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Global AMR Innovation Fund (GAMRIF) Interim Evaluation

Executive Summary

December 2021

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 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.