IMI1 Final Project Report Public Summary

Project Acronym: DRIVE-AB

Project Title: DRIVING RE-INVESTMENT IN R&D AND RESPONSIBLE ANTIBIOTIC USE

Grant Agreement: 115618
Project Duration: 01/10/2014 – 31/12/2017

Abstract

Bacteria are becoming increasingly resistant to many antibiotics, and only few new antibiotics are being developed to combat them. Antibiotic resistance has become a global public health threat. It is estimated that antibacterial drug resistance costs the EU approximately EUR 1.5 billion and 25 000 lives each year. The development of new drugs to treat resistant infections is falling behind due mostly to economic and scientific hurdles. New economic models that offer incentives for the discovery and development of new antibiotics and reconcile these with responsible antibiotic use and access are long overdue.

DRIVE-AB was a public-private consortium funded by the Innovative Medicines Initiative (IMI) and derived from a 2013 IMI1 call for proposals. The project was launched in October 2014 and ended in December 2017. It was funded by IMI with in-kind support from EFPIA partners equivalent to one-third of the total €9.4 million funding awarded. DRIVE-AB was composed of 16 public and 7 private partners from 12 countries.

The overarching objectives of the DRIVE-AB project were to:

- Create, test and validate new economic models to incentivise the discovery and development of new antibiotics;
- Recommend to governments and policy-makers new economic models that stimulate innovation, responsible use and global access of novel antibiotics to meet public health needs;
- Quantify the value of new antibiotics;
- Define standards and metrics for responsible antibiotic use;
- Estimate the current and future impact of antibiotic resistance in order to determine future public health needs.

In its main activity, the consortium assessed more than 30 incentives gathered from different industries for how each would affect antibiotic innovation and sustainable use and equitable availability. The market entry reward, which DRIVE-AB recommends providing in addition to unit sales for qualifying antibiotics, aims to create a more attractive market for investment in antibiotic R&D designed to attract increased and sustainable private-sector funding. Based on its research, DRIVE-AB estimates that two innovative antibiotics addressing priority pathogens identified by the World Health Organization (WHO) could receive a market entry reward in the next five years. DRIVE-AB simulations predict that a market entry reward could bring to market 16 to 20 new truly innovative antibiotics in the next 30 years. Without incentives, some scientifically promising treatments would never make it to patients.

Of the incentives analyzed by the consortium, three additional models were determined to be most effective to stimulate R&D and ensure that critical antibiotics continue to be accessible and can be used sustainably: 1) non-refundable research grants; 2) governmental or non-profit pipeline coordinators that identify and fill gaps in the global antibiotic pipeline; and 3) long-term supply continuity funding to ensure a predictable supply of generic antibiotics over time.

All of the recommended incentives would include mandatory provisions for equitable access and sustainable use in order to ensure these critical medicines are available to patients that need them globally, and remain effective over time. These models are meant to be complementary and do not operate in isolation. Instead, they are designed to form an ecosystem that maximizes research and development while ensuring access and sustainable use of new antibiotics over time.

DRIVE-AB estimates that at least $800 million (Euros 680 million) is needed to fund grants and pipeline coordinators, an increase of about 50 per cent from the current public investments in antibiotic R & D made each year. The consortium posits that the recently-announced G20 Global R&D Collaboration Hub on AMR should be considered as one possible important approach to achieving high-level coordination for incentives. The G20 should work with member states and like-minded countries to agree to implement and finance a market entry reward over a period of 20 years, including common sustainable use provisions, according to DRIVE AB. Target product profiles, set by the WHO or another suitable body could serve to focus public and private investments to the areas of greatest unmet need for patients and society.

While market entry rewards are discussed and put in place, national authorities should address the economic challenges within their existing systems. DRIVE-AB provides suggestions for improving Health Technology Assessment processes to better capture the societal value of antibiotics in coverage and reimbursement decision-making.

DRIVE-AB project partners also compiled and assessed definitions and metrics of responsible antibiotic use across diverse socioeconomic, geographic and clinical settings. They delivered a systematic review of the variation in antibiotic use, analysing barriers to and enablers of responsible use. Finally, they developed a conceptual framework and consensus parameters for a widely accepted international standard of responsible antibiotic use.

Furthermore, DRIVE-AB published new models to describe the spread of resistant organisms. They determined the clinical impact of emerging multi-resistant pathogens across various settings, as well as quantified the economic consequences of antibiotic resistance from the perspectives of patients, health care providers and society. Finally, they expanded the model to predict the impact of propagation of multi-resistant pathogens in order to estimate the need for new antibiotics and inform clinicians and health policy makers.

In summary, DRIVE-AB's purpose was to transform the way policymakers stimulate antibiotic innovation, and to ensure that these new antibiotics are used sustainably and are available equitably. To achieve this vision, DRIVE-AB used a research-based approach with significant stakeholder input to build policy recommendations to incentivize antibiotic R&D. These DRIVE-AB recommendations were not unanimously agreed among all DRIVE-AB members, but do broadly reflect the results of the research carried out.

Executive summary

1. Project rationale and overall objectives of the project

Bacteria are becoming increasingly resistant to many antibiotics, and only few new antibiotics are being developed to combat them. Antibiotic resistance has become a global public health threat. It is estimated that antibacterial drug resistance costs the EU approximately EUR 1.5 billion and 25 000 lives each year. The development of new drugs to treat resistant infections is falling behind due mostly to economic and scientific hurdles. New economic models that offer incentives for the discovery and development of new antibiotics and reconcile these with responsible antibiotic use and access are long overdue.

DRIVE-AB was a public-private consortium funded by the Innovative Medicines Initiative (IMI) and derived from a 2013 IMI1 call for proposals. The project was launched in October 2014 and ended in December 2017. It was funded by IMI with in-kind support from EFPIA partners equivalent to one-third of the total €9.4 million funding awarded. DRIVE-AB was composed of 16 public and 7 private partners from 12 countries (see map below for location of partners).

The public partners included the British Society for Antimicrobial Chemotherapy (BSAC), Chatham House, the Centre for Anti-Infective Agents (CEFAIA), Heidelberg University, the London School of Economics and Political Science, the Norwegian Institute of Public Health, Radboud University Medical Centre, Tel Aviv Sourasky Medical Center, the University of Antwerp, the University of Geneva, the University of Lorraine, the University of Rijeka Medical Faculty, the University of Strathclyde, the University of Tübingen, Uppsala University and Wageningen University.

The EFPIA partners were Astellas Pharma Europe LTD, AstraZeneca AB, Merck Sharp & Dohme (replaced Cubist Pharmaceuticals GmbH), GlaxoSmithKline PLC, F. Hoffmann-La Roche Ltd, Pfizer Limited and Sanofi-Aventis Research & Development.

The overarching objectives of DRIVE-AB were to:

- Define standards and metrics for responsible antibiotic use;
- Estimate the current and future impact of antibiotic resistance in order to determine future public health needs;
- Quantify the value of new antibiotics;
- Create, test and validate new economic models to incentivise the discovery and development of new antibiotics;
- Recommend to governments and policy-makers new economic models that stimulate innovation, responsible use and global access of novel antibiotics to meet public health needs.

2. Overall deliverables of the project

Six work streams were established in parallel and worked together with a wide variety of stakeholders. Their overall deliverables included:

1. **Define "responsible" use of antibiotics:**

Project partners compiled and assessed definitions and metrics of responsible antibiotic use across diverse socioeconomic, geographic and clinical settings. They also aimed to deliver a systematic review of the variation in antibiotic use, analysing barriers to and enablers of responsible use. Finally, they developed a conceptual framework for an international standard of responsible antibiotic use.

2. **Set, communicate and revise public health priorities:**

Project partners developed mathematical prediction models of multidrug-resistant (MDR) pathogen spread from first detection to established endemicity. They then aimed to determine the clinical impact of emerging MDR pathogens and AMR and to generalize the impact across various settings. Finally, they expanded the model to predict the impact of propagation of MDROs in order to estimate the need for new antibiotics and inform clinicians and health policy makers.

3. **Develop antibiotic valuation models:**

Projects partners quantified the economic consequences of AMR from the perspectives of patient, health care providers and society. They developed novel valuation models that can quantify the value of new antibiotics from the perspectives of these different stakeholders.

4. **Create, test and validate new economic models:**

In this largest sub project, DRIVE-AB partners assessed the specific bottlenecks and risk perceptions affecting the development of antibiotics. They evaluated reward and business models in other industries that could also support stewardship and conservation and/or address key challenges similar to antibiotics. Once the most promising models were determined (those that deliver the greatest public health benefit with an acceptable net present value [NPV]), the partners then developed, exhaustively analysed, validated, and explored in detail the implementation of the most promising reward models, including funding sources. A final deliverable was to produce policy recommendations, present them to and gain buy-in from stakeholders.

5. **Stakeholder platform and external communication:**

A group of project partners aimed to identify and engage stakeholders through the development of a broad multidisciplinary stakeholder platform. In order to do that, they had to develop and

implement a comprehensive communication/engagement strategy that involved and engaged all stakeholders needed to support all the technical research work streams. Effective relationships were established via meetings with decision makers central to the implementation of a new business model by engaging them throughout the project. An important deliverable of this work stream was also to communicate effectively the project's findings and advances to the public.

6. Coordinate and manage the project:

A management team established a governance structure for the consortium, coordinated the different work streams and ensured their collaboration, supporting the implementation of any changes in activities of the network. This team also had to ensure and assist in day-to-day operational management of the consortium and monitor the effective execution of tasks and timely achievement of project deliverables and milestones. Finally, it also provided financial management of the consortium.

3. Summary of progress versus plan since last period

During the last year of the project, all research tasks were completed. Some were completed a few months later than planned which led to the request for a 3-month extension of the project (without budget increase) to deliver the final policy report.

Some of the research results have already been published, but some are still in the process of being published in scientific journals.

The final conference took place as planned in Brussels on September 5-6, 2017 to present the final DRIVE-AB recommendations to a wide range of stakeholders. The final policy report was released online on January 24, 2018, together with a news release.

4. Significant achievements since last report

- A commentary in the Lancet ID addressed to the G20 and entitled '*To the G20: incentivising antibacterial research and development*' was published in July 2017, for the G20 meeting that took place in Germany.
- A major achievement of the consortium was the organisation of the final DRIVE-AB conference, "*Revitalizing the antibiotic pipeline: Stimulating innovation while driving sustainable use and global access*", which was held at the Crowne Plaza Le Palace in Brussels, Belgium, on 5-6 September 2017. The conference attracted approximately 200 participants from a wide range of stakeholder groups, including policy-makers, medical professionals, representatives of the pharmaceutical and biotechnology industries, civil society communities, and regulatory and public health experts. The interactive two-day meeting was focused on the communication of the consortium's research results and recommended options to drive investment in antibiotics that included a combination of incentive mechanisms along with finance and governance options to support their implementation. DRIVE-AB presentations were complemented by external keynote speeches and panel discussions with high-level experts. Participants also had the opportunity to view 25 scientific posters summarizing the details of the consortium's research results.
- On January 24th, 2018, the DRIVE-AB consortium published its final policy recommendations in the form of a policy report. The report is entitled "*Revitalizing the antibiotic pipeline: stimulating innovation while driving sustainable use and global access*". This was a major undertaking

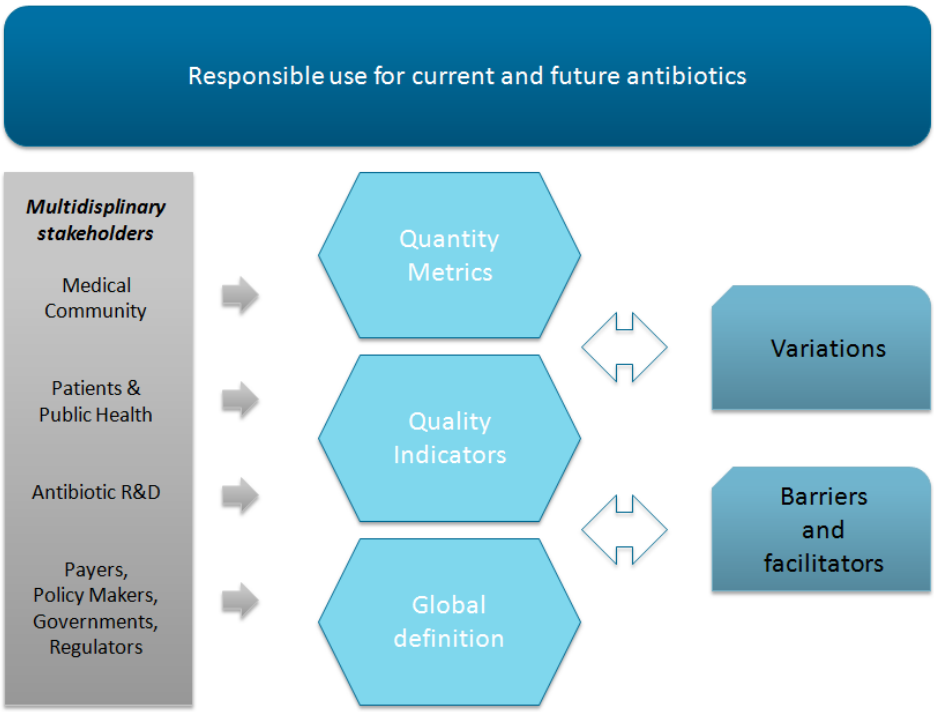
gathering the evidence from each part of DRIVE-AB and presenting it in a coherent and interlinked way.

- Data generated by the systematic review of the impact of AMR formed part of the evidence base that experts used to formulate the WHO's global priority list of antibiotic-resistant bacteria to guide research, discovery, and development of new antibiotics (also called the Priority Pathogens List – PPL). This list ranks the resistant organisms causing acute bacterial infections for which new antibiotics are most urgently needed and has been published both in a WHO report and in a more synthesized Lancet ID article, published online in late Dec 2017.
- Project partners worked actively with Germany as the leader of the G20 in 2017 regarding incentives to stimulate greater antibiotic innovation. Our contributions helped to influence the creation of the G20 AMR R&D Hub.

5. Scientific and technical results of the project

Over the course of the project, 6 work streams worked together with a wide variety of stakeholders to produce the following main results:

- The first work stream that looked at defining responsible antibiotic use provided a common terminology and framework for shared understanding of responsible and sustainable antibiotic use (see figure below). It also delivered broadly accepted metrics to monitor responsible use which could be used to inform stewardship programs, improve use of existing antibiotics, and prevent inappropriate use of newly developed molecules. These outputs are key to ensure that today's antibiotics remain effective for patients as long as possible as well. Using responsibly any new antibiotic will also be key to ensure it remains effective and available to patients as long as possible, especially if public funds have been used to support the R&D of such drugs.



The DRIVE-AB conceptual framework of responsible antibiotic use.

- The second work stream, which had for aim to set, communicate and revise public health priorities, used a novel approach to describe early signals for new emerging AMR, developed novel methodology to predict the spread of resistant organisms, and validated and calibrated these predictions based on updated data and preventive measures. The main results were that informative simulations can be performed on the past and future epidemiologic trends of AMR using already available data sources. Not surprisingly, the number of infections caused by antibiotic-resistant bacteria varies regionally. In Europe it is moderate but expected to rise. Countries with insufficient infection control measures should expect to see large increases. Moreover, the interval from early establishment of resistance to widespread need for new antibiotics may be brief in some countries. Finally, our predictions show that deaths from some resistant bacteria, such as carbapenem resistant *K. pneumoniae*, may double by 2050. These outputs can be used by public health bodies to have an estimate of the burden of antibiotic resistance in their country and maximise the impact of infection prevention measures.

- The third work stream that looked at the value of antibiotics provided novel approaches to evaluating antibiotics and capturing their value to patients, society and the health care system. The analysis revealed that increasing antibiotic resistance potentially threatens the safety and efficacy of surgical procedures and immunosuppressing chemotherapy. Significant value could be overlooked if antibiotics are assessed within the confines of current HTA methodology and without the consideration of the unique value attributes associated with these medicines. Further, this work stream proposes that practical solutions to include them in cost-effectiveness analyses may be feasible. Among more immediate applications, these methods will inform health technology assessment agencies in determining the value of new antibiotics from the payer perspective.

- The largest work stream developed granularity around incentive models that would stimulate antibiotic innovation while ensuring sustainable use and access. These models were quantitatively tested through the development of a computer modelling simulator.
  Looking first at the antibiotics currently in R&D, this work stream found that the current pipeline for innovative antibiotics in various stages of R&D is insufficient, potentially delivering no more than one innovative antibiotic for a "critical" WHO priority pathogen within the next five years.

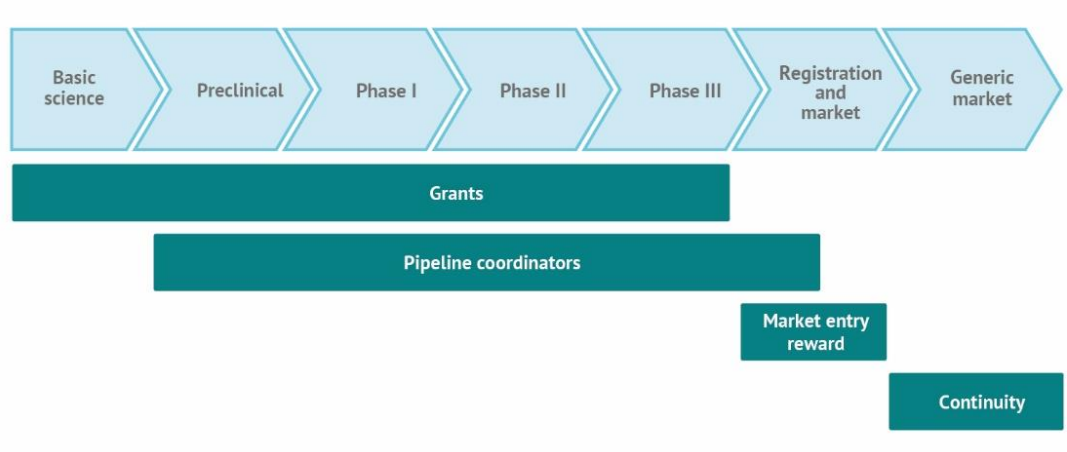
What are the DRIVE-AB proposed solutions?

The effective stimulation of antibiotic innovation requires a balanced combination of both "push" incentives (those designed to support R&D directly) and "pull" incentives (those designed to reward successful outcomes from R&D).
Four incentives were determined to be the most effective in stimulating the entire antibiotic pipeline and ensuring access and sustainable use (see Figure below).

- **Push incentives:**
  - Grants - non-repayable funds for R&D given to academic institutions, companies and others

- Pipeline coordinators - governmental or non-profit organizations that closely track the antibiotic pipeline, identify gaps, and actively support R&D projects both financially and technically to fill these gaps

- **Pull incentives:**
  - Market entry rewards - a series of financial payments to an antibiotic developer for successfully achieving regulatory approval for an antibiotic that meets specific predefined criteria to address a defined public health need, with obligations for sustainable use, equitable availability and supply
  - Long-term supply continuity model - a delinked payment to create a predictable supply of important generic antibiotics



The 4 DRIVE-AB recommended incentives cover all phases of drug R&D.

How can sustainable antibiotic use be embedded in incentives?

It is vital that any innovation incentive promotes the sustainable use antibiotics to ensure the longevity of the public-sector investment and continued benefit to patients. Principal antibiotic R&D funders and developers should agree to standard sustainable use and equitable availability principles that can be included in all pertinent push funding agreements. Sustainable use measures for developers should be contractually linked to both market entry rewards and long-term supply continuity awards.

How can equitable availability be ensured?

The need for novel antibiotics to treat multi-drug-resistant pathogens is global. Low- and middle-income countries are usually the last countries where patented antibiotics receive marketing authorization, delaying patient access. DRIVE-AB recommends that developers who receive a market entry reward be contractually bound to the equitable availability obligations:

- Developer must submit an access plan to the regulator
- Countries or other healthcare providers not included in the access plan can submit a letter of interest
- Developer must commit to provide all necessary data to WHO to develop antibiotic-specific policy guidance
- Developer commits to implement the access plan and monitoring activities.

Recommendations

Here are the twelve policy recommendations from the final DRIVE-AB policy report:

1. The G20 Global R&D Collaboration Hub on AMR should be considered as one possible approach to achieving high-level coordination for both push and pull mechanisms.

This high-level coordination should act to align public funding towards important investment opportunities. The hub is not intended to be an extensive new organization, and will not create a new pooled fund or determine how member states' contributions will be allocated. While the mandate of the hub is still under discussion, this is certainly an excellent opportunity for it to act as a coordinating body for market entry rewards as well as push models. Since it will function at a political level, operational pipeline coordinators can inform the hub about existing gaps.

2. The G20 should work with member states and other like-minded countries to agree to implement and finance a market entry reward for a 20-year period including common sustainable use and equitable availability provisions.

To test the operational implementation, a pilot between two or three countries would be appropriate, to be initiated immediately and lasting for one to three years. When it is fully operational, we recommend a partially delinked market entry reward of $1 billion per antibiotic for innovative antibiotics meeting predefined target product profiles (TPPs). The reward should be paid out over at least five years, with contractual obligations for the lifetime of the intellectual property. If infection control and stewardship programmes are effective, there will always be a need for a market entry reward because the consumption of novel antibiotics should remain modest. We recommend this 20-year period not to indicate that the problem will be solved, but to learn from the implementation and fix any unintended consequences. This period is long enough to determine the impact of the market entry reward on innovation. Any shorter assessment would be biased by the existing antibiotic pipeline.

3. The European Commission should work with member states to gauge interest in implementing a common European market entry reward.

Not all European countries will be interested in or able to contribute to a market entry reward, and those with the highest resistance levels would be better served by investing in improved national infection control and stewardship programmes. The European Union G20 countries are France, Germany, Italy and, until 2019, the United Kingdom. The Netherlands and the Scandinavian countries have also demonstrated strong public interest in AMR, including innovation. All European countries benefit from one overarching regulatory agency – the European Medicines Agency (EMA). They also benefit from the European Investment Bank (EIB), which is mandated to make a difference to the future of Europe and its partners by supporting sound investments that further European policy goals. DRIVE-AB sees potential in a group of like-minded European countries able to commit to pilot a European-based market entry reward paid out by the EIB for qualifying antibiotics approved by the EMA. It can be argued that Europe should be financially responsible for at least one-third of the cost of a global market entry reward. The European Commission's Joint Action on AMR and Healthcare-Associated Infections could be utilized to assist in the implementation of this pilot.

4. Countries should make long-term commitments to continue financing of antibacterial R&D and ideally increase push funding by about 50 per cent.

There may be capacity within existing multinational grant funding agencies – e.g. CARB-X, GARDP, JPIAMR (Joint Programming Initiative on Antimicrobial Resistance) – to absorb and effectively deploy more capital. Owing to the existing pipeline, much of this immediate funding should be placed in early – and mid-stage grants until the pipeline becomes more robust. Granting agencies should have specific calls for research targeting pathogens that pose the most urgent public health threats (e.g. WHO's priority pathogens list for the discovery phase and TPPs for the development phase).

5. To ensure that progress is made on all identified priority pathogens, targeted portfolio-based approaches such as BARDA (Biomedical Advanced Research and Development Authority), CARB-X and GARDP – i.e. pipeline coordinators – should be supported and expanded.

A review of the current antibiotic pipeline demonstrates that not all pathogens are equally attractive for developers. Pipeline coordinators are needed to closely track the antibiotic pipeline (or subsets thereof), identify gaps and actively support R&D projects to fill these gaps. They work at an operational level and should not be confused with entities that work on political coordination, such as the G20's Global R&D Collaboration Hub on AMR.

6. Sustainable use measures for developers should be contractually linked to both market entry rewards and long-term supply continuity awards.

A special working group (potentially under the guidance of the G20's Global R&D Collaboration Hub on AMR) should convene to develop standard sustainable use measures both for developers and for governments. DRIVE-AB has proposed measures that can be used as a starting point.

7. Equitable availability measures for developers should be contractually linked to market entry rewards.

A special working group (potentially under the guidance of the Global Antibiotic Resistance Partnership, given its significant expertise) should convene to develop standard equitable availability measures. Again DRIVE-AB has proposed measures that can be used as a starting point. These measures will require testing and adaptation. This could be done with an approved patented antibiotic that is considered useful in low- and middle-income countries.

8. Principal antibiotic R&D funders (e.g. BARDA, CARB-X, JPIAMR, IMI, the National Institutes of Health (NIH), the Wellcome Trust) and developers should agree to standard sustainable use and equitable availability principles that can be included in all pertinent push-funding agreements.

This will allow developers to begin to plan for making their antibiotics globally and sustainably available.

9. To test the operational implementation of delinkage, interested countries and multilateral bodies (such as UNICEF, the United Nations Children's Fund) should initiate a delinked, joint procurement process of an antibiotic with a fragile supply chain which is included as an "access" antibiotic on WHO's Essential Medicines List (e.g. benzylpenicillin).

Testing a long-term supply continuity model can also test the implementation of a delinked model such as a market entry reward. This could be an immediate concrete action where countries can test the operational difficulties of coordination while waiting for a suitable antibiotic to receive regulatory approval.

10. Grant funding should be allocated to undertake post-approval clinical trials in order to gather evidence concerning uncommon infections and special patient groups.

Pipeline coordinators should map the public health gaps in this area and seek to gather empirical data to fill the gaps. Continued emphasis should be placed on improving clinical trial networks to facilitate the rapid identification of eligible patients.

11. As a part of their ongoing health technology assessment (HTA) processes, countries should begin to integrate methods and frameworks that account for the enablement, option and diversity value for each new antibiotic submitted for regulatory approval.

While market entry rewards are discussed and put in place, national authorities should address the economic challenges within their existing systems. This will ensure that incentives for antibiotic innovation can be improved in the near term to maintain current private investment into antibiotic R&D – for example, by developing HTA processes to better capture the societal value of antibiotics in coverage and reimbursement decision-making.

12. To ensure that antibiotic innovation is targeting the highest-priority public health needs, WHO (or another suitable body) should develop target product profiles (TPPs) for its priority pathogens list.

There should be broad consensus among public health experts and clinicians that these profiles represent unmet public health needs for antibiotic innovation. Developers should be consulted to ensure that TPPs are achievable. The development of TPPs should be an ongoing process as the priority pathogens list is updated over time. Once established, TPPs must remain stable for a decade to ensure predictability within lengthy R&D timelines.

- An important output is finally the clear guidance given by the consortium for implementing this evidence that will provide a persuasive argument to undertake the necessary system changes at the national or supranational level. The long-term impact should be increased financing to re-ignite and maintain the necessary levels of antibiotic R&D over time while ensuring rational use.

- The management work streams set up and managed a multi-disciplinary stakeholder platform to engage at all stages of the DRIVE-AB project and support the implementation of new models. To inform the public and stakeholders of the advances of the project during its whole course, it maintained an active Twitter account and an open public website and regularly published project preliminary outputs in the form of reports, slide sets etc. This team also provided the scientific and administrative leadership and integrated programme management essential to the larger project's success including setting up and managing the steering committee and project management office.

6. Potential impact, main dissemination activities and exploitation of results

To ensure an optimal impact of the DRIVE-AB outputs described in the previous section, several strategies of dissemination were adopted and all meaningful approaches of dissemination were used:

- In terms of oral dissemination, the project was presented (either its scope and aims, its research outputs and/or its policy recommendations) at close to 120 scientific conferences, as

well as small and large stakeholders meetings. Through high-level interactions with governments and decision makers, DRIVE-AB influenced the current political discussion around antibiotic innovation, the need for new economic models, the importance of sustainable use and access, and the difficult balance between regulation and free-market considerations.

- In terms of scientific publications, as of February 2018, 18 articles of primary research, opinions or reviews have been published in scientific journals and about 40 more are submitted or in preparation.
- The DRIVE-AB website presented the project and displayed throughout the project a lot of outputs spanning from scientific publications to meeting slide sets (http://drive-ab.eu/).
- A Twitter account was used during the whole projects to disseminate DRIVE-AB news as well as other interesting AMR-related news (@DRIVE_AB).
- The final conference in which stakeholders from all fields were invited and participated was designed to maximise the dissemination of the recommendations to all stakeholders. The conference attracted approximately 200 participants from a wide range of stakeholder groups, including policy-makers, medical professionals, representatives of the pharmaceutical and biotechnology industries, civil society communities, and regulatory and public health experts. The day and a half conference was focused on the communication of the consortium's research results and recommended options to drive investment in antibiotics that included a combination of incentive mechanisms along with finance and governance options to support their implementation. These presentations were followed by panel discussions with experts from organisations such as the World Health Organization, the European Commission, and the Biomedical Advanced Research and Development Agency, among others, to discuss the feasibility of DRIVE-AB's recommendations and the opportunities and barriers to their implementation across global settings.
- The final DRIVE-AB policy report was released on January 24, 2018 and is freely and openly available online at: http://drive-ab.eu/drive-ab-outputs/drive-ab-reports/. It was a major undertaking gathering the evidence from each part of the project and presenting it in a coherent and interlinked package. The aim of this report is to help policymakers decide upon and implement the best incentives to stimulate antibiotic R&D while ensuring sustainable use and access. Overall, the DRIVE-AB recommendations, if taken up by politicians from the EU and abroad, could have an impact on the health and socio-economic benefits of European citizens.

7. Lessons learned and further opportunities for research

DRIVE-AB was a public-private partnership including 23 partners from large pharmaceutical companies, academia, and civil society, in other words, a contrasting mix of people with different experience, expertise, visions and perspectives. This was the strength and the originality of the project, but also represented its major challenge. The collaboration in this public-private partnership has been a great challenge for DRIVE-AB. During the research phase of the project, important interactions took place between the public and private partners. When it came to reaching convergence on potential

policy recommendations, challenges arose due to the diverging views and agendas of the different partners.

As the project developed, DRIVE-AB had to adapt to a fast-moving environment due to political timelines and the high momentum around AMR policy discussions, to which it contributed. This placed high pressure on participants to deliver and raised the interests at stake considerably since the project was conceived back in 2013. Under these circumstances, we were also faced with the challenging task of weighing data and evidence from all DRIVE-AB participants to find realistic and pragmatic solutions to the project's key questions and present them in a timeframe that was relevant for policy makers.

In May 2017, the Swedish non-governmental organization ReAct which was participating in DRIVE-AB through the official partner Uppsala University, decided to withdraw from DRIVE-AB citing conflicts of interest and governance issues. We regret that ReAct decided to leave the DRIVE-AB partnership. We believe that ReAct contributed positively to the conversations and development of DRIVE-AB's research. With ReAct's departure, we lost an important voice within the project to represent civil society. Although we were aware that aligning such a diverse group of partners behind all recommendations would be difficult, DRIVE-AB was committed to building consensus. All partners were consistently included in meetings and were encouraged to comment on major documents and report drafts. As in all collaborative research-based projects, publications authored by named individuals followed a standard process, including circulation to all Work Package (WP) members and the steering committee for feedback, often with numerous iterations to include participants' positions. When no consensus was achieved, publications were authored with a disclaimer statement saying that it did not represent the view of all DRIVE-AB partners. With regards to those few instances where there were no named authors (for example, policy briefs), all drafts were circulated and feedback incorporated. We also attempted to reflect diverging views when space was limited and reflected them in detail when there was no space limitation (as is the case in this final report and many publications). Conference presentations discussing DRIVE-AB's conclusions reflected this diversity of views.

Overall, the research results and the awareness raised by DRIVE-AB on these issues have reached the goal of DRIVE-AB to be a catalyst for change and to provide food for thought for all stakeholders. Further opportunities for research are manifold in the field. Important upcoming projects in which some DRIVE-AB partners plan to be included are the project part of the currently opened IMI2 call 13 entitled: *The value of diagnostics to combat antimicrobial resistance by optimising antibiotic use*. Several DRIVE-AB partners continue to interact with the recently created G20's Global R&D Collaboration Hub on AMR. Other DRIVE-AB partners are also implicated in a recently funded JPIAMR project on '*Aligning industry incentives with AMR control goals: Exploring the feasibility of an antibiotic susceptibility bonus for drugs to treat Gram-negative infection'.*