit within the wider UK AMR effort.

GAMRIF has funded high risk/high reward projects activities, as called for by its business case. Future funding may present an opportunity to focus in on particularly promising areas and to see some of these areas through to achieving impact. A second area for reflection going forward is the level of risk tolerance of the portfolio. This is linked to the types of innovations funded, their stage in the development pipeline, and the maturity/health of the larger ecosystem for translating the research into products, policies and practices and ultimately health impact. This theme arose under WP 2, where GAMRIF selection within the CARB-X portfolio has resulted in funding relatively costly and riskier (non-traditional) product candidates, the latter with a less clear regulatory and clinical pathway to market. It also arose under Work Packages 3 and 4, which identified that the ecosystem to scale/translate the research to behaviour changes/impact is relatively under-developed and requires a different, socio-economic justification rather than the more traditional microbiological and One Health framing; this may result in the research being published in a journal with less reach or impact, rather than having substantial impact. In the context of the risk appetite set out in the business case, which called for funding high risk/high reward R&D, GAMRIF has achieved this aim. A key consideration for a potential GAMRIF 2.0 is the degree of risk tolerance appropriate for future funding. Funding more exploratory high-risk work and/or without a healthy ecosystem for translation to impact vs funding projects where GAMRIF - given its level of funding and influence – can more likely contribute to nearer-term product delivery and/or changes in policy and practice.

3.8.2 Effectiveness (intermediate results) and efficiency

Documentary and KI evidence suggests that the management of GAMRIF's overall portfolio was effective and efficient, and a considerable amount of work was achieved within budget across a diverse portfolio and geography, and despite the interruptions of the COVID-19 response. Stakeholders praised the responsiveness and expertise of the GAMRIF delivery team, particularly their simultaneous management across seven Work Packages, good dialogue and flexibility in navigating the delays due to the COVID-19 response. GAMRIF's quick responses enabled delivery partners to be flexible and impactful themselves by virtue of being able to make prompt decisions about funding requirements.

GAMRIF chose delivery partners who had pre-existing relationships with grantees, collaborators (e.g CARB-X accelerators), and other funders., expertise, and systems for conducting a rigorous, competitive selection process and facilitating progression of grantees through the R&D process and facilitating dissemination and policy impact. The counterfactual might have been for DHSC to run these competitions themselves, on a project-by-project, reactive grant-funding basis. There is good evidence to show that GAMRIF has achieved greater effectiveness with the funds available by working through expert delivery partners instead.

Through the experience of managing the portfolio, the GAMRIF delivery team has learned about the delivery partners' ability to spend according to forecasted projections, to account for the money and to show results. There were delays to commissioning work within WP 1 (UK-China); this could leave the UK side vulnerable and create challenges for reporting at the end of GAMRIF. Differences in working culture across partners also led to delays and less efficient collaborations. Partners' ability to account for spending and report on its results differed as well; for example, Innovate UK has monitoring officers who perform a monitoring and accountability function whereas BBSRC is less accustomed to this way of working and was more challenged to meet government's M&E needs as well as predicable spend to forecasted budgets. Conversations with the GAMRIF delivery team have provided evidence that the GAMRIF delivery team is evolving its

approach to project selection and partner working, reflecting programme learning and the need to adapt to contexts and constraints.

The GAMRIF delivery team is involved in championing and influencing work which is not featured in the GAMRIF logframe or ToC; this may risk that the work is not fully captured as one of the levers or inputs into the change process. GAMRIF has been an essential part of pushing forward the R&D side of the O'Neill Review on AMR recommendations as well as commitments of the UK AMR National Action Plan[28]. Not only has GAMRIF funded early-stage research to fill the pipelines with AMR-relevant candidate technologies, but team members have also been involved with work to champion and influence antibiotic R&D ecosystems. For example, in light of GAMRIF's Team Leader having dual responsibility for GAMRIF and global AMR diplomacy to provide a 'bridge' between the two teams, work has been done to develop and agree with G7 countries, a set of principles designed to make market systems for antibiotics more sustainable[29]. Team members have worked to highlight and facilitate introductions to the NHS and NHS England and Improvement-led innovative antibiotic reimbursement project currently being trialled in England. As explained within each work package, there was important influencing work as well, to leverage new funding and shape the LMIC orientation of that investment. Although the GAMRIF delivery team acknowledges that GAMRIF was designed to leverage the R&D investments for soft power influence in AMR, and vice versa, to use soft power influence to make the most of the R&D investments, neither the logframe nor the ToC capture these levers and enablers as inputs into the results chain for GAMRIF. It would be appropriate to do so, especially considering that the UN's IACG framework for action on AMR explicitly refers not just to **content areas** (what needs to be done to tackle AMR) but also to **levers** (ways of addressing content areas) and **enablers** (preconditions needed to apply levers successfully).[30] The next refresh of GAMRIF's ToC might better situate GAMRIF within these global AMR frameworks and pick up not just on content areas (what to do) but also on ways that GAMRIF is working to achieve results.

Attempting to quantify VfM results of an early-stage research portfolio should not be a central focus, although there is merit in looking at VfM from a strategic perspective, and there have been intangible benefits to the R&D ecosystem derived from GAMRIF-supported-work. VfM measures being monitored by GAMRIF include counting the number of products that increase TRL levels and the amount of new or follow-on investments which have been leveraged. ODA funded programmes would normally use the 4E + S VfM framework (economy, efficiency, effectiveness, equity and sustainability), looking at quantitative metrics for each parameter. However, on an AMR R&D portfolio funding early-stage research, it would not be useful or credible to conduct such an exercise. Rather, it is more appropriate to talk about strategic VfM, at the WP as well as overall portfolio level, in terms of:

- allocative efficiency – did GAMRIF (and its delivery partners) fund the right activities and the right mix of activities?
- technical efficiency – was the (GAMRIF and the WP) portfolio managed well, turning the inputs into outputs in an efficient and effective way? and
- value/results – what sort of interim results were achieved and what is the likelihood of those results translating into sustainable outcomes and impact?

Those questions map very neatly onto our 3 principal EQs:

- EQ 1 is about strategic focus - has GAMRIF as a whole and within Work Packages focused on the right activities in terms of a) priority needs b) addressing gaps not well filled by others and c) aligned with comparative advantage and does the overall mix of activities produce a "sum greater than parts" - this is allocative efficiency
- EQ 2 is about how well the GAMRIF portfolio and the Work Packages were managed - this is technical efficiency
- EQ 3 is about interim results and the prospect of their sustainability, which is the value part of the equation

In previous sections, we have answered these questions at the WP level, while there are a few additional points to add when looking at VfM/effectiveness and efficiency at a portfolio level. One observation is that there are many intangible - not readily quantifiable - benefits to the entire R&D ecosystem, derived from GAMRIF's work. The development of TPPs

[28] O'Neill Review on AMR 2016, DRIVE-AB Report
[29] See page 7: https://ec.europa.eu/health/sites/default/files/antimicrobial_resistance/docs/amr_ev_20190312_co05c_en.pdf

and diagnostic market assessments provide a basis for further funders to justify involvement in this area. Similarly, the strengthening of clinical trial sites through GARDP and the development of stewardship and access provisions through CARB-X and GARDP improves the entire R&D ecosystem, of benefit to all funders and supportive of health impact. The research partnership-building activities supported through the bilateral programmes, and strengthened diplomatic ties, may produce continued future value. As the portfolio matures and products get closer to market, it may become more credible to quantify the anticipated health benefits or monetary savings from introducing improved AMR technologies.

3.8.3 Impact and sustainability

Here we present the findings from the Contribution Analysis at the overall portfolio level by output and then outcome, followed by a table summarising the gradings across all Work Packages. Outputs and outcomes were assessed against two criteria - the plausibility of whether the result has been/will be delivered ('CA'), and the strength of supporting evidence from the evaluation. We used a five-point scale for the assessment, whereby 1 denotes very weak plausibility or evidence, and 5 very strong plausibility or evidence. Further detail on the Contribution Analysis, by WP, is included in Annex 3.

GAMRIF plausibility of contribution to outputs

Output 1: "Encouragement of international partners to research innovative concepts tackling AMR in LMICs"

Contribution Analysis (CA) score: 5
Strength of Evidence (SoE) score: 5

Output 1: The plausibility of GAMRIF's investment contributing to the outcome "Encouragement of international partners to research innovative concepts tackling AMR in LMICs" was graded as high across all Work Packages, given the additional funding that was leveraged and the value-add GAMRIF has provided in shaping that investment towards LMIC needs. Across the 7 Work Packages, a significant volume of quality work has been funded. Evidence is being generated and disseminated and promising technology candidates are progressing through R&D pipelines, although some of the final outputs and outcomes will still take time to be delivered. Many of the partnerships established are likely to continue. The strength of evidence for this is high, given the strong collaborations established, and well-functioning relationships with delivery partners and sub-grantees reaching across national boundaries.

Although the impact of GAMIF's portfolio on AMR will be realised over the longer-term, there are several indications that suggest GAMRIF is contributing towards having a sustainable impact. Firstly, GAMRIF's work has both raised awareness about AMR issues and promoted new collaborations. For instance, GAMRIF has contributed to BBSRC and NERC expansion into antibiotics in agriculture and the environment, in partnership with other countries. GAMRIF has similarly promoted sustainable partnerships between academic institutions. It has brought people together, connected academia with industry, and built new and better diplomatic relationships between countries as evidenced in WP 4 UK-Argentina. Finally, GAMRIF has leveraged funding from others and in line with its overarching ambition has steered that funding towards the needs of LMICs. In many cases, GAMRIF is providing more than funding - influencing the scope and scale of other funders' investments and the conversations around the table in terms of prioritisation of LMIC needs. These represent intangible benefits beyond the scope of the GAMRIF programme, which would be difficult to quantify.

Output 2: "High-quality research that aims to: Reduce the need for antibiotics through alternative medicines and vaccine development".

Contribution Analysis (CA) score:5
Strength of Evidence (SoE) score: 5

Output 2: The plausibility of contributing towards "High-quality research that aims to: Reduce the need for antibiotics through alternative medicines and vaccine development" is high at the overall portfolio level, with evidence of strong, independent and expert-advised processes for identifying promising antibiotic alternatives, candidates continuing in development in many of the Work Packages, with some showing early signs of efficacy. Strength of evidence for this conclusion is high. For CARB-X, however the relevance of the output focus itself is questioned. The research supported by CARB-X is high quality, but the assumption that riskier alternative medicines and costlier vaccines will reduce the need for antibiotics in LMICs and should be the primary focus of GAMRIF funding can be

questioned.[31] The strength of evidence for the AMR burden being disproportionately felt in LMICs has strengthened only recently with the work by IHME, so by consequence the strength of evidence to question the GAMRIF technology limitation is increased.

Output 3: "High-quality research that aims to: Reduce use of antibiotics in farming of food producing animals"

Contribution Analysis (CA) score: 4
Strength of Evidence (SoE) score: 5

Output 3: The plausibility of contributing towards "High-quality research that aims to: Reduce use of antibiotics in farming of food producing animals" is graded as medium-high at the overall portfolio level. This is a key aim of projects under WP 1, 3 and 4, and one project in WP 5. However, several factors may make achieving this output challenging: the relevance of research outputs beyond Argentina (to the rest of Latin America and other LMICs, given infrastructure requirements); the maturity of the WP 4 projects, since policy outputs must be produced and disseminated first; and for the Zambia One Health middleware project, data availability would need to translate into behaviour change to realise the output. Relevant WP 3 projects include adaptation of existing technologies (e.g nanobubbles in aquaculture) or of differing risk profile (feed additives/neutraceuticals, phages) and these projects need increased industry involvement for regulatory and commercialisation support in order to reduce the use of antibiotics in farming. All this research needs to demonstrate to industry and farmers how it will result in reduced costs or increased yield, in order to encourage reduced use of antibiotics. Strength of evidence for this conclusion is high.

Output 4: "High-quality research that aims to: Reduce the environmental pollution of resistant bacteria and antibiotics"

Contribution Analysis (CA) score: 3
Strength of Evidence (SoE) score: 4

Output 4: The plausibility of achieving "High-quality research that aims to: Reduce the environmental pollution of resistant bacteria and antibiotics" is graded medium at the overall portfolio level, as so few Work Packages focus on this output. This evaluation concluded that plausibility of contribution to this output is high, with strong evidence from the aquaculture/nanobubble project, but less evidence from others. WP 4's plausibility of contribution to this output was graded lower; as the focus was shifted early to animal health aspects due to Argentina's interests.

Output 5: "High-quality research that aims to: Improve the measurement of clinical data and its uptake into national level surveillance"

Contribution Analysis (CA) score: 3
Strength of Evidence (SoE) score: 3

Output 5: The plausibility of contributing to "High-quality research that aims to: Improve the measurement of clinical data and its uptake into national level surveillance" is graded as medium at the overall portfolio level, with only some sub-projects under Work Packages 3, 4 and 5 focused on this output. In WP 4, 3 of 5 projects are looking into establishing surveillance protocols/broad frameworks to understand AMR in animals and environment; however, it is not yet clear how this will be taken up at the national level at this stage. Policy outputs need to be produced and disseminated first. The AMR connectivity projects funded through WP 5 all have the potential to achieve output 5, as does improving drug-resistant gonorrhoea detection. The evidence for this conclusion was graded as medium, as evidence of national uptake as actionable data is produced is not yet clear.

[31] To clarify, this contrasts with the original EAB steer. As explained under WP 2, the technology scope limitation was not a proactive decision by GAMRIF but based upon an EAB recommendation to not fund direct-acting small molecules, since they attract the lion's share of a limited funding pot and therefore not prioritised as neglected and underfunded areas for GAMRIF.

GAMRIF plausibility of contribution to outcomes

Outcome 1: "International focus and funding in tackling AMR in LMICs research increased"

Contribution Analysis (CA) score: 5
Strength of Evidence (SoE) score: 5

Outcome 1: The plausibility of GAMRIF's investment contributing to the increase in "International focus and funding in tackling AMR in LMICs research" is high across the portfolio and the strength of evidence is high. – see also comments under Output 1. This outcome was achieved through: the engagement with IDRC, leveraging Canadian funding; engaging in bilateral partnerships with China and Argentina (although sustaining/translating research conducted under the bilateral partnerships will depend to a large degree on the continuing commitment of the Chinese and Argentinian government and partners as well as HMG's priorities in relation to these countries); through steering the CARB-X portfolio towards LMIC concerns including S&A guidance; through developing the capacity of LMIC-based clinical trials networks; and through fostering connections between LMIC academics and industry/UK partners. Strength of evidence for this conclusion is high.

Outcome 2: "Innovative solutions tested and moved up the TRL through the R&D pipeline"

Contribution Analysis (CA) score: 5
Strength of Evidence (SoE) score: 5

Outcome 2: The plausibility of contributing to "Innovative solutions tested and moved up the TRL through the R&D pipeline" is high across the portfolio, being graded as high for all Work Packages which contribute to this outcome. The right mix of activities are being funded and the delivery partners are delivering efficient and effective portfolio management and wrap-around support to product developers, producing good interim results. The strength of evidence for this conclusion is high.

Outcome 3: "Improved supply of appropriate and affordable products & tools for combatting AMR available to LMICs"

Contribution Analysis (CA) score: 5
Strength of Evidence (SoE) score: 5

Outcome 3: The plausibility of contributing to "Improved supply of appropriate and affordable products & tools for combatting AMR available to LMICs" is high for those products which make it to market. The research is high quality as graded by expert review panels. However, the likelihood of reaching the market is limited by the fact that the portfolio is largely early-stage, will experience high attrition rates and will require significant funding contributions by others. This has implications for GAMRIF's contributions to ultimately result in product market entry, use, health impact and savings. The ecosystem supporting development of other technologies is similarly challenged: reimbursement plans would need to change to promote use of diagnostics and incentivise development and the diagnostics would need to be rapid, accurate, cheap and easy to use if they are to deter unnecessary antibiotic consumption. Non-traditionals (e.g phages, microbiome) face an uncertain regulatory and clinical pathway, and vaccines are very costly to develop and are also challenged by incentives for investment and barriers to uptake. However, the plausibility is higher now than it was even a year ago, due to several recent positive developments in the ecosystem. GARDP's antibiotics candidates are later stage and therefore have a higher chance of resulting in product market entry, use, health impact and savings. There is still a need to secure manufacturing and market authorisation holder partners, determine other specifics of commercialisation including a complementary diagnostic strategy, and secure further funding.

Some of GAMRIF's partners have instituted stewardship and access contractual provisions which have set a new norm globally and are influencing the commercialisation strategies in LMIC geographies towards public health objectives. Even once new products are commercialised and available, funds for product uptake and health systems strengthening will be required due to the significantly different levels of resources and infrastructure in LMICs.

In animal health, the eventual relevance of the funded projects to AMR mitigation relies on i) assumptions that reduction in, and/or modification of, antibiotic use in animal health and farming practices will result in reduced pressure on AMR in human health, and will depend on ii) downstream challenges - implementation and supply lines for non-antibiotic interventions, and animal stewardship (such as environmental exposure, feed quality, zoning) and human behaviour

change - being addressed in the future. A risk to the eventual value added is the lack of emphasis on downstream coordination and knowledge-sharing.

Outcome 4: "Behaviour change in industry and clinical practice ion LMICs from research evidence into economic incentives and national policy; Food security evidence; Clinical practice pilot programmes"

Contribution Analysis (CA) score: 4
Strength of Evidence (SoE) score: 4

Outcome 4: The plausibility of contributing to "Behaviour change in industry and clinical practice in LMICs from research evidence into economic incentives and national policy; Food security evidence; Clinical practice pilot programmes" is graded as medium at the overall portfolio level. Ensuring that research can be translated into policy will require further programming activity and funding beyond GAMRIF 1.0. KIs acknowledged that publications alone will not change policies and practice; there needs to be dissemination activity to raise awareness and engagement of policy makers and/or users (e.g farmers) - in research formulation and implementation, and/or through the delivery of engaging workshops and seminars. As mentioned, the framing of One Health AMR issues as a socio-economic problem would also help raise awareness of and attention to research findings. The following observations on contribution to this outcome were made at the WP level.

- WP 1 noted that the choice of MoST as a partner reflects the research focus of the work; as the portfolio matures, GAMRIF may need to reflect on whether different or additional partners are needed, who can ensure health policy relevance and behaviour change.
- WP 2 is a "push" incentive which has increased the volume and quality of work at the pre-clinical and first stage. However, there are many other influences on economic incentives and national policy. We know CARB-X has created an economic incentive to engage in pre-clinical and early clinical work but influencing clinical practice is a long way off and more substantive industry behaviour change will require a mix of push and pull incentives as well as support to the enabling environment for AMR R&D, some aspects of which DHSC is working to influence, as noted earlier.
- WP 3 highlighted that increased industry interaction with products nearer to market would be needed to develop the commercialisation strategy, and to clear regulatory hurdles; increased focus will also be needed to demonstrate that interventions are beneficial to farmer incomes through efficiencies, cost-reduction or increased yield.
- WP 4 noted the need to frame the AMR problem as a socioeconomic issue, as opposed to maintaining focus on the microbiological linkages of humans, animals, and the environment. The social science component of the research under this WP has been recognised as very beneficial and is widely seen as the key to translating evidence into policy – including considering how evidence and tools can be used in LMICs.
- WP 5 noted that the projects have yet to demonstrate change or influence practice but could do so in the future.
- WP 6 observed that GARDP has focused on a few, targeted priority AMR needs in LMICs. Because of this narrow prioritisation and focus on LMICs, it cannot be expected to have wide economic incentive effects. Although within the narrow indications of neonatal sepsis and STIs, GARDP's work may indeed influence national policies, treatment algorithms and clinical practice. Even though GARDP's work is closer to market, influencing clinical practice is a long way off and more substantive industry behaviour change will require a mix of push and pull incentives extending beyond a few LMIC-targeted priority needs.
- WP 7 supports early-stage R&D so for the same reasons as WP 2, the plausibility of contribution to more downstream impact at this stage is graded as moderate.

Score	Descriptor
5	Highly plausible / Strong evidence
4	Plausible / Moderate evidence
3	Somewhat plausible / Weak evidence
2	Not clear / No evidence
1	Negative evidence

Table 2 Portfolio-level CA matrix

Portfolio-level CA matrix

		WP 1		WP 2		WP 3		WP 4		WP 5		WP 6		WP 7	
		Plausibility of contribution	Strength of evidence	Plausibility of contribution	Strength of evidence	Plausibility of contribution	Strength of evidence	Plausibility of contribution	Strength of evidence	Plausibility of contribution	Strength of evidence	Plausibility of contribution	Strength of evidence	Plausibility of contribution	Strength of evidence
1	Encouragement of international partners to research innovative concepts tackling AMR in LMICs	4	4	5	5	5	5	5	5	5	5	5	5	4	4
2	High-quality research that aims to: Reduce the need for antibiotics through alternative medicines and vaccine development	4	4	5	5	5	4	-	-	-	-	-	-	5	4
3	High-quality research that aims to: Reduce the need for antibiotics in farming of food producing animal	4	4	-	-	4	5	4	4	4	5	-	-	-	-
4	High-quality research that aims to: Reduce the environmental pollution of resistant bacteria and antibiotics	-	-	-	-	5	4	4	4	-	-	-	-	-	-
5	High-quality research that aims to: Improve the measurement of clinical data and its uptake into national level surveillance	-	-	-	-	3	4	3	3	5	4	-	-	-	-
1	International focus and funding in tackling AMR in LMICs research increased	3	4	5	5	5	5	4	3	4	5	5	5	4	3
2	Innovative solutions tested and moved up TRL through the R&D Pipeline	4	5	5	5	5	5	-	-	5	5	5	5	4	3
3	Improved supply of appropriate and affordable products & tools for combatting AMR available to LMICs	4	3	4	3	4	5	-	-	5	5	4	4	4	3
4	Behaviour change in industry and clinical practice on LMICs from: research evidence into economic incentives and national policy; Food security evidence; Clinical practice pilot programmes	3	3	3	3	4	5	4	4	4	5	3	3	3	3
	Average Score	4	4	4	4	4	5	4	4	5	5	4	4	4	3

4.0 Conclusions and recommendations

4.1 Conclusions and lessons learnt

Interim results are very positive for GAMRIF. GAMRIF is filling important investment gaps in AMR-relevant R&D, including driving a greater focus on LMICs and the One Health approach. Through the global initiatives and PDPs, the design and structure of GAMRIF has allowed funding to go to the best science – selected competitively by expert groups - regardless of geographic location. It has allowed GAMRIF to combine funding with other partners and resources, to achieve more than could be achieved alone, and to channel that funding via fit-for-purpose delivery mechanisms and industry partnerships, leveraging external expertise and reducing the need for GAMRIF to duplicate.

Based upon the evaluation evidence, we conclude that the plausibility of GAMRIF's investments contributing to the first three outcomes in its ToC is high. These include:

(i) *International focus and funding in tackling AMR in LMICs research increased.*

(ii) *Innovative solutions tested and moved up the TRL through the R&D pipeline.*

(iii) *Improved supply of appropriate and affordable products and tools for combatting AMR available to LMICs*.

Contribution to the fourth portfolio-level outcome *(iv) behaviour change in industry and clinical practice on LMICs* was graded slightly lower. This is because the human health-focused work is at too early a stage to expect changes in LMIC policy or clinical practice. GAMRIF animal and environmental health-focused projects require additional investment and partnering (including with industry) to achieve this outcome.

Given GAMRIF's focus on funding early-stage research, expectations need to be managed about GAMRIF's ability to demonstrate impact, as well as (quantitative) VfM. Within the next few years, it may be possible to quantify expected results more credibly (e.g averted morbidity, mortality), through some of the nearer to market technologies being developed by PDPs. Until then, the focus should be on delivering interim results and assessing value-for-money at a strategic level (are GAMRIF and its delivery partners investing in the right activities, in the right way, and obtaining the right results?). The evaluation also found intangible benefits to the R&D ecosystem from GAMRIF. Over time, the aggregate value of enhanced diplomatic ties, UK visibility internationally, and leveraging of wider (and future) funding from GAMRIF-supported work is likely to be significant.

Overall, GAMRIF has been managed efficiently. A diversified portfolio, employing a variety of delivery partner mechanisms and funding schedules, has spread the risk of slippage, and facilitated spending to meet ODA targets. However, some delivery partners' ways of working – in terms of predictable funding disbursement and accounting for results – are better aligned with GAMRIF needs than others. Consideration of this alignment, and the managerial effort required to compensate for misalignment, should be a consideration for a potential GAMRIF 2.0.

Further lessons learnt are that the AMR themes and content areas funded by GAMRIF 1.0 have been very broad and the risk tolerance has been high. GAMRIF 2.0 presents an opportunity to learn from this diversity and focus in on particularly promising areas - some projects for example require further support to sustain and broaden their reach, while greater engagement with international stakeholders will be important to facilitate expansion across borders. The GAMRIF business case also made a strategic decision to engage with early-stage development, to help enrich the product development pipeline, rather than concentrating on reducing downstream barriers and market readiness. This presents a challenge since GAMRIF funding is likely to end for most funded projects before they reach the phase where they can commercialise their products (SMEs may not have the resources to support the rest of the project through to commercialisation). By contrast, the likelihood of market entry within the GARDP WP is heightened by its regulatory and commercialisation strategy, alongside the partnership's approach to clinical trials.

There is potential for DHSC to support more promising areas through to achieving impact at higher levels of the ToC, driving products to completion for example through helping to address regulatory hurdles and the causes of market

failure. DHSC appears well placed to contribute to all this work, through its convening power and reach, and ability to work with all the major sectors involved. For example, there may be potential to further leverage or learn from GARDP's work across GAMRIF Work Packages, to better support challenges in the enabling environment – looking at regulatory challenges, clinical trial capacity in high AMR burden countries and developing and piloting commercialisation opportunities

Below, we provide further summary conclusions and lessons from GAMRIF's individual Work Packages:

- Work Packages 2, 6 and 7: GAMRIF has encouraged LMIC-led projects, or partnerships between HICs and LMICs, resulting in increased relevance of R&D of products useable in LMIC health system contexts. GARDP's work also has the potential to make the overall R&D ecosystem more efficient (and which fall out of the earlier-stage scope of other Work Packages). Lessons learnt include that the ability to attract and engage LMIC-based researchers to product-focused work and develop LMIC-based clinical trial sites may require additional effort
- Work Package 3: GAMRIF support has successfully driven early-stage product development in the globally important but poorly supported livestock and aquaculture field in LMICs. The research capacity and collaborations built, across a range of countries, also fulfil GAMRIF's aims. The paucity of down-stream support and recognised barriers to commercialisation and knowledge dissemination increase the risk of market failure. Identifying ways to address these will be necessary to ensure the impact of GAMRIF-supported product pipelines - for example improving knowledge-sharing mechanisms between academia, industry and farmers and helping to improve regulatory efficiency.
- Work Package 5: STI Diagnostic development has been well-targeted, and the groundwork undertaken to facilitate market entry. AMR connectivity projects to improve information access have also been well-conducted, with the Zambia One Health Middleware Project breaking new ground in integrating AMR-relevant data. By their nature, impact on antibiotic use and AMR will be dependent on successful health system integration and take considerable time to realise. Further investment is needed to bring the STI diagnostic products to market, and the identification of this will be important to secure value from the current investment. The Zambia One Health Middleware Project is an exception, where its uniqueness enhances potential for early adoption and impact.
- Work Packages 1 and 4: The bilateral partnerships with China and Argentina have proved to be more challenging managerially and, compared to other Work Packages, have taken longer to establish. There are several reasons for this, a principal one being that these were completely new partnerships, as opposed to the global initiatives and PDPs, which have established portfolio management mechanisms supported by a range of funders. Funded projects, however, are now on-schedule and beginning to yield positive outputs and results. As with other Work Packages, there is a need to consider how to ensure any products successfully developed through GAMRIF funding can reach commercialisation. For WP 4, the embedded social science component should help to better understand the AMR problem and shape appropriate policies.

4.2 Recommendations

Below we present our recommendations for the GAMRIF portfolio and individual Work Packages. Across the portfolio, the key recommendation themes relate to ensuring the future GAMRIF ToC links to influencing the wider R&D ecosystem; that longer-term GAMRIF funding or continued investment could be prioritised specifically for projects that show potential to reach commercialisation; and that further synergies should be explored with UK funding bodies and other AMR initiatives with a complementary focus on product R&D and market shaping.

Portfolio Level

- Based upon the evaluation evidence, it is recommended that DHSC continues to fund the GAMRIF programme due to its role in filling important investment gaps in AMR-relevant R&D.
- The next refresh of GAMRIF's ToC should better situate GAMRIF within global AMR frameworks and plans and include not just content areas but also wider ways that GAMRIF is working (and could work) to influence the R&D

ecosystem (i.e. levers and enablers), and help achieve its intended impact. This includes for example driving opportunities to support wider LMIC research engagement, as well as research uptake across Work Packages.

- Explore opportunities for providing longer-term GAMRIF funding to projects that show potential to reach commercialisation - successful projects would benefit from continued investment and downstream support to enter the market. Alternatively, consider how to link supported projects with other funding opportunities, national and international partners and/or knowledge to help increase their impact (including strengthening and communicating linkages across Work Packages). Particularly for those demonstrating early potential, projects could be required to (and receive support for) outlining their plans for continuing the research after the end of GAMRIF funding and the project's potential pathways to market/impact.
- Explore further synergies with complementary UK funding bodies - e.g UKVN, NIHR/GHR, FCDO/RED, Fleming Fund, Wellcome Trust - with other AMR initiatives, and/or with other funders which have a possible complementary focus on product R&D and market shaping, such as UNITAID, UKVN and the BMGF, to support these portfolio level recommendations.

Work Package 1: UK-China

- Review whether MoST represents an appropriate choice of partner for any future collaboration with China with regards to future collaboration, providing longer-term objectives continue to relate to AMR and public health policy. Future iterations of GAMRIF – especially if they include a focus on later-stage development projects – would benefit from linkages with the Chinese National Health Commission (NHC) and a more explicit focus on public health policy.
- Alternatively, GAMRIF could consider different strategies for partnership in China, such as the regional approach that has been adopted by the Newton Fund[32].
- Consider whether GAMRIF should continue working with China through a bilateral partnership. Although a bilateral partnership model has been useful for keeping China involved in the conversation around AMR, bringing in an additional LMIC partner through another arrangement – such as a trilateral partnership – could help guarantee projects remain relevant to the AMR priorities of LMICs more broadly.
- Consider how to ensure any products successfully developed through GAMRIF funding can reach commercialisation. Practical examples of this include support from GAMRIF on linking with potential funding opportunities and/or requiring projects to outline plans for continuing research after the end of GAMRIF funding. GAMRIF could also explore opportunities for providing direct longer-term funding to projects that show potential to reach commercialisation.

WP 2: CARB-X

- Consider widening the technology scope that is eligible to be funded by GAMRIF, to consider small molecule direct-acting antibiotics and diagnostics as eligible to apply for ODA funding.
- Support efforts to widen CARB-X geographic networks, in order to expand the pool of applicants.
- Explore further synergies with GARDP and FIND, and within the CARB-X portfolio, around complementary diagnostic and therapeutic development.

WP 3: InnoVet-AMR

- Increase involvement of large multi-lateral partners and industry in existing projects, to improve their potential for regulatory passage, market entry and knowledge dissemination. This will require individual project assessment to determine whether measures already taken through 'wrap-around' activities are sufficient, given the diverse nature and state of readiness of projects.

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[32] https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1055511/newton-fund-evaluation-case-study-china.pdf

- Develop handover plans for further funding of current projects, to minimise the risk of failure to progress once this round of GAMRIF support is ended.
- Consider convening a forum to identify the key drivers of AMR in the animal health area, and existing innovations to build upon. Including industry, academia, and farmer organisations, this process would form the basis of future priorities, ensure that DHSC funding is strategically aligned with those of other funders, and provide a platform to broaden interest and involvement in current projects in WP 3.

WP 4: UK–Argentina

- Adopt learning from reported imbalances (in terms of resources/workload) between UK/Argentine researchers, and domestic resource constraints. A better understanding of differences in research cultures at an earlier stage of the programme, and potentially more flexibility for transferring funds/re-allocating resources, could help support more equitable partnerships. For example, considering an in-country delivery partner could potentially facilitate more flexibility in allocation/ transferring of resources.
- Continue efforts to understand and communicate the socio-economic factors behind AMR and farming practices (e.g use of antibiotics in farming environments), as well as developing practical and innovative solutions to tackle AMR in low-resource settings, through embedded social science research.

WP 5: FIND

- The current AMR connectivity projects should be assessed against competitors to determine their suitability for further investment/recruitment of downstream funders. Where considered viable, expansion efforts should concentrate on countries with large populations that are major AMR policy influencers e.g Kenya, Nigeria and South Africa.
- The implications of delayed roll-out of the drug-resistant gonorrhoea diagnostic with respect to Zoliflodacin need to be understood and factored into the market plans for both.
- The health care delivery positioning of improved STI diagnostics as well as improved connectivity needs more work in order to ensure use in clinical patient management and improved surveillance. Expert consultation including with in-country clinicians should inform potential use cases and guide the prioritisation of further investment.

WP 6: GARDP

- Going forward, focus on the most promising projects – including those which improve the overall enabling environment for R&D and product uptake - and discourage dilution of management effort/funding into potentially tangential areas.
- Continue to encourage partnering/synergy with AMR Action Fund, BARDA, CARB-X, CHAI and DNDi to help achieve greater VfM.

WP 7: BactiVac

- BactiVac has demonstrated considerable output for a relatively low investment, whilst also promoting awareness of LMIC needs. Building further on these efficiencies through providing further support (through a successor GAMRIF programme) should be considered.
- Continue efforts to engage industry partners early in vaccine development, to ensure early consideration of manufacturing, regulatory and market barriers.
- Expand communication with other funding bodies and structures such as CARB-X to promote uptake of promising early-stage candidates for further development.

Annexes

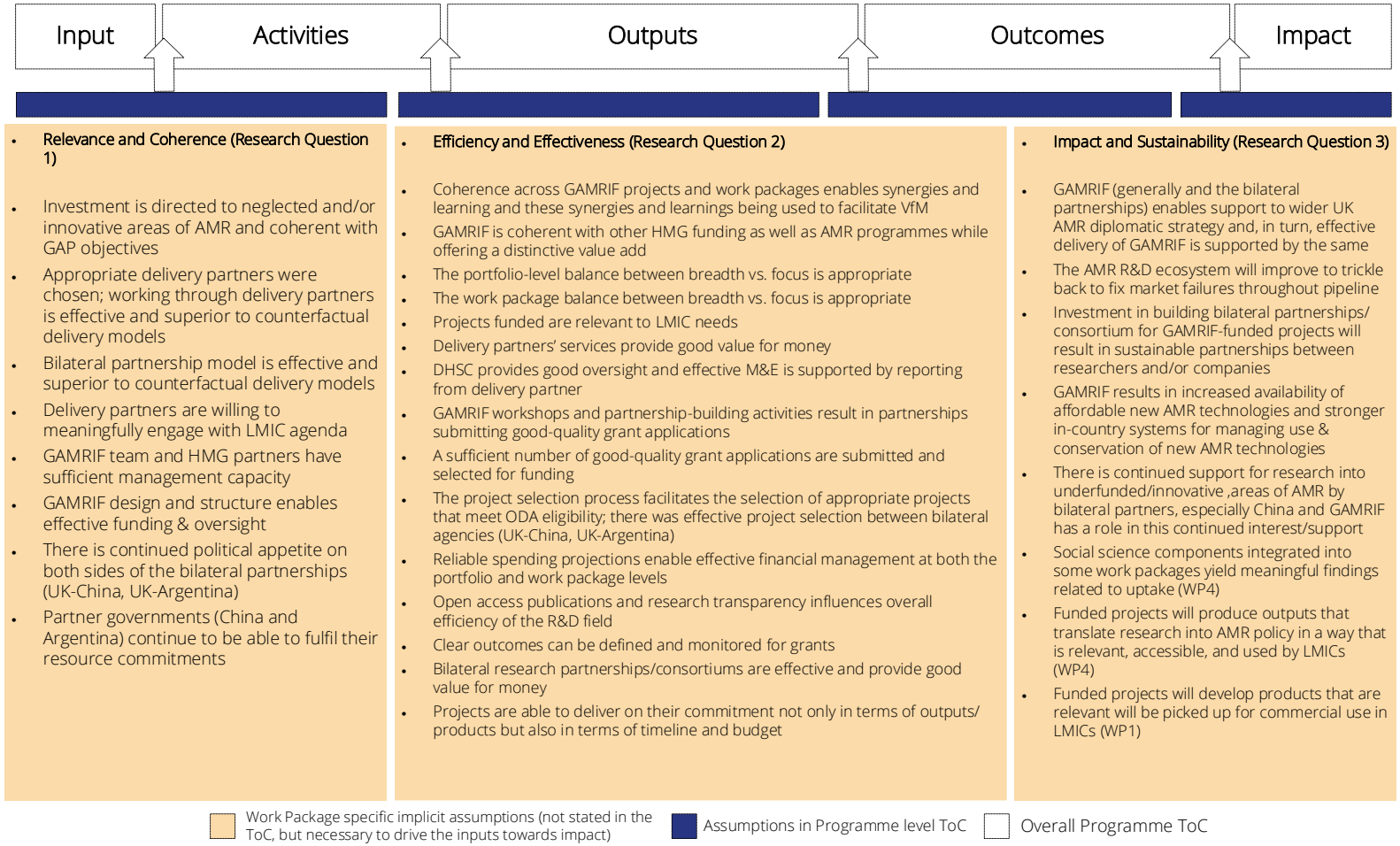
Annex 1: Final Evaluation Framework

Overall EQs and sub-EQs	Key Methodological Approaches	Source(s) of Evidence
Question 1 (DAC criteria: Relevance and Coherence): Has GAMRIF allocated resources strategically towards potentially high impact activities aligned with global priorities, taking into consideration needs and gaps not already well filled by others, and considering GAMRIF's comparative advantages and goals?		
To what extent have GAMRIF investments been aligned and are coherent with AMR needs outlined in GAP and considering gaps not filled by other funders/partners, representing a clear value-add?	Systematic review of the aims, objectives, and activities of GAMRIF, and its assumptions outlined in the ToC (e.g evidence of wider leadership/ coordination, funding leverage, quality and relevant research, access and stewardship plans, information sharing, LMIC engagement), mapped against global priorities, needs and gaps.	Desk Review (annual reviews, M&E data, research outputs) Stakeholder Interviews with DHSC staff, delivery partners, project teams, other project stakeholders. FGDs with research team members
How is GAMRIF different to other AMR research programmes? What are its unique selling points? To what extent has GAMRIF's comparative advantages influenced choice of investments?		
What other/alternative things should GAMRIF be doing to achieve its goal and objectives?		
Question 2 (DAC criteria: Effectiveness and Efficiency): Does the current design and management of GAMRIF's portfolio (and the delivery partners' efficiency and effectiveness) allow it to effectively maximise its impact and objectives? Are there opportunities to improve ways of working towards better efficiency/effectiveness?		
How effective is GAMRIF's multiple delivery mechanism at achieving its objective? Are there any other delivery mechanisms that could be explored? How efficient and effective is DHSC in managing GAMRIF? Are there any constraints to effective management of any of the Work Packages? To what extent do delivery partners' services (admin, technical oversight, financial reporting/, running competitions etc.) provide good VfM? Does reporting from each delivery partner provide DHSC with sufficient information to manage the programme efficiently?	Interrogating the ToC assumptions related to effective management, delivery, and monitoring mechanisms (across DHSC and partners), and what has worked/not worked. VfM assessment - focus on: ▶ The relationship between outputs and the resources required to produce them (economy and efficiency), relationship with the delivery mechanism, and any required changes. ▶ The relationship between the programme's intended and actual	Desk Review (annual reviews, business case, external literature) Stakeholder Interviews with DHSC staff, delivery partners, project teams, other project stakeholders, wider stakeholders in the AMR R&D field FGDs with research team members

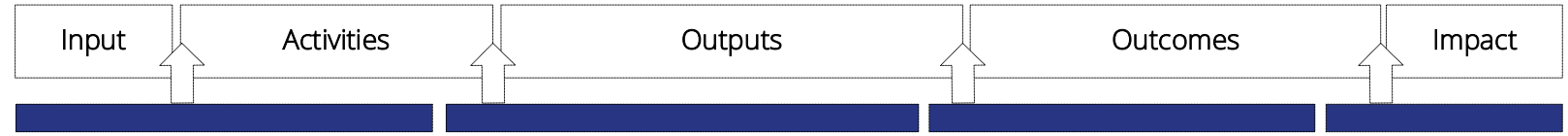
Are there any changes required to the programme and Work Packages' design to improve its VfM (economy, efficiency, effectiveness and equity)?	outcomes (effectiveness, equity), relationship with the delivery mechanism, and any required changes	
Question 3 (DAC criteria: Impact and Sustainability): Are there indications that the GAMRIF programme has produced positive change likely to contribute to sustainable impact?		
To what extent have programme outputs and outcomes been achieved / are likely to be achieved? What factors have provided: i) most support; and ii) the primary challenges to GAMRIF staying on track to achieve its desired objectives? What evidence is there that demonstrates the potential for LMIC access and uptake of products when they are developed in years to come? What more could be done to ensure access and uptake? How could GAMRIF maximise R&D outputs that will lead to successful product development? How can GAMRIF and/or a potential successor R&D programme adapt in line with learning from the ToC and its assumptions?	CA – using the programme's ToC and impact pathways to help map the impact of the intervention, and other influences, on outcomes (and identify where GAMRIF's contribution to product development and uptake is strongest). This approach will also help define and measure actual and potential research outcomes at different stages in the research process, and across different partnership models, GAMRIF Work Packages and project types, based upon indicators of: ▶ Contribution to knowledge ▶ Benefits to future research and research use ▶ Benefits to informing policy and product development. Contribution Analysis – to understand: (1) to what extent ToC assumptions were consistent with the reality of programme implementation; and (2) how important these assumptions are to the achievement/non-achievement of key outcomes and the contribution of programmes such as GAMRIF. Case studies - providing within-case analysis of how the causal processes and assumptions in the ToC play out in practice.	Desk Review (annual reviews, business case, external literature) Stakeholder Interviews with DHSC staff, delivery partners, project teams, other project stakeholders, wider stakeholders in the AMR R&D field

Annex 2: Work Packages - Nested Theories of Change

Work Packages 1, 4



Work Packages 2, 6, 7



Relevance and Coherence (deciding what to do)

- Investment is directed to neglected areas of AMR and aligned/coherent with GAP objectives
- External coherence with other UK govt funding (leveraging expertise and advice); GAMRIF also coherent with other AMR research programmes (e.g. BMGF & WT), offering distinctive value add
- Process by which investment options are appraised and preferred delivery mechanisms selected is effective and enables flexible and nimble approach
- Delivery mechanism choice is superior to counterfactual delivery models (e.g. UK focused competition) in terms of e.g. Identifying lead candidates with best potential based on PPL criteria & facilitating transition to clinical evaluation
- Delivery partners willing to engage with LMIC agenda (with implications for candidate and developer selection/support and ODA justification)
- Sufficient funds raised for DHSC to gain "seat at the table" (e.g. £40m at Carbx)
- GAMRIF team/UK govt partners have sufficient mgmt. capacity
- Continued political appetite, strong multinational leadership and policy and advocacy work

Efficiency and (intermediate) effectiveness (deciding how to do it)

- Strategic partnerships and international AMR diplomacy results in leveraged funding; additional funders make the overall programme of work possible
- GAMRIF design and structure (incl. monitoring approaches – content and frequency of reporting, financial disbursement mechanisms and financial controls, timely contracting) enables effective funding & oversight
- Researcher appetite/pool of expertise sufficient to engage in LMIC relevant research;
- Partner mgmt. capacity and (independent) SAB are able to apply selection criteria and vet proposals for ODA eligibility; evidence of effective go/no-go decision making
- Reliable spending projections enable effective financial management
- Delivery partner portfolio management assures adequate number and quality of projects (latter defined according to LMIC relevance/TPP, PPL priority, innovation degree, LMIC researchers). Portfolio balance between breadth vs. focus is appropriate and innovations supported are those most relevant to LMIC needs.
- Delivery partners' services (admin, technical oversight, financial reporting/ running competitions etc.) provide good value for money
- Developers put effective stewardship and access plans in place to ensure LMIC access (without negative impact on incentives)
- Continued focus on innovative candidates (this requirement is not weakened over time with pressure to spend)
- Open access publications and research transparency influences overall efficiency of the R&D field, enabling better targeting of future research
- Clear outcomes can be defined and monitored for CARBX grants, incl. TRLs
- "Accelerator" initiative has influence over attracting LMIC researchers and tailoring support to their specific needs
- Coherence within portfolio enables synergies and learning, facilitates VfM

Impact and Sustainability (results)

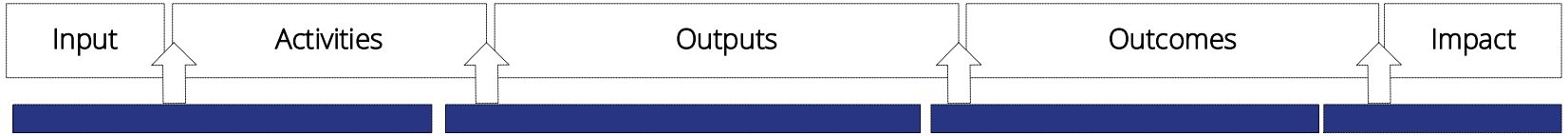
- R&D ecosystem (e.g Initiatives such as U.S. PASTEUR Act) will improve to trickle back to bridge the valley of death/fix market failures throughout pipeline incl. for SMEs
- PDP Pipeline coordinators or private firms will take up the most promising products post CARBX and see them through to market
- The (non-binding?) S&As in the CARBX agreements are eventually operationalised to sufficiently influence pricing, product presentation, registration/supply capacity in LMICs
- Increased availability of affordable new AMR technologies and stronger in-country systems for managing use & conservation of new AMR technologies (incl. related to animal health)
- Implementation science conducted to develop contexts for innovations; social sciences integrated into some work packages (WP3 and WP4) yield meaningful findings related to uptake
- GAMRIF enables support to UK wider international AMR diplomatic strategy and in turn effective delivery of GAMRIF is supported by the same

Work Package specific implicit assumptions (not stated in the ToC, but necessary to drive the inputs towards impact)

Assumptions in Programme level ToC

Overall Programme ToC

Work Package 3



- **Relevance and Coherence (deciding what to do)**
- Investment is directed to neglected areas of AMR and aligned/coherent with GAP objectives
- External coherence with other UK govt funding (leveraging expertise and advice); Also coherent with the Livestock Vaccine Innovation Fund (LVIF) program also housed at IDRC, and other AMR research programmes, offering distinctive value add
- Process by which investment options are appraised and preferred delivery mechanisms selected is effective and enables flexible and nimble approach
- Delivery mechanism choice is superior to counterfactual delivery models (e.g. UK focused competition) in terms of e.g. Identifying lead candidates with best potential based on PPL criteria &facilitating transition to clinical evaluation
- Delivery partners willing to engage with LMIC agenda (with implications for candidate and developer selection/support and ODA justification)
- Sufficient funds raised for DHSC to gain "seat at the table" (e.g. influence on IDRC activities including LVIF, and wider AMR activities in OneHealth)
- GAMRIF team and IDRC have sufficient mgmt. capacity
- Continued political appetite, strong multinational leadership and policy and advocacy work

- **Efficiency and (intermediate) effectiveness (deciding how to do it)**
- Strategic partnerships and international AMR diplomacy results in leveraged funding; additional funders make the overall programme of work possible
- GAMRIF design and structure (incl. monitoring approaches – content and frequency of reporting, financial disbursement mechanisms and financial controls, timely contracting) enables effective funding & oversight
- Researcher appetite/pool of expertise sufficient to engage in LMIC relevant research;
- Partner mgmt. capacity and (independent) SAB are able to apply selection criteria and vet proposals for ODA eligibility; evidence of effective go/no-go decision making
- Reliable spending projections enable effective financial management
- Delivery partner (IDRC) portfolio management assures adequate oversight and quality management of projects (latter defined according to LMIC relevance, innovation degree, LMIC researchers, local farming relevance).
- Delivery partners' services (admin, technical oversight, financial reporting/ running competitions etc.) provide good value for money
- Developers put effective stewardship and access plans in place to ensure LMIC access (without negative impact on incentives)
- Continued focus on innovative candidates (this requirement is not weakened over time with pressure to spend)
- Grantees provide high likelihood of innovation success and influence over wider field of vaccine and vaccine-related technology use to reduce and improve antimicrobial use.
- Open access publications and research transparency influences overall efficiency of the R&D field, enabling better targeting of future research
- Clear outcomes can be defined and monitored for IDRC grants.
- Coherence within portfolio enables synergies and learning, facilitates VfM

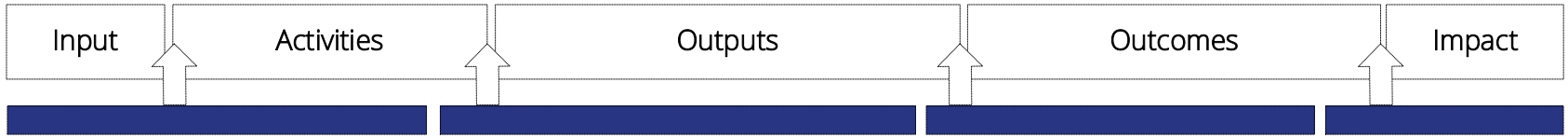
- **Impact and Sustainability (results)**
- Demand and use ecosystem for AMR-relevant vaccines and vaccine-related technologies for livestock and aquaculture will find boarder use, fixing market failures throughout the development pipeline incl. for SMEs
- Vaccine developers not involved will be incentivised to develop and expand offerings to the livestock and aquaculture sectors
- Development of new vaccines that mitigate antimicrobial use, and more efficient systems for administering vaccines and supporting vaccination.
- Trial countries and sites take up technologies tested within their own health practices and expand nationally.
- New vaccine products and implementation practices established are taken up more broadly and facilitate higher quality and standardized management practices.
- GAMRIF investment stimulates wider investment from other sources, increasing the overall long-term investment in the livestock and aquaculture vaccine fields.

Work Package specific implicit assumptions (not stated in the ToC, but necessary to drive the inputs towards impact)

Assumptions in Programme level ToC

Overall Programme ToC

Work Package 5



- **Relevance and Coherence (deciding what to do)**
- Investment is directed to neglected areas of AMR and aligned/coherent with GAP objectives
- External coherence with other UK govt funding including funding to FIND (leveraging expertise and advice); GAMRIF also coherent with other AMR research programmes (e.g. BMGF & WT), offering distinctive value add
- Process by which investment options are appraised and preferred delivery mechanisms selected is effective and enables flexible and nimble approach
- Delivery mechanism choice is superior to counterfactual delivery models (e.g. UK focused competition) in terms of e.g. Identifying lead candidates with best potential based on PPL criteria &facilitating transition to clinical evaluation
- Delivery partners willing to engage with LMIC agenda (with implications for candidate and developer selection/support and ODA justification)
- Sufficient funds raised for DHSC to gain "seat at the table" (e.g. impact on FIND priorties)
- GAMRIF team/UK govt partners have sufficient mgmt. capacity
- Continued political appetite, strong multinational leadership and policy and advocacy work

- **Efficiency and (intermediate) effectiveness (deciding how to do it)**
- Strategic partnerships and international AMR diplomacy results in leveraged funding; additional funders make the overall programme of work possible
- GAMRIF design and structure (incl. monitoring approaches – content and frequency of reporting, financial disbursement mechanisms and financial controls, timely contracting) enables effective funding & oversight
- Researcher appetite/pool of expertise sufficient to engage in LMIC relevant research;
- Partner mgmt. capacity and (independent) SAB are able to apply selection criteria and vet proposals for ODA eligibility; evidence of effective go/no-go decision making
- Reliable spending projections enable effective financial management
- Delivery partner portfolio management assures adequate design and quality of projects (latter defined according to LMIC relevance/TPP, innovation degree, LMIC researchers, health system relevance).
- Delivery partners' services (admin, technical oversight, financial reporting/running competitions etc.) provide good value for money
- Developers put effective stewardship and access plans in place to ensure LMIC access (without negative impact on incentives)
- Continued focus on innovative candidates (this requirement is not weakened over time with pressure to spend)
- Field partners and sites provide high likelihood of long-term engagement and influence over wider field of AMR and diagnostics implementation and effective use.
- Improved diagnostic tests to distinguish gonorrhoea +/- chlamydia alone (intermediate aim) attain market share lead to improved use of antibiotics.
- New antibiotics emerging from GARDP and CARB-X are successful in finding market share, providing a relevant market for corresponding diagnostics for microbial susceptibility developed with support through FIND.
- Open access publications and research transparency influences overall efficiency of the R&D field, enabling better targeting of future research
- Clear outcomes can be defined and monitored for FIND grants.
- Coherence within portfolio enables synergies and learning, facilitates VfM

- **Impact and Sustainability (results)**
- Demand and use ecosystem for AMR-relevant diagnostic and data management technologies will improve to trickle back to bridge the valley of death/fix market failures throughout pipeline incl. for SMEs
- Diagnostic firms not involved will be incentivised to develop and expand offerings to a broader AMR market
- Increased availability of affordable new AMR technologies and stronger in-country systems for capturing and using data relevant to AMR management.
- Trial countries and sites take up technologies tested within their own health practices and expand nationally.
- Clinical algorithms, TPPs and data transfer standards established are taken up more broadly and facilitate higher quality and standardized management practices.
- GAMRIF investment stimulates wider investment from other sources, increasing the overall long-term investment in the AMR diagnostics field.

Work Package specific implicit assumptions (not stated in the ToC, but necessary to drive the inputs towards impact)

Assumptions in Programme level ToC

Overall Programme ToC

Annex 3: Contribution Analysis per Work Package

Work Package 1

Based on the evaluation evidence, the plausibility of GAMRIF's bilateral partnership with China contributing to the relevant output and outcome measures has been summarised in the text and table below.

WP 1 CA matrix			
		Plausibility of contributing to outcome	Strength of evidence
Output	1. Encouragement of international partners to research innovative concepts tackling AMR in LMICs	4	4
	2. High-quality research that aims to: Reduce the need for antibiotics through alternative medicines and vaccine development	4	4
	3. High-quality research that aims to: Reduce the need for antibiotics in farming of food producing animal	4	4
	4. High-quality research that aims to: Reduce the environmental pollution of resistant bacteria and antibiotics	-	-
	5. High-quality research that aims to: Improve the measurement of clinical data and its uptake into national level surveillance	-	-
Outcomes	6. International focus and funding in tackling AMR in LMICs research increased	3	4
	7. Innovative solutions tested and moved up TRL through the R&D Pipeline	4	5
	8. Improved supply of appropriate and affordable products & tools for combatting AMR available to LMICs	3	3
	9. Behaviour change in industry and clinical practice on LMICs from: research evidence into economic incentives and national policy; Food security evidence; Clinical practice pilot programmes	3	3

Plausibility of Contribution key: 1 - Negative; 2 – Not Clear; 3 – Somewhat Plausible; 4 – Plausible; 5 – Highly Plausible **Strength of Evidence key**: 1 – Negative Evidence; 2 – No Evidence; 3 – Weak Evidence; 4 – Moderate Evidence; 5 – Strong Evidence

- Output 1: The plausibility of GAMRIF's bilateral partnership with China contributing to the output ***"Encouragement of international partners to research innovative concepts tackling AMR in LMICs"*** is reasonably high. WP 1 has encouraged international partners to research innovative concepts tackling AMR, since MoST entered into a bilateral partnership to fund innovative, early-stage AMR projects. The strength of evidence is also reasonably high, although it is not fully clear how easy it will be to take research and/or products developed as part of WP 1 into other LMICs. Moreover, it is not clear what the impact will be on funding this kind of AMR research – in China or in other LMICs – beyond the lifespan of GAMRIF itself.
- Output 2-3: The plausibility of contributing towards ***"High-quality research that aims to: Reduce the need for antibiotics through alternative medicines and vaccine development"*** and ***"High-quality research that aims to: Reduce the need for antibiotics in farming of food producing animals"*** is reasonably high. The scopes of projects funded under WP 1 are relevant to reducing the need for antibiotics through alternative medicines and vaccine development. Moreover, 8 of the 14 funded projects were specifically focused on farming and food producing animals. A rigorous, tested project selection process was used to select projects, suggesting that the quality of research is high. The strength of evidence for this is also reasonably high. However, given the bilateral project selection process it is possible that some projects with higher-quality research were not selected and that projects with somewhat lower-quality research were included in WP 1.

- Outcome 1: The plausibility of GAMRIF's bilateral partnership with China contributing to ***"International focus and funding in tackling AMR in LMICs research increased"*** is moderate and the strength of evidence for this is reasonably high. The country and topic focus of WP 1 was at least partially political, and it is not clear if or how China will remain engaged in this area of AMR research following the end of GAMRIF. Given how different the Chinese context is from other LMICs, it is also not clear how WP 1 will increase focus and funding in research related to tackling AMR in LMICs at the international level.
- Outcome 2: The plausibility of contributing to "***Innovative solutions tested and moved up the TRL through the R&D pipeline"*** is reasonably high as projects funded under WP 1 are generally progressing well and developing innovative solutions that could be moved up the R&D pipeline. The strength of evidence demonstrating this progression is high. However, this progression will largely be dependent on the availability of funds to support the next stage of research.
- Outcome 3: The plausibility of contributing to ***"Improved supply of appropriate and affordable products & tools for combatting AMR available to LMICs"*** is medium because research funded under WP 1 is early stage and will require significant contributions outside the current GAMRIF funding to ultimately result in market-ready products. It does not appear that any of the projects will be at the commercialisation stage on completion of the current funding period. Moreover, interviewees expressed some scepticism about whether products and tools developed for the Chinese market could be affordable and relevant to LMICs more generally. Strength of evidence for this conclusion is medium, again because the products are so early stage.
- Outcome 4: The plausibility of contributing to ***"Behaviour change in industry and clinical practice on LMICs from research evidence into economic incentives and national policy"*** is medium at this stage. This objective is very long term, and it is not clear from the available evidence how WP 1 will connect to policy or longer-term product development beyond prototypes. There are many other influences on economic incentives and national policy outside of GAMRIF's control. Strength of evidence is medium for this conclusion; KIIs and reporting indicate projects generally achieving initial objectives, but evidence on commercial success and impact on national policy, food security, etc. is not currently available.

Work Package 2

Based on the evaluation evidence, the plausibility of GAMRIF's CARB-X investment contributing to the relevant output and outcome measures has been summarised in the text and table below.

WP 2 CA matrix			
		Plausibility of contributing to outcome	Strength of evidence
Output	1. Encouragement of international partners to research innovative concepts tackling AMR in LMICs	5	5
	2. High-quality research that aims to: Reduce the need for antibiotics through alternative medicines and vaccine development	5	5
	3. High-quality research that aims to: Reduce the need for antibiotics in farming of food producing animal	-	-
	4. High-quality research that aims to: Reduce the environmental pollution of resistant bacteria and antibiotics	-	-
	5. High-quality research that aims to: Improve the measurement of clinical data and its uptake into national level surveillance	-	-
Outcomes	1. International focus and funding in tackling AMR in LMICs research increased	5	5
	2. Innovative solutions tested and moved up TRL through the R&D Pipeline	5	5

	3. Improved supply of appropriate and affordable products & tools for combatting AMR available to LMICs	4	3
	4. Behaviour change in industry and clinical practice on LMICs from: research evidence into economic incentives and national policy; Food security evidence; Clinical practice pilot programmes	3	3

Plausibility of Contribution key: 1 - Negative; 2 – Not Clear; 3 – Somewhat Plausible; 4 – Plausible; 5 – Highly Plausible **Strength of Evidence key**: 1 – Negative Evidence; 2 – No Evidence; 3 – Weak Evidence; 4 – Moderate Evidence; 5 – Strong Evidence

- Output 1. The plausibility of GAMRIF's CARB-X investment contributing to the outcome ***"Encouragement of international partners to research innovative concepts tackling AMR in LMICs"*** is high, for reasons summarised in the EQ 1/value add section. The strength of evidence is high, based on solid evidence collected through KIIs and JOC minutes.
- Output 2. The plausibility of contributing towards ***"High-quality research that aims to: Reduce the need for antibiotics through alternative medicines and vaccine development"*** is high. The research supported by CARB-X is high quality and GAMRIF's funding targets alternatives to antibiotics. However, as discussed in WP section, the assumption that riskier alternative medicines and costlier vaccines will reduce the need for antibiotics and should be the primary focus of GAMRIF funding may be questioned. The strength of evidence for the AMR burden being disproportionately felt in LMICs has strengthened only recently with the work by IHME, so by consequence the strength of evidence to question the GAMRIF technology limitation is strengthened.
- Outcome 1. The plausibility of GAMRIF's investment through CARB-X contributing to ***"International focus and funding in tackling AMR in LMICs research increased"*** is high and strength of evidence is high – see comments under Output 1.
- Outcome 2. The plausibility of contributing to "***Innovative solutions tested and moved up the TRL through the R&D pipeline"*** is high; the right mix of activities are being funded and the delivery partner is delivering efficient and effective portfolio management and support to PDs, producing good interim results. Strength of evidence for this conclusion is high, based on JOC minutes, funders reports, KIIs and other data reviewed.
- Outcome 3. The plausibility of contributing to ***"Improved supply of appropriate and affordable products & tools for combatting AMR available to LMICs"*** is slightly lower, only because CARB-X's candidates are early stage and will require significant contributions by others outside of GAMRIF and CARB-X's direct control, in order for GAMRIF's contributions to ultimately result in product market entry, use, health impact and savings. However, for reasons explained under EQ 3, the plausibility is higher now than it was even a year ago, due to several recent developments. Strength of evidence for this conclusion is medium, again because the products are so early stage and Pew Trust's pipeline coverage will only start to pick up the presence of CARB-X graduates in the clinical development pipeline in a few years' time.
- Outcome 4. The plausibility of contributing to ***"Behaviour change in industry and clinical practice on LMICs from research evidence into economic incentives and national policy"*** is medium at this stage. CARB-X is a "push" incentive which has increased the volume and quality of work at the pre-clinical stage, however for the same reasons as outcome #2, there are many other influences on economic incentives and national policy, outside of GAMRIF and CARB-X's control. Strength of evidence is medium for this conclusion; we know CARB-X has created an economic incentive to engage in pre-clinical work but influencing clinical practice is a long way off and more substantive industry behaviour change will require a mix of push and pull incentives as well as support to the enabling environment for AMR R&D.

Work Package 3

GAMRIF investments in WP 3/InnoVet-AMR are assessed on plausibility and strength of evidence to lead to overall GAMRIF programme ToC outputs of:

WP 3 CA matrix			
		Plausibility of contributing to outcome	Strength of evidence
Output	1. Encouragement of international partners to research innovative concepts tackling AMR in LMICs	5	5
	2. High-quality research that aims to: Reduce the need for antibiotics through alternative medicines and vaccine development	5	4
	3. High-quality research that aims to: Reduce the need for antibiotics in farming of food producing animal	4	5
	4. High-quality research that aims to: Reduce the environmental pollution of resistant bacteria and antibiotics and antibiotics	5	4
	5. High-quality research that aims to: Improve the measurement of clinical data and its uptake into national level surveillance	3	4
Outcomes	1. International focus and funding in tackling AMR in LMICs research increased	5	5
	2. Innovative solutions tested and moved up TRL through the R&D Pipeline	5	5
	3. Improved supply of appropriate and affordable products & tools for combatting AMR available to LMICs	4	5
	4. Behaviour-change in industry and clinical practice on LMICs from: research evidence into economic incentives and national policy; Food security evidence; Clinical practice pilot programmes	4	5
	5. Innovative solutions tested and moved up TRL through the R&D Pipeline	5	5
	6. Improved supply of appropriate and affordable products & tools for combatting AMR available to LMICs	4	5
	7. Behaviour-change in industry and clinical practice on LMICs from: research evidence into economic incentives and national policy; Food security evidence; Clinical practice pilot programmes	4	5

Plausibility of Contribution key: 1 - Negative; 2 – Not Clear; 3 – Somewhat Plausible; 4 – Plausible; 5 – Highly Plausible **Strength of Evidence key**: 1 – Negative Evidence; 2 – No Evidence; 3 – Weak Evidence; 4 – Moderate Evidence; 5 – Strong Evidence

- Output 1: The plausibility of GAMRIF's investment in InnoVet-AMR contributing to achievement of Output 1 ***"Encouragement of international partners to research innovative concepts tackling AMR in LMICs"*** is high, with a range of effective inter-country collaborations established, including novel product areas. The strength of evidence is high with a strong collaboration with IDRC established, and well-functioning relationships with 11 Implementing Partnerships reaching across national boundaries.
- Output 2: The plausibility of achieving Output 2 ***"High-quality research that aims to: Reduce the need for antibiotics through alternative medicines and vaccine development"*** is high, evidenced by field projects having identified candidates, one showing signs of early efficacy in reducing anti-microbial requirements.
- Output 3: The plausibility of achieving ***"High-quality research that aims to: Reduce use of antibiotics in farming of food producing animal"*** is moderate as it will require evidence of strong uptake and behaviour change. The evidence is strong.

- Output 4: The plausibility of achieving ***"High-quality research that aims to: reduce the environmental pollution of resistant bacteria and antibiotics"*** is high, with high likelihood of reduced antibiotic use in aquaculture and some livestock projects. Evidence is strong in the aquaculture /nanobubble project, less strong in others.
- Output 5: The plausibility of achieving ***"High-quality research that aims to: Improve the measurement of clinical data and its uptake into national level surveillance"*** is low, as this is not addressed strongly in WP 3, which concentrates on upstream product development. Evidence of lack of impact is moderate – more detail on wrap-around work would benefit this area.
- Outcome 1: The plausibility of achieving Outcome 1 ***"International focus and funding in tackling AMR in LMICs research increased"*** is high, this was achieved through the engagement with IDRC, leveraging Canadian funding, and the inter-country collaborations established (evidence strength is high).
- Outcome 2: The plausibility of the outcome ***"Innovative solutions tested and moved up through the R&D Pipeline"***, is high, with most projects showing likelihood of achieving milestones justifying further support. The strength of evidence is high, based on IDRC reporting and KII information.
- Outcome 3: The plausibility of achieving Outcome 3 ***"Improved supply of appropriate and affordable products & tools for combatting AMR available to LMICs"*** is moderate, as no projects are likely to be at stage of commercialisation on completion of the current funding period. The strength of evidence of this is high, based on IDRC reporting and KIIs.
- Outcome 4: The plausibility of achieving ***"Behaviour change in industry and clinical practice on LMICs - Food security evidence; Clinical practice pilot programmes"*** is moderate. While KIIs and reporting indicates projects achieving initial objectives, but commercial success and impact on food production are not shown. The evidence of this is high.

Work Package 4

Based on the evaluation evidence, the plausibility of GAMRIF's WP 4 investment contributing to the relevant output and outcome measures has been summarised in the text and table below.

WP 4 CA matrix			
		Plausibility of contributing to outcome	Strength of evidence
Output	1. Encouragement of international partners to research innovative concepts tackling AMR in LMICs	5	5
	2. High-quality research that aims to: Reduce the need for antibiotics through alternative medicines and vaccine development	-	-
	3. High-quality research that aims to: Reduce the need for antibiotics in farming of food producing animal	4	4
	4. High-quality research that aims to: Reduce the environmental pollution of resistant bacteria and antibiotics	4	4
	5. High-quality research that aims to: Improve the measurement of clinical data and its uptake into national level surveillance	3	3
Outcomes	1. International focus and funding in tackling AMR in LMICs research increased	4	3
	2. Innovative solutions tested and moved up TRL through the R&D Pipeline	-	-
	3. Improved supply of appropriate and affordable products & tools for combatting AMR available to LMICs	-	-
	4. Behaviour change in industry and clinical practice on LMICs from: research evidence into economic incentives and national policy; Food security evidence; Clinical practice pilot programmes	4	4

Plausibility of Contribution key: 1 - Negative; 2 – Not Clear; 3 – Somewhat Plausible; 4 – Plausible; 5 – Highly Plausible **Strength of Evidence key**: 1 – Negative Evidence; 2 – No Evidence; 3 – Weak Evidence; 4 – Moderate Evidence; 5 – Strong Evidence

- Output 1: The plausibility of GAMRIF WP 4 investment to contribute to the output "***Encouragement of international partners to research innovative concepts tackling AMR in LMICs"*** is very high, and the strength of evidence is very high as shown under section EQ 1 above. The partnership with Argentine institutions has worked well and high likelihood to collaborate again in the future, while researchers felt that they could pursue gaps in AMR research and appreciate that GAMRIF was encouraging and funding this.
- Output 3: The plausibility of WP 4 contributing to the output ***"High-quality research that aims to: Reduce use of antibiotics in farming of food producing animal"*** is high, and the strength of evidence is high, as shown in section EQ 1 above. The key aim of most funded projects as they focus on animal AMR and farm settings while high quality was ensured, as a committee selected the highest scored projects based on ODA relevance and Policy potential. The only concern is the application of research outputs beyond Argentina, in the rest of Latin America and other LMICs. More evidence is needed to evaluate if the research will have an impact, as policy outputs will have to be produced and disseminated first
- Output 4: The plausibility of GAMRIF's investments on output ***"High-quality research that aims to: reduce the environmental pollution of resistant bacteria and antibiotics"*** is high, and the strength of evidence is high as shown in section EQ 1. Not as many projects focused on plant-based research on environmental AMR, as focus shifted more to animal health and farm-specific environmental AMR due to Argentina's interests. It was however considered potentially more relevant to LMICs as farm settings/ agriculture might be more relevant to LMICs. There is however still a need for more evidence to evaluate if the research will have an impact, as policy outputs will have to be produced and disseminated first
- Output 5: The plausibility of GAMRIF WP 4 investments contributing to the output ***"High-quality research that aims to: Improve the measurement of clinical data and its uptake into national level surveillance"*** is medium, and the strength of evidence is medium as well. 3 of 5 funded projects are looking into establishing surveillance protocols/ broad frameworks to understand AMR in animals and environment. KIIs also suggested that findings will be presented/ disseminated within Argentina and globally but it is not yet clear if this will/can have an impact on national level systems. As above, policy outputs need to be produced and disseminated first, while there is a concern about different levels of LMICs and how uptake will be affected
- Outcome 1: The plausibility of GAMRIF WP 4 contributing to the outcome ***"International focus and funding in tackling AMR in LMICs research increased"*** is high, although the strength of evidence is at a medium level at this stage. WP 4 funding focuses on areas not as commonly funded in AMR (animal health and environment), which is already appreciated by stakeholders interviewed, and there is evidence to suggest that GAMRIF is raising awareness about AMR in general. WP 4 is an innovative partnership with Argentina which had never been done before, also aiming to influence more broadly in Latin America, while all projects are producing LMIC-relevant outputs. However, there is not much evidence yet on how GAMRIF can lead to more funding besides influence of policy makers through project outputs (which are not completed nor disseminated yet)
- Outcome 4: The plausibility of GAMRIF's investments on WP 4 contributing to the outcome ***"Behaviour change in industry and clinical practice on LMICs from: research evidence into economic incentives and national policy; Food security evidence; Clinical practice pilot programmes"*** is high and the strength of evidence is high as well. One of the key aim of WP 4 to translate evidence into policy, while each project has planned to produce such outputs and has considered how such evidence and tools can be used in LMICs, as well as produced joint proposal through integration project. A social science component is embedded and is key to better understand the problem and help shape appropriate policies. However, there is uncertainty about the applicability of such evidence/ tools due to the different levels of resources and infrastructure in LMICs, while policy briefs and other outputs are not yet produced, which means that the stakeholder reach or policy influence cannot be assessed at this stage. More evidence is needed to assess how likely it is that GAMRIF will lead to behaviour change.

Work Package 5

The plausibility and strength of evidence of GAMRIF investments in WP 5/FIND to lead to the overall GAMRIF programme ToC Outputs are assessed as follows:

WP 5 CA matrix			
		Plausibility of contributing to outcome	Strength of evidence
Outputs	1. Encouragement of international partners to research innovative concepts tackling AMR in LMICs	5	5
	2. High-quality research that aims to: Reduce the need for antibiotics through alternative medicines and vaccine development	-	-
	3. High-quality research that aims to: Reduce need for antibiotics in farming of food producing animals	4	5
	4. High-quality research that aims to: reduce the environmental pollution of resistant bacteria and antibiotics	-	-
	5. High-quality research that aims to: Improve the measurement of clinical data and its uptake into national level surveillance	5	4
Outcomes	1. International focus and funding in tackling AMR in LMICs research increased	4	5
	2. Innovative solutions tested and moved up TRL through the R&D Pipeline	5	5
	3. Improved supply of appropriate and affordable products & tools for combatting AMR available to LMICs	5	5
	4. Behaviour change in industry and clinical practice on LMICs from: research evidence into economic incentives and national policy; Food security evidence; Clinical practice pilot programmes	4	5

Plausibility of Contribution key: 1 - Negative; 2 – Not Clear; 3 – Somewhat Plausible; 4 – Plausible; 5 – Highly Plausible **Strength of Evidence key**: 1 – Negative Evidence; 2 – No Evidence; 3 – Weak Evidence; 4 – Moderate Evidence; 5 – Strong Evidence

- Output 1: The plausibility of GAMRIF's investment in FIND contributing to achievement of Output 1 ***"Encouragement of international partners to research innovative concepts tackling AMR in LMICs"*** is high. The strength of evidence for this is high with a strong collaboration with FIND and FIND's relationships with international NGOs within the project, and with GARDP and WHO.
- Output 3: The plausibility of achieving ***"High-quality research that aims to: Reduce use of antibiotics in farming of food producing animal"*** is currently moderate – only the Zambia One Health middleware project is relevant to this output, and requires data availability to translate into behaviour change.
- Output 5: The plausibility of achieving: ***"High-quality research that aims to: Improve the measurement of clinical data and its uptake into national level surveillance"*** is high. The digital projects all raise opportunity to achieve this, as does improving drug-resistant gonorrhoea detection. Evidence is moderate, as evidence of national uptake as actionable data is not yet clear.
- Outcome 1: The plausibility of achieving outcome 1 ***"International focus and funding in tackling AMR in LMICs research increased"*** is moderate, as the potential to leverage external funds is not yet realised. The strength of evidence is high.
- Outcome 2: The plausibility of achieving ***"Innovative solutions tested and moved up through the R&D Pipeline"*** is high, as this has been demonstrated for both outputs (Documentation and KIIs). The evidence strength is high.
- Outcome 3: The plausibility of achieving ***"Improved supply of appropriate and affordable products & tools for combatting AMR available to LMICs"*** is high, as it is likely one or more projects will prove sustainable. The strength of the evidence from KIIs and documents is high.

- Outcome 4: The plausibility of achieving Outcome 4 ***"Behaviour change in industry and clinical practice on LMICs from clinical practice pilot programmes"*** is moderate, as the projects have yet to be demonstrated to change or influence practice but could do so. The strength of evidence, from KIIs and documentation, is high.

Work Package 6

Based on the evaluation evidence, the plausibility of GAMRIF's GARDP investment contributing to the relevant output and outcome measures has been summarised in the text and table below.

WP 6 CA matrix			
		Plausibility of contributing to outcome	Strength of evidence
Output	1. Encouragement of international partners to research innovative concepts tackling AMR in LMICs	5	5
	2. High-quality research that aims to: Reduce the need for antibiotics through alternative medicines and vaccine development	-	-
	3. High-quality research that aims to: Reduce the need for antibiotics in farming of food producing animal	-	-
	4. High-quality research that aims to: Reduce the environmental pollution of resistant bacteria and antibiotics	-	-
	5. High-quality research that aims to: Improve the measurement of clinical data and its uptake into national level surveillance	-	-
Outcomes	1. International focus and funding in tackling AMR in LMICs research increased	5	5
	2. Innovative solutions tested and moved up TRL through the R&D Pipeline	5	5
	3. Improved supply of appropriate and affordable products & tools for combatting AMR available to LMICs	4	4
	4. Behaviour change in industry and clinical practice on LMICs from: research evidence into economic incentives and national policy; Food security evidence; Clinical practice pilot programmes	3	3

Plausibility of Contribution key: 1 - Negative; 2 – Not Clear; 3 – Somewhat Plausible; 4 – Plausible; 5 – Highly Plausible **Strength of Evidence key**: 1 – Negative Evidence; 2 – No Evidence; 3 – Weak Evidence; 4 – Moderate Evidence; 5 – Strong Evidence

- Output 1. The plausibility of GAMRIF's CARB-X investment contributing to the outcome ***"Encouragement of international partners to research innovative concepts tackling AMR in LMICs"*** is high, for reasons summarised in the EQ 1/value add section. The strength of evidence is high, for reasons summarised under EQ 1&2. The strength of evidence is high, based on solid evidence collected through KIIs and document review
- Outcome 1. The plausibility of GAMRIF's investment through CARB-X contributing to ***"International focus and funding in tackling AMR in LMICs research increased"*** is high and strength of evidence is high – see comments under Output 1.
- Outcome 2. The plausibility of contributing to "***Innovative solutions tested and moved up the TRL through the R&D pipeline"*** is high; the right mix of activities are being funded and the delivery partner is delivering efficient and effective portfolio management and support to PDs, producing good interim results. Strength of evidence for this conclusion is high, based on GARDP reporting to GAMRIF, KIIs and data reviewed.
- Outcome 3. The plausibility of contributing to ***"Improved supply of appropriate and affordable products & tools for combatting AMR available to LMICs"*** is medium-high, as GARDP's candidates are later stage and therefore have a higher chance of resulting in product market entry, use, health impact and savings. However, there is still a need to secure manufacturing and market authorisation holder partners, determine other specifics of commercialisation

including a complementary diagnostic strategy, and secure further funding. Strength of evidence for this conclusion is medium-high.

- Outcome 4. The plausibility of contributing to ***"Behaviour change in industry and clinical practice on LMICs from research evidence into economic incentives and national policy"*** is medium at this stage. GARDP is a "push" incentive which has focused on a few priority AMR needs in LMICs. Because of this narrow prioritisation and focus on LMICs preferentially, it cannot be expected to have wide economic incentive effects, although within the narrow indications of neonatal sepsis and STIs it may indeed influence national policies, treatment algorithms and clinical practice. Strength of evidence is medium for this conclusion; even though GARDP's work is closer to market, influencing clinical practice is a long way off and more substantive industry behaviour change will require a mix of push and pull incentives extending beyond a few LMIC-targeted priority needs.

Work Package 7

GAMRIF investments in WP 7 are intended to lead to the overall GAMRIF programme ToC outputs of 1. ***"Encouragement of international partners to research innovative concepts tackling AMR in LMICs"*** and 2. ***"High-quality research that aims to: Reduce the need for antibiotics through alternative medicines and vaccine development"***. Based on the evaluation evidence, the plausibility of GAMRIF's BactiVac investment contributing to the relevant output and outcome measures has been summarised in the text and table below.

WP 7 CA matrix

		Plausibility of contributing to outcome	Strength of evidence
Output	5. Encouragement of international partners to research innovative concepts tackling AMR in LMICs	4	4
	6. High-quality research that aims to: Reduce the need for antibiotics through alternative medicines and vaccine development	5	4
	7. High-quality research that aims to: Reduce the need for antibiotics in farming of food producing animal	-	-
	8. High-quality research that aims to: Reduce the environmental pollution of resistant bacteria and antibiotics	-	-
	9. High-quality research that aims to: Improve the measurement of clinical data and its uptake into national level surveillance	-	-
Outcomes	1. International focus and funding in tackling AMR in LMICs research increased	4	3
	2. Innovative solutions tested and moved up TRL through the R&D Pipeline	4	3
	3. Improved supply of appropriate and affordable products & tools for combatting AMR available to LMICs	4	3
	4. Behaviour change in industry and clinical practice on LMICs from: research evidence into economic incentives and national policy; Food security evidence; Clinical practice pilot programmes	3	3

Plausibility of Contribution key: 1 - Negative; 2 – Not Clear; 3 – Somewhat Plausible; 4 – Plausible; 5 – Highly Plausible **Strength of Evidence key**: 1 – Negative Evidence; 2 – No Evidence; 3 – Weak Evidence; 4 – Moderate Evidence; 5 – Strong Evidence

- Output 1. Based on the evaluation evidence, the plausibility of GAMRIF's WP 7 investment contributing to the outcome ***"Encouragement of international partners to research innovative concepts tackling AMR in LMICs"*** is medium, for reasons summarised in the EQ 1/value add section. The strength of evidence is medium, based on consistent but relatively limited evidence collected through the funders' reports, KIIs and one FGD.

- Output 2. The plausibility of GAMRIF's WP 7 contributing towards ***"High-quality research that aims to: Reduce the need for antibiotics through alternative medicines and vaccine development"*** is high, for reasons summarised under EQ 2. The strength of evidence is medium, based on consistent but relatively limited evidence collected through the funders reports, KIIs and one FGD.
- Outcome 1. The plausibility of GAMRIF's investment through BactiVac contributing to ***"International focus and funding in tackling AMR in LMICs research increased"*** is high and strength of evidence is medium – BactiVac delivery team and grantee feedback suggests connections between LMIC academics and industry/UK partners are being further solidified through direct collaboration as well as meetings or webinars where bacterial vaccines have been promoted and communicated through social media.
- Outcome 2. The plausibility of GAMRIF's WP 7 investment contributing to ***"Innovative solutions tested and moved up the TRL through the R&D pipeline"*** is high; the right mix of activities are being funded and the delivery partner is delivering efficient and effective portfolio management and support to PDs, producing good interim results. Strength of evidence for this conclusion is medium, based on the funders' reports, KIIs and one FGD.
- Outcome 3. The plausibility of WP 7 contributing to ***"Improved supply of appropriate and affordable products & tools for combatting AMR available to LMICs"*** is low-medium, only because BactiVac's candidates are early stage and will require significant contributions by others outside of GAMRIF and BactiVac's direct control, in order for GAMRIF's contributions to ultimately result in product market entry, use, health impact and savings. However, for reasons explained under EQ 3, BactiVac research grants are exploring new tools in LMIC settings, such as "pain free, practical and cheap" needleless vaccine under WP 7 which demonstrated equally effective results to a direct injection, with less resource and time required for administering the treatment. Strength of evidence for this conclusion is medium, based on the funders' reports, and KIIs with delivery team.
- Outcome 4. The plausibility of WP 7s investments contributing to ***"Behaviour change in industry and clinical practice on LMICs from research evidence into economic incentives and national policy"*** is low at this stage, only because BactiVac's candidates are early stage and will require further time and contributions by others outside of GAMRIF and BactiVac's direct control, in order to demonstrate translation from research evidence into policy and clinical practice. Strength of evidence for this conclusion is medium, based on KIIs and one FGD.

Annex 4: List of stakeholders

	KIIs	FGDs	Stakeholder group	
WP 1	8 (9 interviewees)	2 (5 participants)	Cardiff University CIEL Innovate UK – delivery team KTN Moredun Research Institute Hong Kong University UKRI China Warwick University	Antibiotic R&D funders JPIAMR German Federal Ministry of Education and Research (BMBF) ReAct MRC Research project grantees
WP 2	9 (12 interviewees)	0	BARDA Boston University CARB-X delivery team FCDO FCO (UK Consulate, Boston)	Wellcome Trust Newton Fund Grand Challenges Fund NIH/NIAID Fleming Fund
WP 3	9 (13 interviewees)	3 (8 participants)	IDRC delivery team FAO FCDO Dimagi FCDO FIND project ILRI IVVN Wilton Park Research project grantees	LVIF (IDRC) Nanobubble project OIE RA-ELECT Royal Veterinary College The Pew Trust Charitable Trust VMD Wellspring Development Capital
WP 4	5 (5 interviewees)	2 (2 participants)	BBSRC BEIS FCDO CONICET Loughborough University McGill University NERC	University of Bristol University of Calgary University of Edinburgh University of Exeter University of Nottingham University of Warwick Research project grantees
WP 5	6 (8 interviewees)	0	CARB-X CGIAR (Grant recipient) CHAI Dimagi	FIND GARDP LSHTM Nesta
WP 6	4 (7 interviewees)	0	GARDP delivery team BARDA NIH/NIAID	
WP 7	4 (4 interviewees)	2 (5 participants)	BactiVac delivery team Research project grantees	
Portfolio Level / Cross-cutting	13 (17 interviewees)	0	GAMRIF staff BEAM Alliance / DaVolterra BEIS BMGF bioMerieux Bloomsbury SET BSAC DIT Drug Discovery Unit, Dundee EPSRC FAO (UK embassy, Hanoi) FCDO	GALVmed Health Innovation in a Virtual Environment (HiVE) Independent Academics IDS Janssen Diagnostics JPIAMR Lion's Head London School of Economics LSHTM Nesta PHE University of Cape Town

			Swedish University of Agriculture UKCDR Zoetis Independent AMR academics	University of Dundee Wellcome Trust WHO
TOTAL	58 (75 interviewees)	10 (21 participants)		

Annex 5: Topic Guide

▶ Overarching EQ and sub-EQs	Across entire portfolio	Work Packages 2, 6 & 7	Work Packages 1 &4	Work Package 3	Work Package 5
Question 1: Relevance and coherence: Has GAMRIF allocated resources strategically towards potentially high impact activities aligned with global priorities, taking into consideration needs and gaps not already well filled by others, and considering GAMRIF's comparative advantages and goals? Sub-EQs: To what extent have GAMRIF investments been aligned and are coherent with AMR needs outlined in GAP and considering gaps not filled by other funders/partners, representing a clear value-add? How is GAMRIF different to other AMR research programmes?	How well is GAMRIF aligned with global frameworks and priorities? Have investments been aligned or has there been duplication or overlap? What needs were identified? How were activities to address these prioritised? Have needs and priorities changed? Has GAMRIF responded flexibly to these changes? Are stakeholders aware of GAMRIF funded activities? What is their view of the relevance of these? What are GAMRIF's strengths and comparative advantage relating to this WP? Is it important that GAMRIF (as opposed to others) funds this work? How is GAMRIF complementing and	In your view, what is the comparative advantage of GAMRIF as compared to other partners? Conversely, what AMR challenges are not strong for GAMRIF (should be left to other partners)? What features of the R&D ecosystem are within vs. outside the direct control of CARB-X, GARDP and BactiVac which are enabling/hindering R&D and progression to market? (e.g regulatory environment, finance) Which partners are working/should be working on these "eco-system" areas? Any role for GAMRIF? (Q for GAMRIF and other UK partners) How have investment decisions been aligned/synergised with any similar programming supported through e.g JPIAMR, Newton Fund, Grand Challenges Fund, Fleming Fund, DHSC GHR programme etc, FCDO research and evidence directorate team (RED). Any opportunities for improvement in synergy?	In your view, what have been the strengths of using a bilateral partnership model as compared to other approaches used in GAMRIF (global initiatives, product development partnerships) or in the sector more generally? What have been the challenges? Are the projects funded by WP 1 and 4 relevant to LMIC needs in relation to AMR? Why or why not? How did the bilateral partners (UK-China/UK-Argentina) ensure that selected projects were relevant to LMIC needs? How have investment decisions been aligned with those of other HMG funds working in AMR, especially with ones specifically working in China/Argentina (ex: Newton Fund work in China)? How have investment decisions been aligned/synergised with any similar programming through the	In your view, what is the GAMRIF-IDRC partnership offering to AMR mitigation in the farming/veterinary field that is not being sufficiently addressed elsewhere? Is the InnoVet-AMR project complementing or adding value to the LVIF program? Are the (known) projects sufficiently integrated with the broader farming industry and with national programs, and what is the likelihood of learnings from the projects being disseminated and taken up more widely within farming communities? Are the projects selected and the overall programme relevant beyond the partners selected for funding? More specifically, are (specific known projects) of relevance across farming	Is GAMRIF funding to FIND likely to significantly influence diagnostic development towards reducing AMR pressure? Are the paths mapped out in the proposal likely to impact antibiotic use? Will the proposed areas of work – new diagnostics development and data management – be likely to reduce pressure towards AMR in LMICs? (i.e., Are the major factors leading to AMR likely to be reduced through improved diagnosis?) Is the project to assess screening technologies for medicine quality (detection of sub-standard and fake medicines) likely to complement work already in this area? How will it complement and support the work of WHO in particular? How will the proposed funding leverage and complement other projects under way within FIND?

What are its unique selling points? To what extent has GAMRIF's comparative advantages influenced choice of investments? What other/alternative things should GAMRIF be doing to achieve its goal and objectives?	reinforcing other UK investments in AMR? In what areas can/has GAMRIF most effectively played a leadership role? How has GAMRIF worked in partnership with others to ensure complementarity and coordinated efforts? Are there other areas of work that might make a greater contribution to the objectives?	Where is the greatest risk for duplication or misalignment? Conversely, what examples can you think of where the sum has been greater than the parts?	Chinese/Argentinian government? Are there any opportunities for improvement in synergy/alignment within UK funded programmes or with other China/Argentinian work? What is the greatest risk for duplication or misalignment?	and geographic boundaries? Are the individual projects selected for funding likely to compete or are they complementary to each other in addressing AMR? (i.e., is there redundancy if all projects are successful). Are there any major gaps in the field that are not being addressed by the projects funded? If so, what are these? Would they add greater or lesser VfM than those selected? Are there known competitor technologies or approaches that are likely to render the *known) project(s) redundant and/or ineffective?	What difference in outcomes can be expected to existing projects? Are there significant changes in the landscape since the program was formulated that require a rethink of priorities and purpose? Is FIND an appropriate organisation to address each of the purposes of the funding (data capture and transfer from diagnostics, diagnostic development), or are other groups better positioned in one or other of these areas? Are there obvious gaps that FIND is not addressing in the areas covered by the investment?
Question 2: Effectiveness (intermediate results) and efficiency: Does the current design and management of GAMRIF's portfolio (and the delivery partners' efficiency and effectiveness) allow it to effectively maximise its impact and objectives?	Has GAMRIF struck the right balance of resource allocation (time and budget) between Work Packages and activities, to achieve the intended objectives? Does the mix of activities funded produce a sum greater than its parts?	How is continual engagement and synergy maintained with JPIAMR, Newton Fund, Grand Challenges Fund, Fleming Fund, DHSC GHR programme etc, FCDO research and evidence directorate team (RED). Any opportunities for improvement? How does CARB-X, GARDP and BactiVac ensure continued focus on innovation? (e.g novelty of applications against WHO 4 criteria, #	How is continual engagement and synergy maintained with other HMG funds working in AMR, especially with ones specifically working in China/Argentina (ex: Newton Fund work in China)? In your view, how has the bilateral partnership model	How likely are reduction or modifications in the specific (known) projects funded likely to translate into reduction in pressure towards AMR in humans should they achieve their objectives? Are the timelines sufficient to achieve tangible outcomes for the (known)	Is the timeline and funding envelope likely to be sufficient to achieve intended outcomes for 1. Data management activities, 2. Diagnostic development Are these activities likely to complement each other? Are there other mechanisms and programmes that could be leveraged to improve the

Are there opportunities to improve ways of working towards better efficiency/effectiveness? Sub-EQs How effective is GAMRIF's multiple delivery mechanism at achieving its objective? Are there any other delivery mechanisms that could be explored? How efficient and effective is DHSC in managing GAMRIF? Are there any constraints to effective management of any of the Work Packages? To what extent do delivery partners' services (admin, technical oversight, financial reporting/, running competitions etc.) provide good VfM? Does reporting from each delivery partner provide DHSC with sufficient information to manage the programme efficiently?	Are there synergies of an operational or strategic nature to the mix of activities chosen? If there were any weaknesses in the mix of Work Packages chosen, what were the lessons learnt? Has GAMRIF had to shift its approach owing to changing context or unexpected challenges, which caused a rethink? Are there any cases where a refocus was warranted but didn't happen? What are the challenges vs opportunities in GAMRIF working across technology types (therapeutics, diagnosis and preventatives) and across the entirety of one-health? Can you point to any examples of GAMRIF acting as facilitator or influencer in this space (i.e., performing a role beyond that of solely a grant organisation)? Is GAMRIF working with/trying to influence, the right partners/actors?	of repeat submissions, geographic concentration). Does CARB-X do anything to understand who is not applying and why e.g avoidance of access provisions, IP concerns, avoidance of paperwork/extra hoops required by funders? How has the addition of GAMRIF ODA funding affected CARB-X's portfolio (candidate selection in terms of non-traditionals and alternatives to anti-biotics?) and developer profile? What have been the implications (of the addition of GAMRIF/ODA funding) in terms of CARB-X, GARDP and BactiVac management capacity and managerial processes? What have been the benefits vs burdens or risks of these changes? Is CARB-X tracking and reporting on how long does it take to pass from one stage to next of development, e.g Hit to lead, lead optimisation etc. How does this compare to industry benchmarks? Is CARB-X/GARDP/BactiVac able to track and report on the cost of each R&D stage? Is CARB-X/GARDP/BactiVac able to compare what the research partners are budgeting/spending for key R&D inputs and compare this to	worked from a WP management perspective? How is progress by different project teams being tracked by and reported to GAMRIF? How much synergy is there between GAMRIF's oversight and M&E systems and the management processes of their bilateral partners (MoST/CONICET)? Have suitable processes been put in place for administering and monitoring grants on both the UK and the China/Argentina sides? Are there examples of areas where this has worked particularly well? Any particular areas of challenge? Why is this the case? What – if any – impact did GAMRIF workshops and partnership-building activities (will tailor to WP) have on the quantity and quality of grant applications received? Do you think these activities represented good VfM in supporting effective bilateral partnerships/consortiums? What	projects? What strategies could be applied to ensure continued progress after the funding period? Is contact and feedback with IDRC addressing grantee needs and improving the likelihood of success? Are there ways in which quality and efficiency of monitoring and feedback can be improved? Are there significant farmer groups that will be excluded from access to the proposed products due to the nature of the product or other areas within or beyond the purview of the program? Are funded projects on track to deliver on their commitments – not only in terms of outputs/products but also in terms of timeline and budget? If no, what have been the main challenges in meeting these expectations? Is the financial and data flow from IDRC sufficient and timely in order to ensure smooth operation of the (known) project?	effectiveness of the GAMRIF investment? Are there known redundancies or duplications in the three areas of activity that are being better addressed by other groups, or likely to become redundant due to development of other technologies? Is the programme sufficiently complementary to, or synchronised with, the work of WHO in this area and that of other relevant agencies? Are funded projects on track to deliver on their commitments – not only in terms of outputs/products but also in terms of timeline and budget? If no, what have been the main challenges in meeting these expectations? Are the projects sufficiently integrated into national health systems and the work of major stakeholders in this area? Is there sufficient dialogue between FIND and other players to ensure this? Is the funding complementing other UK HMG funding to FIND? Is there any duplication or opportunities that could be

Are there any changes required to the programme and Work Packages' design in order to improve its VfM (economy, efficiency, effectiveness and equity)?	Is the sequencing of activities supported appropriate? How has GAMRIF leveraged its ability to be flexible and responsive?	benchmarks to ensure not overpaying? How does the CARB-X accelerator process work? Who are the accelerators, what expertise do they provide? How many grantees have accessed accelerator support, what sort of support is being accessed (& specifically by LMIC firms) at what cost & what impact it has had e.g on speed to complete the stage? Is CARB-X tracking how many projects are terminated, at what stage and why? Are post-mortems conducted on projects that fail – would it have been possible to terminate that project earlier? (e.g was there a critical experiment that could have stopped that project earlier?) What are current plans for how to better catalyse work on treatment and diagnosis targeting LMIC pathogens & presentations/ platforms appropriate to LMIC health systems? Has any thought been given to widening CARB-X technology scope to consider innovations in primary	could have been done differently to improve effectiveness? Were enough good-quality grant applications submitted during the competition for WP 1/4 projects? If yes, what factors do you think contributed to this? If no, what do you think could have been done to improve the quantity and quality of applications received? How did the project selection process work? How did the bilateral partner agencies (UK-China, UK-Argentina) choose projects? How effective was that system at ensuring GAMRIF priorities were represented by selected projects? How did GAMRIF make sure that selected projects met ODA eligibility? Are funded projects on track to deliver on their commitments – not only in terms of outputs/products but also in terms of timeline and budget? If no, what have been the main challenges in meeting these expectations? Has the bilateral partnership model had any impact (positive or negative) on projects' ability to	Is the 'wrap-around' programme to support grantees in product development for market and market entry strategy fit for purpose, and effectively being utllised?	leveraged to increase efficiencies? Was the selection process of FIND in line with expectations of GAMRIF? Were there high-quality proposals that clearly fitted the purposes? Is the support and feedback from FIND to the project partners clear, timely and sufficient for purpose? Are the skill sets available for support from within FIND appropriate and adequate? Are there competitors or potential partners /collaborators that should also be engaged to provide better VfM for health systems? Are the data management apps compatible with current digital data standards and likely to remain so for the foreseeable future? Are the funded projects likely to deliver the intended products within the time period of the funding package?

		care (bearing in mind BMGF investments here)? What efforts if any are being made to improve quality of discovery science, e.g any partnering with others with wider geographic presence as conduits for applications? How does the Scientific Advisory Board (SAB) process work in terms of ensuring best projects proceed and others are killed? What influence does GAMRIF have at the governance level? How has this influence been used? What have been the progress and challenges with regard to open access publications and research transparency & what has been GAMRIF's role?	deliver expected outputs/projects on time and within budget?		
Question 3: Effectiveness, impact, and sustainability: Are there indications that the GAMRIF programme has produced positive change likely to contribute to sustainable impact? Sub-EQs	[*Following review of M&E data*] Have logframe indicators been met? Is the trajectory suggesting they will be met? What have been the main challenges/risks relating to the logframe target? Were initial assumptions correct? Have other stakeholders done what was expected?	(In addition to the portfolio level questions) What evidence is there on indicators such as: TRL progression; engagement of LMICs researchers; pilots (incl. clinical trials) in LMICs underway; research publications & presentations; funding leveraged Does CARB-X monitor what happens to graduates, including their access to follow-on funding, to better	What evidence is here on indicators such as TRL progression; pilots (incl. clinical trials underway); research publications, presentations, policy briefings, and best practice position papers, particularly as they relate to accessibility and relevance to LMICs? In your opinion, have the bilateral partnerships enabled	In documents reviewed, there was reference to social science being integrated into some Work Packages (WP 3 and WP 4) related to stewardship and uptake – what is the nature of the work? Are the expected outcomes likely to be transferable to other farming communities and /or livestock areas?	Are there plans in place to ensure continuity and/or expansion of programmes after GAMRIF funding ends? Is there sufficient market opportunity to sustain the diagnostics tests under development in an open market? Are there major competitor technologies that may affect their viability?

To what extent have programme outputs and outcomes been achieved / are likely to be achieved? What factors have provided: i) most support; and ii) the primary challenges to GAMRIF staying on track to achieve its desired objectives? What evidence is there that demonstrates the potential for LMIC access and uptake of products when they are developed in years to come? What more could be done to ensure access and uptake? How could GAMRIF maximise R&D outputs that will lead to successful product development? How can GAMRIF and/or a potential successor R&D programme adapt in line with learning from the ToC and its assumptions?	What else needs to happen for medium- and longer-term outcomes to be achieved? Looking within the WP, is anything missing that would enhance catalytic impact? Looking across the Work Packages, is anything missing that would enhance catalytic impact? What have been the main achievements and successes of GAMRIF? What would have happened without GAMRIF support or involvement? Is there any evidence of impact on policies, systems, institutions, practices? Have there been any unexpected impacts or benefits? Will impact achieved be sustained? What is GAMRIF doing to ensure sustainability of activities, initiatives and outcomes? Are there any Work Packages or activities that have not performed/delivered results as expected? Why?	understand how to support towards impact? What is the guidance given to grantees/developers on stewardship & access (S&A)? How was this guidance developed (incl. GAMRIF role)? Is any support given to developers to draft the plans? What happens if the plans are not of adequate quality? What options (if any) would CARB-X, GARDP and BactiVac have if the plans are not eventually operationalised (any IP claw back clauses?) What do you see as the key risks with the plans not being operationalised? Are the S&A agreements only applicable to ODA funded work or to all CARB-X, GARDP and BactiVac grantees? Looking at the value chain/pipeline from early discovery through to access and stewardship, where are the biggest gaps that may impede the trajectory towards outcomes and impact? GAMRIF + partners early-stage investment will be wasted if the market failures persist – what	support to the wider UK AMR diplomatic strategy? Has the UK's wider UK AMR diplomatic strategy supported effective delivery of GAMRIF bilateral partnerships? If yes (in either case), please provide examples. Do you expect the GAMRIF bilateral partnerships to enable support to the wider UK AMR diplomatic strategy in the long term? Why or why not? Do you think the investments made in building bilateral partnerships and consortium for GAMRIF-funded projects will result in sustainable partnerships between researchers and/or companies in the UK and bilateral partners (China/Argentina)? Why or why not? What could be done to further support the sustainability of these partnerships? What is the likelihood that there will be continued support for research into under-funded/innovative areas of AMR covered by WP 1 and/or 4 by GAMRIF's bilateral partners (China/Argentina)? What has	Are there reasonable expectations of continued use and expansion of products once the funding period is completed – or is there a clear need for extended funding to ensure a credible chance of success? Will LVIF have mechanisms to consider support for projects after the GAMRIF funding period is compete? What other mechanisms are available to give such support? What are the major risks that would result in failure to operationalise the products of the (known) projects? What mitigation strategies could be considered to reduce these risks? What is the likelihood that the work funded by GAMRIF will stimulate wider investment in the field and improved product development and delivery of other vaccine and antibiotic replacement products more widely?	Who are the likely procurers of diagnostic tests and apps developed under this WP and are they sufficiently engaged in the process of TPP development and market strategy development? Are there clear paths to improve antibiotic use from the current projects under the two purposes? Is there a clear path for the TPPs developed under this WP to be adopted by future developers and manufacturers? Is there WHO support in place for this? Are country infrastructures sufficient to take advantage of improved data flow arising from the initiatives funded in this WP? Are there other parallel developments that need to be implemented, or supported, to ensure this and achieve better VfM?

	What developments are there in relation to implementation science conducted to develop contexts for innovations? GAMRIF enables support to UK wider international AMR diplomatic strategy and in turn effective delivery of GAMRIF is supported by the same – any case studies here to tell this story?	opportunities might there be for GAMRIF to address?	GAMRIF's role been in generating any continued interest/support? WP 4 Only: How was social science work related to stewardship and uptake integrated into projects funded through this WP? Has it had any relevance/synergy with other Work Packages? What is the nature of the work? How likely is this work to yield meaningful findings related to stewardship and uptake that are both relevant and accessible to LMICs? Why is this the case? WP 4 Only: In your opinion, how likely are funded projects to produce outputs that translate research into AMR policy in a way that is relevant, accessible, and used by LMICs? Why is this the case? What, if anything, could be done to increase relevance, accessibility, and/or use?		

Annex 6: Contribution Analysis – Judgement Criteria

The below table sets out scoring against judgement criteria for assessing strength of evidence. The assessment of plausibility of contribution towards linked outcomes against high level EQs was undertaken through a summary of high-level findings from the Work Packages, as outlined in Annex 3.

Score	Descriptor	Judgement criteria for Strength of Evidence
5	Strong evidence	Clear, direct causal association between specific GAMRIF inputs/activities and outcomes, with detailed examples provided as to how the programme has supported change. Corroborated by multiple sources and stakeholders, including official documentation (e.g policy, strategy or programme documentation) and stakeholder interviews and focus groups. The team will judge strength of evidence based on quantity of evidence (number of people who share the perspective), alignment with other pieces of evidence, as well as the source and centrality of stakeholders to the evidence content area. If a source is highly credible and central to the content, it may be appropriate to include the perspective of a single KI rather than dismiss it, even if there is deviation from the dominant narrative presented in GAMRIF reporting.
4	Moderate evidence	Some indication of direct causal association between specific GAMRIF inputs/activities and outcomes, although link is inferred rather than concrete. Corroborated by more than one source (e.g documentation and two-three stakeholder interviews), but with limited examples as to how the programme has supported change
3	Weak evidence	Indication of direct causal association between specific GAMRIF inputs/activities and outcomes, but no detailed examples of provided as to how the programme has supported change. Only cited by one-two sources (e.g one stakeholder or unofficial documentation)
2	No evidence	Very limited/no information to form judgements about the pathway between GAMRIF inputs, activities and outcomes
1	Negative evidence	Evidence that GAMRIF inputs and activities have had a negative impact in achieving specific outcomes.

Annex 7: Documents Consulted, by WP

Work Package (WP)	Documents Consulted by Work Packages
WP 1	• Memorandum of Understanding between DHSC and Innovate UK. • Memorandum of Understanding between DHSC and MoST. • 2018-2019 Annual Report. China-UK Antimicrobial Resistance Collaboration
WP 2	• Pre-grant assessment report. Boston University (CARB-X) • Year 1 Programmatic Report. CARB-X • Year 2 GAMRIF R&D Report. CARB-X • Year 3 CARB-X Annual Report. GAMRIF • CARB-X 2020 Conflict of Interest Audit Report • CARB-X Monthly Funders Reports 2018 to 2021 • GAMRIF Delivery Chain Map, June 2020 & May 2019-July 2019 • CARB-X Grant Proposal • CARB-X Assessment of Proposal • Memorandum of Understanding between DHSC and Boston University, and amendment • CARB-X Joint Oversight Committee Minutes • CARB-X Stewardship & Access Plan (SAP) Development Guide and email exchanges during the development process
WP 3	• InnoVet-AMR: Innovative Veterinary Solutions for Antimicrobial Resistance. InnoVet-AMR IDRC. • DHSC Joins global fight to tackle antimicrobial resistance in animals. DHSC Blog. • Report of the Meeting ff the OIE Ad Hoc Group on Prioritisation of Diseases for Which Vaccines Could Reduce Antimicrobial Use in Animals, Paris, 21 – 23 April 2015. OIE. • Prioritisation of Diseases for which Vaccines Could Reduce Antimicrobial Use in Animals. Dr Elisabeth Erlacher–Vindel (Head of Science and New Technologies Department OIE). • Global Call for Research Proposals: Innovative Veterinary Solutions for Antimicrobial Resistance (InnoVet-AMR) in Food-Producing animals: Livestock and Aquaculture, 2018. IDRC, DHSC. • InnoVet-AMR Interim Report to DHSC, December 2019. • IDRC Update, August 2019 • InnoVet Annual Technical Report, June 2019 • Wilton Park Inaugural Meeting • http://www.idrc.ca/en • Judicious Animal Antibiotic Use Requires Drug Label Refinements. PEW Trusts • Antibiotic Resistance Project. PEW Trusts • Alternatives to Antibiotics in Animal Agriculture. PEW Trusts • https://wellspring-development.com/ • http://www.fao.org/antimicrobial-resistance/en/

	• Antimicrobial Resistance Multi-Partner Trust Fund: Forging Tripartite collaboration for urgent global and country action against antimicrobial resistance (AMR). FAO • Innovative Veterinary Solutions for Antimicrobial Resistance Annual Report, April 1, 2020–March 1, 2021. IDRC • Programme Business Case (PBC) (Redacted version), 28 June 2019. Global Antimicrobial Resistance (AMR) Innovation Fund. • Innovations to reduce the use of antimicrobials in food-producing animals in LMICs (Workshop Report), Wilton Park, 11 – 13 April 2018 • InnoVet-AMR Innovative Veterinary Solutions for Antimicrobial Resistance, Governance Steering Committee Meeting, 20 May 2021 • GAMRIF Portfolio • IDRC Assessment of Proposal • Grant Agreement between DHRC and IDRC, and amendments • Innovative Veterinary Solutions for Antimicrobial Resistance Annual Report, June 2021. DHSC
WP 4	• Memorandum of Understanding between DHSC and BBSRC, April 2018 • Programme Business Case, June 2019. GAMRIF • Annual Review, 2017-19. GAMRIF • Annual Review, 2019-20. GAMRIF • BBSRC-CONICET Argentina AMR funding paper, March 2019 • UK-Argentina Project Application presentation, November 2018 • WHO Global Action Plan on AMR, 2015 • Drug-Resistant Infections: a threat to our economic future, March 2017. World Bank, • https://devtracker.fcdo.gov.uk/projects/GB-GOV-10-GAMRIF-WP 4-UK-Argentina • Projects supported by DHSC through the Global AMR Innovation Fund. DHSC • GBP 5 million given to AMR research partnerships between UK and Argentina. DHSC • Convocatorias y Oportunidades (Calls for Expression of Interest and Opportunities). CONICET • Evidence synthesis on the conditions needed to translate research and drive innovation. RAND Europe • Global Action Plan on Antimicrobial Resistance: two years of progress. WHO • Contained and controlled The UK's 20-year vision for antimicrobial resistance. HMG
WP 5	• UK Government Collaborates With Find To Boost Diagnostic Connectivity To Help Combat The Global Threat Of Antimicrobial Resistance. FIND • Memorandum of Understanding between DHSC and FIND, 2018 • MOU Amendment Variation Agreement for Grant Agreement Dated 18 January 2019. • One Health Surveillance Platform for Antimicrobial Resistance Launched in Zambia. FIND • Ferreyra, Cecilia MD; Redard-Jacot, Maël MSc; Wi, Teodora MD; Daily, Jennifer MBA; Kelly-Cirino, Cassandra PhD. Barriers to Access to New Gonorrhea Point-of-Care Diagnostic Tests in Low- and Middle-Income Countries and Potential Solutions: A Qualitative Interview-Based Study, Sexually Transmitted Diseases: October 2020 - Volume 47 - Issue 10 - p 698-704 doi: 10.1097/OLQ.0000000000001238 • DHSC Progress Report FIND, April 2019 - September 2019

	• DHSC Progress Report FIND, October 2019 - March 2020 • Slides to accompany Q call FIND • DHSC Progress Report FIND, 6 December 2018 • DHSC Progress Report FIND, 14 June 2019 • DHSC Progress Report FIND (Updated Finances), October 2019 - March 2020 • DHSC Progress Report FIND April 2020 – September 2020
WP 6	• GARDP Business Justification • Grant Agreement between DHSC and GARDP • Uniting against antibiotic resistance - 5 by 25 Strategy. GARDP • GARDP 2020-21 Grant Application • Memorandum of Understanding between DHSC and GARDP • GARDP Assessment of Proposal • DHSC GARDP Grant Proposal • GARDP DHSC Meeting Slides & Presentations • GARDP DHSC FINAL Narrative Report. 26 July 2019 • GARDP DHSC FINAL Narrative Report, November 2019 • GARDP Delivery Chain Mapping, January 2020 • GARDP DHSC Narrative Report, May 2020 • GARDP DHSC Slides Meeting, May 2020 • GARDP DHSC STI Financial Report, May 20 • GAMRIF Quarterly Review • GARDP DHSC Slides, May 2021 • GARDP STI report to DHSC Oct 2020, March 2021
WP 7	• BactiVac End of Project Report. University of Birmingham & BactiVac • Application for a Department of Health & Social Care Grant For Financial Year(s) 2018/19 & 2019/20 - Bacterial Vaccinology (BactiVac) Network • Vaccines to tackle drug resistant infections an evaluation of R&D opportunities. Wellcome & The Boston Consulting Group • Catalyst Pump-Priming Projects. BactiVac Network, University of Birmingham
Portfolio Level	• Summary of Scope Prioritisation. GAMRIF • GAMRIF Project Board Terms of Reference. DHSC • GAMRIF Theory of Change Slides • GAMRIF Risk Register • GAMRIF Logframe

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