CHATHAM HOUSE
The Royal Institute of International Affairs

BIG INNOVATION CENTRE

Business Model Options for Antibiotics

Learning from Other Industries

Ella Jaczynska

Kevin Outterson

Jorge Mestre-Ferrandiz

February 2015

Launched in September 2011, the Big Innovation Centre brings together a range of companies, universities and public bodies to research and propose practical reforms with the ambition of making the UK a global open innovation hub as part of the urgent task of rebalancing and growing the UK economy and with the vision of building a world-class innovation and investment ecosystem by 2025.

CONTENTS

Appendices available at:
www.biginnovationcentre.com/publications

Summary

As resistance to antibiotics continues to grow, there is a well-recognized misalignment between the clinical need for new antibiotics and the incentives for their development. The returns from investment in antibiotics research and development (R&D) are perceived as too small. Partly as a result, the number of large multinational companies researching antibiotics has fallen drastically in the past 20 years and few high-quality antibiotics have been developed.

In looking at the antimicrobial resistance (AMR) situation, we were aware that other industries have faced conceptually similar challenges and that they might offer helpful lessons and possible solutions that could be adapted to the problems of antimicrobial R&D. Our focus was particularly on learning about models in which the incentive for R&D is *delinked* from the volume of sales.

A Big Innovation Centre and Chatham House workshop brought together on 1 September 2014 six companies that are members of the Big Innovation Centre: BAE Systems (defence), Allianz (insurance), Barclays Bank (finance), EDF Energy (energy), Dun & Bradstreet (corporate information) and Knowledge Unlatched (academic publishing). These companies presented business and incentivization models they had implemented or devised that could be explored further for their applicability to antibiotics R&D. It was made clear to them that any models shared might be adapted so that they a) provide the pharmaceutical industry with an incentive to invest in antibiotics R&D, b) offer insight to health services about how to fund and to maintain the availability of appropriate antibiotics and c) ensure that both new and existing antibiotics are used appropriately and wisely.

Learning from other industries has been a very fruitful exercise. They have offered a different perspective on how to tackle the AMR issue and have provided relevant analogies to consider.

This research report offers a number of innovative models and ideas that address many of the critical questions facing policy-makers in the EU and the US as they seek solutions. It also contributes to key new initiatives globally and in Europe and the US specifically, including the World Health Organization's Global Strategy on AMR, the Innovative Medicines Initiative DRIVE-AB project in the EU, the UK's Review on Antimicrobial Resistance and, in the US, the President's Advisory Council and the National Strategy for Combating Antibiotic-Resistant Bacteria.

This report highlights important lessons about how these other industries have adapted to diverse challenges in their environment. Based on this work and on our own review over the past few months, we see a clear need for a 'bucket' of various funding mechanisms that can exist in parallel. There should be separate funding mechanisms in place during the R&D phase of developing an antibiotic and a different mechanism to fund the maintenance, delivery and distribution of the antibiotic after regulatory approval.

The report articulates three essential messages:

1) Global collaboration is required on a scale not seen before in relation to antimicrobial resistance. Many independent initiatives are under way nationally and regionally, but they need to be brought together in a concerted worldwide effort to engage on a global scale. The report is designed to help bridge these various efforts and move towards consensus on global action. We propose four initiatives:
    a. Creating a global antibiotics public–private partnership (GAPPP). A GAPPP should involve private companies, academic institutions and public bodies. It must be a sustainable, independent and self-funding operation with a focus on the research and early development of antibiotics in response to identified global public health needs.
    b. Creating a global antibiotics fund (GAF), which would be set up to be an over-arching umbrella fund (potentially consolidating all the pre-existing small funds that exist globally). It could exist alongside or in collaboration with major existing funding sources, such as BARDA and IMI, that have very pre-defined targets for funding.. A GAF would provide monetary support to a GAPPP in order to enable its R&D effort. A GAF would work with existing funders for better awareness of the work each is supporting and for collaboration in funding priorities, options and courses of action. Ultimately, proposals for a GAPPP and a GAF are a possible way forward to pool skills, resources and funding so as to ensure a sustainable long-term solution.
    c. Exploring the Gavi (the Vaccine Alliance)-type model and determining whether or not an independent global body should serve as the global procurement and distribution entity for antibiotics.
    d. Becoming better stewards of antibiotics, as they are valuable drugs. Otherwise, boosting the production of new antibiotics will be futile. Antibiotics must be used appropriately everywhere around the globe. A worldwide effort to conserve them and to ensure appropriate access and use requires international coordination and the participation of every country. Some form of an international treaty or framework agreement is called for.
2) There is a need to explore ‘service-availability’/’option-to-use’ types of agreements/contracts between developers/manufacturers and health care systems as a means to support the ‘delinkage’ concept. As in the defence sector, products are developed but kept on the shelf, maintained and ready when needed, including all the services to deliver them effectively and efficiently. Long-term contracts with customers ensure that the services they require are available when needed. Innovators of new antibiotics should not be rewarded with the traditional ‘price x volume’ model but should focus more on delivering the product, resources and services when needed. Governments would pay an annual ‘service-availability’ fee/premium delinked from the volume of sales. Lessons from the insurance industry indicate how these annual ‘premiums’ could be calculated.
3) There is a need to engage customers (in the broadest sense) and ensure that the right incentives, both financial and non-financial, are aligned from the bench to the

bedside. We should not focus on incentives just for the pharmaceutical companies; we must include prescribers, health systems, patients and all other stakeholders.

1 Introduction

As resistance to antibiotics continues to grow, there is a well-recognized misalignment between the clinical need for new antibiotics and incentives for their development. The returns from investment in antibiotics research and development (R&D) are perceived as too small: prospective sales revenues are judged unlikely to cover the cost and risk of investing in R&D.[1] And the attempt to restrict the use of antibiotics in order to counter the spread of resistance further reinforces this negative perspective.[2] As a result, the number of large multinational companies researching antibiotics has fallen drastically in the past 20 years and few new antibiotics have been developed.[3] Apart from the poor economic return, there are specific scientific challenges to developing antibiotics. Recently, however, there has been improved dialogue among stakeholders about regulatory requirements and how they can be adapted for new antibiotics, and discussions are continuing. But there is some concern that current regulatory requirements may compound the problem of inadequate returns.

As sales of new antibiotics are likely to be restricted, particularly when an antibiotic must be held in reserve, incentives for R&D need to be considered that do not depend on sales volumes and revenues.[4] Many groups are now seeking solutions to this problem. Given the seriousness of this issue for global health and the active engagement of many healthcare stakeholders, we thought it wise to expand the scope of inquiry and look for guidance beyond the boundaries of the pharmaceutical industry. Our thought was that other industries have faced conceptually similar challenges and might offer helpful lessons and solutions that could be adapted to the problems of antibiotics R&D. There was particular interest in learning about models in which the incentive for R&D is *delinked* from the volume of sales.

Acting on this premise, the Big Innovation Centre and Chatham House held a workshop in London on 1 September 2014 with presentations from six companies that are members of the Big Innovation Centre: BAE Systems (defence), Allianz (insurance), Barclays Bank (finance), EDF Energy (energy), Dun & Bradstreet (corporate information) and Knowledge Unlatched (academic publishing).

---

[1] Sertkaya, A., Eyraud, J., Birkenbach, A., Franz, C., Ackerley, N., Overton, V. and Outterson, K., Analytical Framework for Examining the Value of Antibacterial Products, Eastern Research Group, April 2014. Available at http://aspe.hhs.gov/sp/reports/2014/antibacterials/rpt_antibacterials.cfm.

[2] Kesselheim, A.S. and Outterson, K., 'Improving antibiotic markets for long-term sustainability', *Yale Journal of Health Policy, Law and Ethics*, 2011, 11(1): 101–67.

[3] Boucher, H.W., Talbot, G.H., Bradley, J.S. et al., 'Bad bugs, no drugs: No ESKAPE! An update from the Infectious Diseases Society of America', *Clinical Infectious Diseases*, 2009, 48(1): 1–12.

[4] Outterson, K., Powers, J.H., Daniels, G.W. and McClellan, M.B., 'Repairing the broken market for antibiotic innovation', *Health Affairs*, 2015, 35(2): 277–285.

The companies were given some background on the current problem but no further prompting, in the hope of innovative solutions arising from the experience of the different industries. It was specified that the models explored needed a) to provide the pharmaceutical industry with an incentive to invest in antibiotics R&D, b) to provide insight to health services as to how to fund and to maintain the availability of appropriate antibiotics and c) to ensure that both new and existing antibiotics are used appropriately and wisely.

We were not disappointed. The report offers a number of innovative models and ideas that address many of the important questions facing pharmaceutical policy-makers in the EU and the US as they seek solutions. It tackles not only *funding models* but also *organizational infrastructure, collaboration and process models across public–private partnerships* (PPPs). Some of the proposals are novel; others build on existing fund and partnership models and ideas in ways that could be globally applicable and relevant. We focus on the EU and the US because we believe that they are pivotal in terms of offering incentives for innovation although the challenge of promoting appropriate access and use is global in scope.

The purpose of this report is to make a contribution to major new initiatives globally and in Europe and the US specifically, including the Innovative Medicines Initiative (IMI) DRIVE-AB project in the EU,[5] the UK's Review on Antimicrobial Resistance,[6] the US President's Advisory Council, the World Health Organization's (WHO) Global Strategy on AMR[7] and the US National Strategy for Combating Antibiotic-Resistant Bacteria (CARB).[8] To this end, the report addresses key research questions and proposes areas in which further work and modelling, testing and validation are needed. It identifies gaps that were noted and how they could be addressed.

Background to the problem

The economic model underpinning R&D for antibiotics and sales is more problematic than for other classes of drug. In order to obtain a return for the major sums invested in developing a new antibiotic, pharmaceutical companies must sell as many antibiotics as possible. A pharmaceutical company's revenue is the number of units of antibiotics sold multiplied by their price. When government sets the price, the only way to increase revenue is to sell more antibiotics. But higher sales of antibiotics increase the likelihood of accelerating the development of resistance.

For most other classes of drug, a powerful new drug will realize significant sales in early years. For antibiotics, stewardship measures will increasingly restrict the uptake of new drugs until the older ones lose their efficacy. And higher prices are not a plausible option for

[5] DRIVE-AB, Driving reinvestment in research and development and responsible antibiotic use. Available at http://drive-ab.eu/about/.
[6] Review on Antimicrobial Resistance. Available at http://amr-review.org/.
[7] World Health Organization, Antimicrobial resistance, Geneva, Switzerland, 24 May 2014 [cited 23 December 2014], Sixty-seventh World Health Assembly, WHA67.25, Agenda item 16.5. Available at http://apps.who.int/gb/ebwha/pdf_files/WHA67/A67_R25-en.pdf.
[8] See http://www.whitehouse.gov/sites/default/files/docs/carb_national_strategy.pdf.

increasing returns for antibiotics.[9] Important concerns about this approach include the impact on health service budgets and consequent complaints from payers, accessibility in low- and middle-income countries and the fact that high prices for a small, targeted population may be insufficient to raise the return on investment to the needed level.

Although some conventional measures are being tried, such as increasing direct public-sector investment in R&D and making efforts to streamline the regulatory pathway,[10] they are unlikely to be enough. In particular, systemic changes are needed in the ways that R&D investment is rewarded. Research undertaken in recent years shows that antibiotics are woefully undervalued relative to their importance to society: the health and economic benefits to society generated by the use of antibiotics vastly exceed their cost.[11] Innovative commercial models are required that drive investment in R&D by providing a viable, sustainable return while preserving and extending the utility and responsible use of antibiotics.[12,13] The proposals in this report focus specifically on options for 'delinkage', ones that reward companies for R&D on a basis other than price and sales volumes. They also look beyond the single-company approach and include novel methods of collaboration for driving R&D forward.

In the US, a recent report commissioned by the government from the Eastern Research Group (ERG) examined economic incentives for the development of antibiotics.[14] The report's econometric analysis demonstrated that in the absence of additional incentives, the expected return on investment in R&D for the six bacterial infections studied was inadequate.

The ERG report also examined intellectual property (IP) incentives such as patents and marketing exclusivities; streamlined clinical trials; reductions in the cost of capital such as tax credits; and cash flow awards such as contracts, grants and prizes. Owing to the powerful effect of discounting on distant future benefits, IP incentives always failed in this model to achieve a minimum return on investment. Reductions in the cost of capital would need to be quite substantial, on the order of 50–70 per cent. Reductions in clinical trial development times would need to be improbably radical, in many cases cutting them by 75 per cent.

---

[9] Love, J., 'Prizes, not prices, to stimulate antibiotic R&D', Science and Development Network, 26 March 2008. Available at http://www.scidev.net/en/opinions/prizes-not-prices-to-stimulate-antibiotic-r-d-.html.

[10] Rex, J.H., Goldberger, M., Eisenstein, B.I. and Harney, C., 'The evolution of the regulatory framework for antibacterial agents', *Annals of the New York Academy of Sciences*, 2014, 1323: 11–21.

[11] O'Neill, J., 'Antimicrobial resistance: Tackling a Crisis for the Health and Wealth of Nations', *The Review on Antimicrobial Resistance*, 11 December 2014. Available at http://www.jpiamr.eu/wp-content/uploads/2014/12/AMR-Review-Paper-Tackling-a-crisis-for-the-health-and-wealth-of-nations_1-2.pdf.

[12] Outterson, K., New business models for sustainable antibiotics, Chatham House, February 2014. Available at http://www.chathamhouse.org/sites/files/chathamhouse/public/Research/Global%20Health/0214SustainableAntibiotics.pdf.

[13] Clift, C., Gopinathan, U., Morel, C., Outterson, K., Røttingen, J.A. and So, A., eds, Report of the Chatham House Working Group on New Antibiotic Business Models, Chatham House, February 2015 (forthcoming).

[14] Sertkaya, A., Eyraud, J., Birkenbach, A. et al., Analytical Framework for Examining the Value of Antibacterial Products. Available at http://aspe.hhs.gov/sp/reports/2014/antibacterials/rpt_antibacterials.cfm.

According to the ERG report, the most effective incentives by far are cash flow awards spread across a product's life cycle, including payments during clinical trials as well as enhanced reimbursement once a product gets regulatory approval (post-approval). The model suggested that a cumulative aggregate of awards would need to be in the range of US$1 billion in order to incentivize the development of one successful new antibiotic.

For Europe, Towse and Sharma carried out a similar exercise, with similar results in terms of expected rates of return without additional incentives.[15] Their baseline net present values (NPVs) were negative for all antibiotics projects studied. They modelled the size required of various incentives, including direct funding for R&D, IP, higher prices and an advanced market commitment (AMC), in order to raise the NPV to a more acceptable level. They recommended a combination of cash flow incentives, reducing R&D costs and some kind of priority review, both at the stage of regulatory approval and when setting pricing and reimbursement levels. A suggested alternative package (not mutually exclusive with the first recommendation) could include an upfront payment for registration (rather than for volume of use) in the form of an AMC 'prize', akin to the 'delinkage' concept mentioned above. Two versions were modelled: a one-year AMC in which the award is given as a lump sum to the developer at launch and a five-year AMC in which the award is given to the developer over five years after launch. The necessary prize levels to bring the prospective economic return to an acceptable level were €985 million and €1.4billion (€280 million per year) respectively.

It should be noted that many existing incentive packages offer cash flow awards prior to approval of the drug (pre-approval), including grants for basic research from medical research councils or foundations and contracts for clinical development, such as from the IMI in Europe and the Biomedical Advanced Research and Development Authority (BARDA) in the US. The data support an expansion of these efforts, as recently recognized in Europe with the establishment of the New Drugs 4 Bad Bugs (ND4BB) programme under IMI and by the White House when it expanded BARDA's mission and recommended a significant expansion of its funding.[16] In this report, we propose an expansion in the size of these cash awards, as well as an expansion of their scope. Identified problems with reimbursement for antibiotics suggest that these efforts should include delinked post-approval payments too. This is also a focus of the DRIVE-AB project.

Some of the models in this report are further examples of types of cash award. They build on work and proposals made in the US and the EU, with the aim to help us specify model parameters more clearly.

[15] Towse, A. and Sharma, P., Incentives for R&D for New Antimicrobial Drugs, Office of Health Economics, April 2011; available at https://www.ohe.org/publications/incentives-rd-new-antimicrobial-drugs and Sharma, P. and Towse, A., New Drugs to Tackle Antimicrobial Resistance: Analysis of EU Policy Options, April 2011. Available at https://www.ohe.org/publications/new-drugs-tackle-antimicrobial-resistance-analysis-eu-policy-options.

[16] Available at http://www.whitehouse.gov/the-press-office/2014/09/18/fact-sheet-obama-administration-takes-actions-combat-antibiotic-resistan.

2 Business Models from Other Industries

Table 1 below summarizes the business models presented at the Workshop along with a topline description of how each could be applied to antibiotics. Details of the business models from the six different industries are described further below and in Appendix 2.

Table 1: Business models from other industries

Company	Industry	Model name	Description	Application
Allianz	Insurance	Pandemic insurance	a) New policy, in which premiums are collected and spent to create antibiotics and help to prevent bacterial epidemics resulting from resistance to current antibiotics b) Catastrophe insurance	Funding, underwriting and risk-spreading mechanism at the national level; also indicates the value of avoiding pandemics
BAE Systems	Defence	Long-term availability	Some defence procurement has shifted from simple product delivery (e.g. a ship) to long-term availability and service provision (a ship, maintained with levels of availability for decades).	Society needs antibiotic drug classes to be available and effective for generations; moves from a simple product to a long-term service
Barclays Bank	Finance	Antibiotic corporate bond (ACB)	Public entity sells 10-year bonds; net proceeds are used to fund antibiotics R&D; repayment comes from sales of wildcard patent certificates granted for successfully approved antibiotics.	A financing mechanism for antibiotics R&D that is detached from the sale of antibiotics; external investors are also rewarded. The repayment portion shifts much of the cost on to other areas of the health sector or to other potential sectors. Need to model system so as to understand and overcome concerns about efficiency and fairness.
Dun & Bradstreet	Corporate information	Value-based sales	D&B has moved from revenues built on unit sales to bundled products priced on value.	Antibiotics need to be reimbursed more in line with value. Delinking revenue from sales volume could reduce the rate of resistance and reduce uncertainty for developers and healthcare systems.
EDF	Energy	Conservation incentives	Utilities need to boost customer conservation in order to meet climate change goals but customers do not adopt energy-savings measures without direct financial incentives; companies need a mechanism by which to create equal conditions among companies for these costs.	Antibiotics companies need to incentivize their customers to use less of their products; financial incentives might be necessary; government might need to require proportionate efforts by all companies (branded and generic) to prevent free-riding.
Knowledge Unlatched	Academic publishing	Collaboration	Instead of creating books that are then sold to customers (academic libraries), collaborate with customers to	Antibiotics have high fixed costs and low marginal costs; collaboration with customers (governments) could make the

			collect upfront revenues that are then used to fund open-access e-books to be shared without marginal costs.	market much more predictable.

In the sections that follow, we divide the results and proposals from the Workshop into two categories, distinguishing between funding-design options and process-orientated considerations:

- **Funding-design options**: how funding could be collected and spent at various points in the life cycle of an antibiotic (see Section 3) and

- **Process-design considerations:** management lessons for transforming the antibiotics business model (see Section 4).

Throughout the report, we give our view about which key programmes and initiatives, such as DRIVE–AB, the UK's Review on AMR, the US National Strategy CARB group and the WHO Global Action Plan, could take up these recommendations and work with them.

3 Funding-design Options

The focus of funding-design options is on the whole life cycle of a new antibiotic, i.e. including pre-approval and post-approval. It is important to keep in mind that various funding mechanisms may support different parts of the life cycle. Numerous funding options must be available in order to allow a flexible menu of options. But the first questions are whether or not funding should come from a stand-alone fund and whether or not that fund should be self-sustaining.

Stand-alone sustainable funds

An important design choice for any proposed funding scheme is whether or not it requires support from a stand-alone, self-sustaining fund. Although a significant amount of funding is available globally to support R&D into antibiotics, many funds are not self-sustaining. Insecurity in the funding stream causes companies to discount projected future cash flows for political risk, which decreases the efficiency of any incentive scheme. It has been shown across many industries that the stronger the political support is, the more companies believe there is a credible commitment and thus the more willing they will be to invest.

The current crisis in antibiotics has taken decades to emerge, and AMR will need to be addressed continually over further decades, in view of which the funding solution must be stable over long periods of time. Moreover, a regular stream of new antibiotics is required to replace the old ones as resistance builds. The time lag from bench to bedside is at least a decade and sometimes much longer. Human capital, such as university research teams, physicians, scientists, expertise in the private sector specializing in infectious diseases, and clinical trial networks, cannot be rebuilt quickly and it needs long-term stability. It is

essential, therefore, to have a scheme that supports a long-term, self-sustaining fund. A scheme needs to support the development of many products so that the development risk is spread more widely (the optimal number of antibiotics required both in the market and in development is unknown). The target products must include diagnostics, vaccines, infection-control technologies and biopharmaceuticals in addition to traditional antibiotics.

At the Workshop, the six companies described their revenue models, with particular attention to how their experience might help to provide sustainable funding for antibiotics markets. The proposals in the report take this need into account.

R&D funding models

Although efforts have been made to increase funding through public–private partnerships (PPPs), the success rate of antibiotics (e.g., 72 leads required to generate one product launch compared to 15 on average for other therapy areas)[17] indicates that without significant further incentives, the supply of new ones will remain thin.[18] Numerous funding models need to exist in parallel so as to fund the cost of research and early development, to reduce the risk of this investment and to encourage re-entry into this area.

Insurance model

Allianz made two proposals. The first proposal discussed using insurance premiums from a specific newly created, individual antibiotic insurance cover (see Appendix 2 for details) to create a funding pot that is then used to help assure the continued availability of effective antibiotics. The second proposal offered models of Allianz' catastrophe insurance policies that could be applied to a bacterial epidemic or pandemic. The insurance-type model makes funding very predictable over time through the well-known mechanism of annual insurance premiums. Making these commitments over many years, perhaps over decades, would level out the cost of premiums even more. This funding pot would be provided in part to pharmaceutical companies and research organizations to fund development costs. The authors of this report, along with some participants in the Workshop, modified the individual antibiotic insurance cover proposal in order to source premiums from governments as opposed to individuals.

If antibiotics R&D is viewed as an insurance premium, governments could invest sizeable funds (for example, €1–2 billion/year in the EU, in line with the prize-level amounts the research has shown are needed) to prevent the catastrophic consequences of a post-antibiotics era. Governments, businesses and individuals understand that insurance is a financial mechanism to prepay for the assumption and distribution of risk. Catastrophe insurance policies show how annual premiums can be calculated to ensure that adequate funding is collected in the upfront years in order subsequently to cover all the costs of

[17] Based on Paul et al., 'Hit to Phase 2 based on novel mechanism AB discovery (GSK)', *Nature Reviews Drug Discovery*, 2010 (9): 203–14.

[18] We acknowledge that just increasing further funding on R&D (either public or private or both) will not necessarily increase the rate of success and reduce risk. As stated throughout this report, other initiatives are required.

delivering the antibiotic and all the required support and services when there is a crisis. This links with the discussion of post-approval funding models below. If insurance-type schemes were put in place, they would need to be set up as soon as possible so as to allow the system to accumulate the annual premiums over the years when no catastrophe has occurred. This would enable companies to further inject funds into the development of new antibiotics and to have adequate funds to put manufacturing and distribution in place in the event of a pandemic or a regional resistance crisis.

Corporate bond funding model

The Barclays model was based on its expertise in designing financial products for customers. Its proposal was the issuance of 10-year government-guaranteed corporate bonds (antibiotic corporate bonds or ACBs), repaid from the sale of patent-extension certificates (PECs). Antibiotic corporate bonds would be sold by an independent agency, possibly a quasi-governmental entity, to generate a research fund. That fund would be used to pay for R&D of antibiotics across their life cycle to many entities, including academic groups, small and medium-sized enterprises (SMEs) and large pharmaceutical companies.

A PEC would be generated when regulators approve a new antibiotic for marketing. PECs would be saleable and transferable and may be sold to the highest bidder, allowing the successful bidder to extend a patent on an existing medicinal product within its portfolio by up to three years. As patents are a national system, the complex logistics and feasibility of making this model work globally may be difficult.

The model sets a controversial precedent in breaking the *direct* link between investment in innovation and the award of patent rights for any inventions that arise, although it does sustain a link between innovation and reward more generally. In the UK, it has been highlighted that patent-extension certificates could be applied not only to the pharmaceutical sector but also to various industries if that were decided to be appropriate and beneficial. In the US, breaking the direct link might raise serious legal issues under the US Constitution.

The funds generated from the sale of PECs would provide a revenue stream that is disconnected from the sale of the new antibiotic coming to market. Some, including the authors of this report, consider the PEC proposal to be a controversial idea on grounds of fairness, efficiency and political reality.

It is necessary to determine the costs to a national health system that a PEC could generate and then to model how those costs could be offset. In the corporate bond model, the PEC is funded essentially through national public budgets and private health budgets. But only a fraction of the costs to the system are spent directly on the targeted R&D; the balance goes to transaction and financing costs associated with the bond issue.

Some groups have raised concerns that stand-alone transferable patent-extension certificates are not ethical, as the patent extension being applied to another medicine in a different disease area means that part of the health system and those health insurance payers will pick up the cost of the antibiotic reward.[19] In the EU, this may be less salient because whatever the disease area, the cost is picked up by national health services. In the US, this cost is split among government, private insurers and paying individuals, and thus there is a need to determine how the impact of a PEC on them could be reduced.

Wildcard patent schemes have been proposed in the US and Europe several times over the past decade. They have never gained substantial political acceptance because they represent a fundamental change in the patent system. Patents always reward innovation with exclusivities over that invention. Wildcards break that essential link, awarding exclusivities on another product that bears no relationship to the invention. On this basis, there may be significant barriers, especially in the US, that would greatly limit the appeal of the scheme. The specifics of these barriers need to be researched further, and whether or not there are ways to overcome these barriers must be explored too.

As indicated above, there are known difficulties with the PEC system and with making this repayment mechanism work globally. It is important here to look at other mechanisms for how an antibiotic corporate bond could be repaid, to understand the issues those mechanisms raise and any ways they can be overcome or addressed in this or other repayment mechanisms and to ensure that any system is efficient, has more benefits than funding antibiotics directly and offsets the potentially unpredictable consequences for healthcare budgets of a wildcard extension and associated transaction costs.

Within the ACB–PEC model proposed by Barclays Bank, attempts were made to address some of the concerns raised about PECs by ensuring that they are intrinsically part of an overall scheme that feeds back into further research and support for the antibiotics development ecosystem and that an independent agency would administer the sale and collection of the funds from a sale of the various PECs with clear governance criteria.

A further proposal from Barclays Bank was that some of the funds generated from the PEC sale could also go towards offsetting some of the impact of the patent extension in the different disease area that the patent extension is applied to. The extra funding could be put towards paying for programmes in the other disease areas where the patent has been extended, i.e. to support research into further improving patient outcomes and further reducing the cost of treating and supporting patients. The efficiency and fairness of this scheme should be evaluated and modelled against direct funding options. Alternative bond repayment mechanisms could also be explored within this model, such as direct payments by governments or health systems.

[19] Outterson, K., Samora, J.B. and Keller-Cuda, K., 'Will longer antimicrobial patents improve global public health?', *The Lancet Infectious Diseases*, 2007 (7): 559–66.

The feedback from the Workshop was that in order to make a funding model such as this work, an independent, supranational organization would be required to administer it, for example a central global administrative fund. This would be necessary for various reasons, one being that individual national coordination and multiple national patent-extension certificates would not be a feasible approach. The independence of a global third-party administrator would be vital.

Post-approval funding models

Some of the funding options considered were deemed to be more appropriate once an antibiotic had been approved for marketing or once a package of antibiotics had become available. There is a requirement to ensure that any future business model for antibiotics also addresses incentives and accountabilities for maintaining the approved antibiotic, for delivery and for any services contracted for that may aid deployment, stewardship and delivery when needed.

BAE Systems and Dun & Bradstreet shared examples of ways in which they moved from selling products to setting up 'availability' agreements with customers, payers and governments. These agreements include the provision of value-adding services. This shift in model could be uniquely appropriate for antibiotics: products are developed but kept on the shelf, maintained and ready when needed, including all the services to deliver them effectively and efficiently. Long-term contracts with customers ensure that the services they require are available when needed.

'Service-availability' contracts model

BAE Systems has a funding model that is secured from national defence budgets under a contract for delivery of a service, which can include a portfolio of products and services. The UK defence industry has contractor-logistics-support contracts with its primary customers (governments). The US equivalent is a performance-based logistics contract. They have been called 'contracting for availability'.[20] This is the defence industry's version of an option-to-use contract in which a contractor is remunerated on the basis of service performance in view of the user's desired needs rather than for selling a specific product. For example, what is sold will be not just the ship but also the services of a ship, and the necessary ancillary support over a period of years may also be contracted. Remuneration is determined through a set of agreed key-performance indicators (KPIs). A simple example of a KPI would be the number of aircraft in a fleet ready for service at any one time. However, KPIs can be tailored for many different forms of availability.

As defence is a core national task of government, this funding mechanism is seen as reliable over the long term. But it was also mentioned that given the long development time frames, 'goalposts' can be changed by governments, which increases uncertainty for companies. Although core healthcare and defence budgets are fairly protected from political pressures,

[20] 'Contracting for availability' is an output-focused commercial arrangement that incentivizes improvement in asset availability rather than the traditional sale of products and spares and repairs.

the detailed funding for antibiotics R&D does not enjoy the same protection. A possible exception (or a future way in which to ensure it) is 'global health security': funding that emphasizes the security aspects of strategic health spending. Much of the White House's recent efforts on AMR have been coordinated with the National Security Council, in recognition of the importance of ensuring US security.

The setting up of these contracts must be considered during the development of the product, not just after approval, in order to allow for clarity on exactly what the 'product' to be developed should be. These contracts should also avoid some of the well-known weaknesses with defence procurement, including cost overruns and management difficulties. Achieving these goals for antibiotics will require much further work.

Dun & Bradstreet sells corporate information, primarily to help companies make credit decisions. Historically customers paid on a piecemeal basis for each credit report. Its new revenue model requires shifting customers from a pay-as-you-go basis to paying for annual access to its databases and reports, and thus revenue has been delinked from the volume of use. Customers now pay for value, for access to valuable intelligence and information rather than for units (reports). Dun & Bradstreet needed to make this transition to a delinked revenue model quickly, as it saw looming competition from new internet platforms. For antibiotics, the threat is resistance rather than competition, but the urgency is similar.

Pre-purchase collaborative-marketing model

Knowledge Unlatched presented a model in which funding commitments to pre-purchase academic electronic books (e-books) were secured from academic libraries in advance on a project-by-project basis. Although these agreements are relatively short term in character, the funding is collaborative and more secure than existing alternatives for academic publishers. This collaboration has resulted in a reduction of costs for libraries thanks to shared costs, and publishers have had their costs covered and risks shared. This revenue model emphasizes the power of long-term relationships with customers (academic libraries) for a portfolio of products (academic e-books). Given the severe revenue constraints throughout academic publishing, any new source of funding was entirely welcome.

A key lesson here for antibiotics research and development might be (the value of) collaborative relationships with customers (here the libraries), enabling them to have a strong voice in what products come to market. Also, creating a 'central' fund set up and managed by a third party to pay for the e-books whereby libraries each pay a fixed fee per book was deemed to be essential. The advantage of wider engagement is also seen in achieving reduced prices per book as more libraries join the scheme. The analogy for antibiotics is that there is a need for collaboration among countries to contribute to the 'central' pot and that the more countries that join, the lower the payment required per country. Antibiotics, like academic e-books, have high fixed costs and low marginal costs.

The changes that BAE Systems and the defence industry underwent in order to enable 'service-availability' contracts also fit a pre-purchase collaborative-marketing model. The members of the industry needed to work together and move to this model of agreement

with their key customers; they could not deliver the capabilities needed and the products on their own. Companies that did not embrace this collaboration and way of working from the outset soon realized that they would be disadvantaged. Furthermore, the expense of the products means that governments may partner with other countries to produce a product. In consequence, national industries can end up partnering on programmes. The combination of partners on a product may mean that a partner on one product could be a competitor on another. For example, Lockheed Martin contends with competitor products to the multinational Typhoon aircraft but it partners with BAE Systems on the Lightning F-35.

Government-mandated target-framework model

Antibiotics companies share a common problem with energy utilities such as EDF Energy in that both sectors need their customers to buy fewer of their products. The UK energy industry is obliged as a matter of government policy (the Energy Company Obligation [ECO]) to improve the heating efficiency of the UK housing stock. This requires large investments that will result in customers using less of their product. Currently in a competitive market, any money that EDF Energy spends on energy-efficiency measures must ultimately be recovered from the customer. If EDF Energy raised its tariffs unilaterally to fund a non-mandated energy-efficiency programme, it would lose customers to competitors. This problem of collective action prevents energy efficiency unless all companies are required to participate at specified levels. To catalyse sufficient incentives, it has therefore been necessary for the government to mandate energy-efficiency measures across the industry, although only for larger firms.

In antibiotics, many free-rider problems exist that may be beyond the capacity of any company or country to solve. Similarly this may require a government framework and funding that helps to align incentives throughout the supply and use chain.

See Section 6 for how these various lessons need to be translated and tested further to address AMR.

In boxes 1–4 below are key points summarizing the models presented by the various industries.

Box 1: The Allianz model: Catastrophe cover and reinsurance

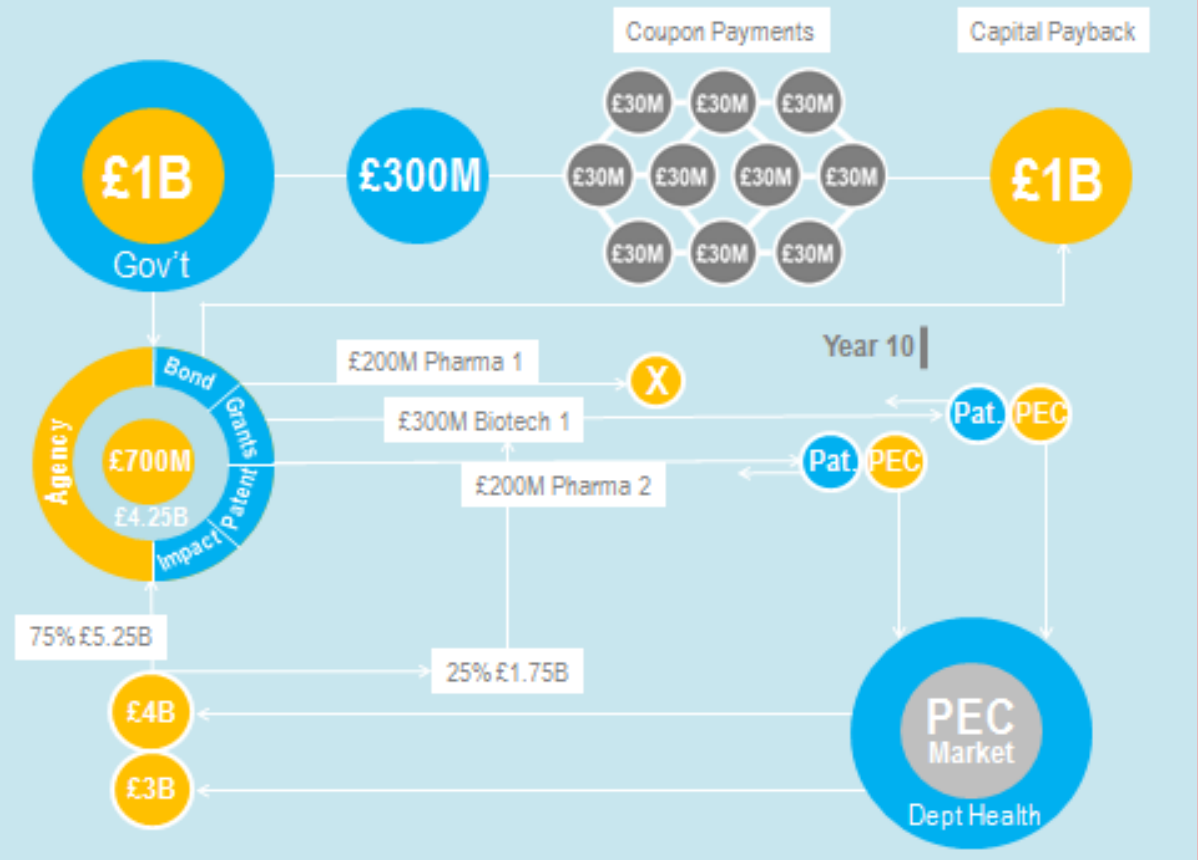
Owing to the volatility of situations being covered, insurance companies load up the annual premiums by about 30–50 per cent in expectation that insurance cover will be needed only every few years but then will be sizeable. This loading-up is to ensure that the expected payout should equate to about 70 per cent of the premiums paid over the years. For an event that occurs roughly once every five years, there is 0 per cent payout of the premium for four years of the scheme and then roughly 350 per cent of the premium paid out in the year when the event occurs. Insurance companies typically manage these types of risk through diversified investment, as well as by covering different types of catastrophe. They use reinsurance to cover extreme events – in essence this pools the risk between companies – and to ensure geographic spread. For a microbial

epidemic/pandemic insurance cover, the risk is managed in two ways: by an aggressive R&D programme to prevent the epidemic/pandemic in the first instance and by having the tools in hand (antibiotics) to monitor and prevent infection and to treat patients if and when required.

Box 2: The Barclays model: An antibiotic corporate bond

Barclays Bank shared a model borrowed from investment banking, in the form of an antibiotic corporate bond (ACB).

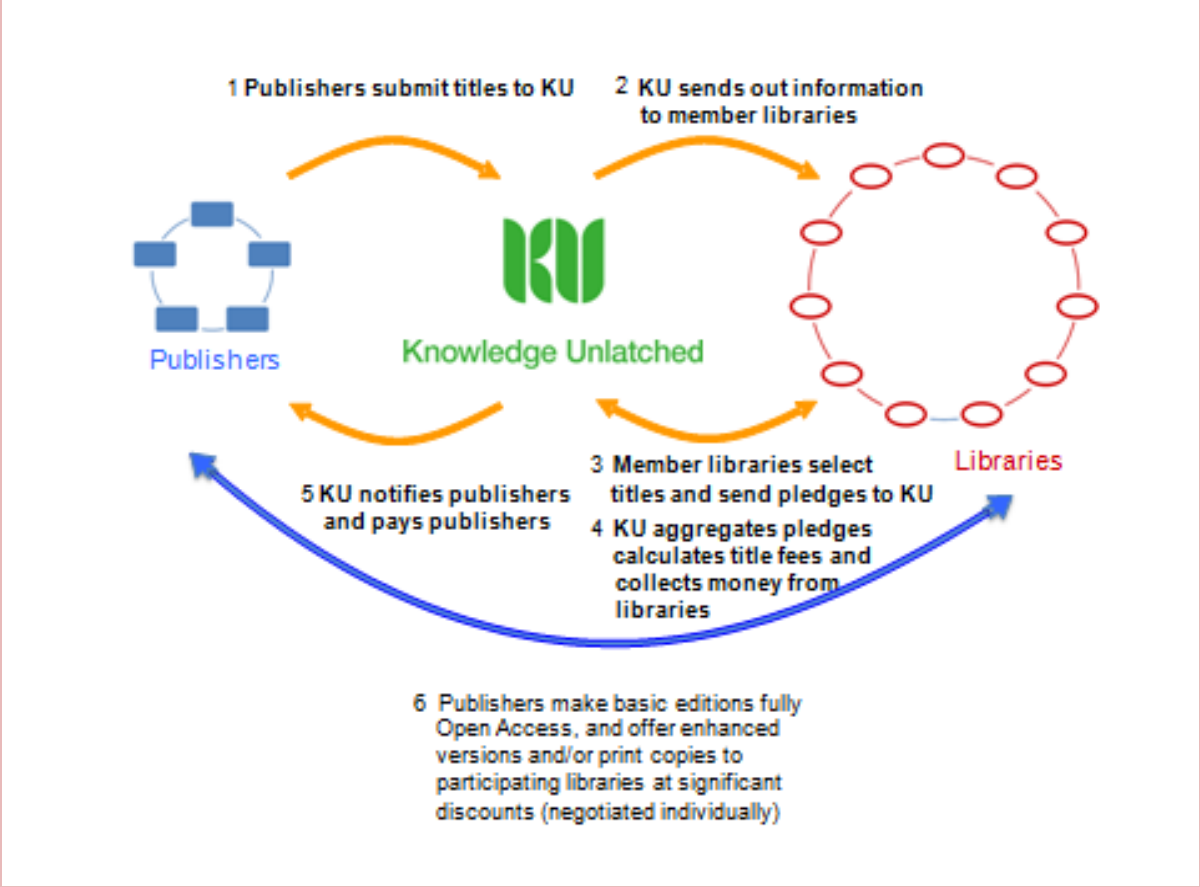
A 10-year bond is purchased by private investors and is government-backed, thereby reducing the risk for investors. Funds from the ACB are injected into research companies that have fulfilled the criteria for early development of an appropriate antibiotic against a profile of an identified public health need. The company does not need to pay back the funds it receives. The bond principal is repaid from the sale of patent-extension certificates, a controversial idea that delays generic entry for another drug.



Source: Barclays Bank.

Box 3: The Knowledge Unlatched model: A global consortium

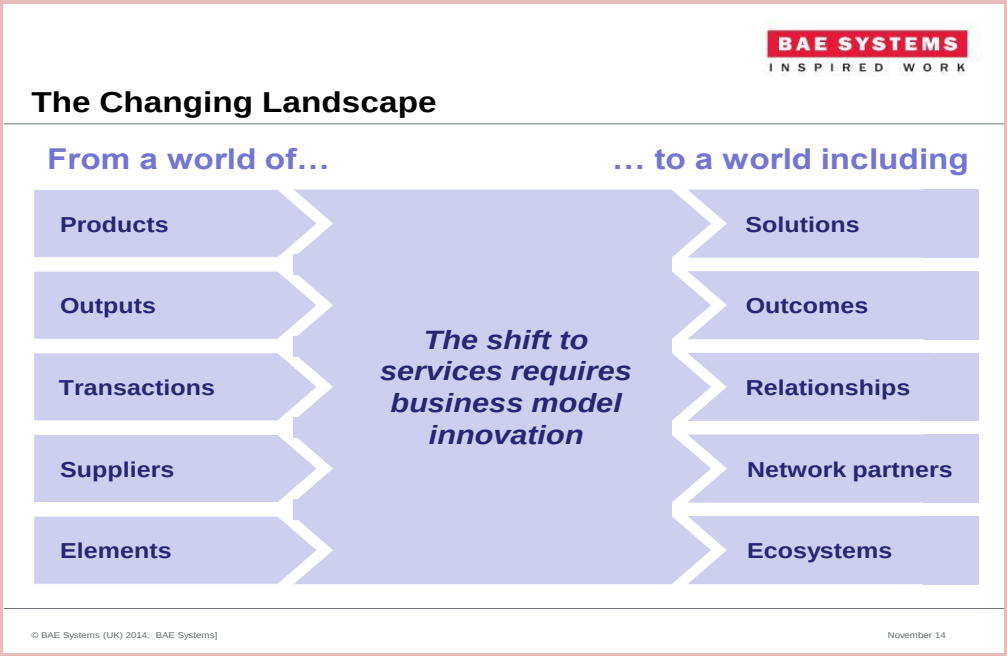
Knowledge Unlatched's model shows the power of developing a global consortium (in its case with academic libraries) that would pay the upfront costs of the product (the e-book). The consortium invests enough money to pay the costs from manuscript to the first digital file. In return, the publisher places the digital file in open access upon publication. Discovery tools find the content and readers can read the monograph with no pay barriers. The publisher can generate additional income through the sale of print versions, tablet versions and other formats. In some cases, these paid versions may have enhanced features or functionality. The upfront payment by the consortium of libraries covers publishers' investment costs, removing or reducing their financial risk. This model provides upfront funds, is self-sustaining for customers and producers and can be used for the delivery of many products. It also ensures open access as opposed to the older copyright-based model.



Source: Knowledge Unlatched.

Box 4: The BAE Systems model

The BAE Systems model addresses the transition from product development to service contracts with government. Every major aspect of its business model had to be reworked in view of the shift to services from products. Fifty per cent of its global revenue now comes from these service contracts, i.e. 'contracting for availability' and 'contracting for capability'.



Source: BAE Systems.

4 Process-design Considerations

This section provides further details on the models presented in Section 3 based on discussions at and since the Workshop about the lessons from these models and their applicability.

A clear message from the different models is that the path to the solution, including its simplicity and transparency, is as important as the solution itself. In view of that, this section focuses on four process-design considerations: new partnership collaboration models; drivers and facilitators for change; barriers and challenges to change; and timelines for change.

Where relevant, each subsection discusses the models and then the implications for antibiotics.

New partnership collaboration models

From the models it was clear that all stakeholders need to work together to address specific challenges and bring about wholesale change in their industry. Companies and organizations committed themselves to a specific infrastructural change (either organizational or industry-wide) to support a potential future event. For antibiotics, key stakeholders include

governments and companies but also physicians, pharmacists, healthcare systems, health payers, health technology assessors, patients and civil society.

For antibiotics, success is not measured solely by the approval of new antibiotics. We need high-quality antibiotics, directed at the greatest threats to human health.[21] In view of antimicrobial resistance, we must consider incentives and accountabilities for maintaining the approved antibiotic, for delivery and for any services contracted that may aid deployment, stewardship and delivery when needed. These post-approval issues are important and require special collaboration that aligns them with long-term incentives for society. And this is not a one-time effort; a regular and adequate supply through the research pipeline is needed.

The models highlight in what ways collaboration is needed and what factors can actually help to achieve it. With the insights gained from the Workshop, we identify three challenges in setting up, administering and sustaining appropriate collaborative partnerships for antibiotics. The challenges are:

- Managing global collaborations effectively
- Moving from selling 'products' to 'option-to-use'/'availability' agreements with key stakeholders
- Building trust with stakeholders, governments, the public and customers

These issues are taken in turn, within the model options described below. They illustrate how the different companies addressed these challenges and they show that there are linkages across the three.

Managing global collaborations effectively

Given the nature of the AMR problem, global collaborations must be thought about at four levels: 1) a global collaborative research effort led by a public–private partnership; 2) a global antibiotics fund to spur research and conservation; 3) a global procurement mechanism, akin to Gavi, the Vaccine Alliance; and 4) a global treaty or framework agreement to support improvements in appropriate access and use in every country.[22]

1. Creating independent third-party collaboration, a global antibiotics PPP, between companies and research bodies focused on R&D

There is significant support from major antibiotics stakeholders for much deeper collaboration among life science companies, academic institutions, research funders, universities and other stakeholders. This could take the form of a global PPP focused on the research and early development of antibiotics: a PPP entity would be set up either as an

[21] Outterson, K., Powers, J.H., Seoane-Vasquez, E., Rodriguez-Monguio, R., Kesselheim, A.S., 'Approval and Withdrawal of New Antibiotics and Other Antiinfectives in the U.S., 1980-2009', The *Journal of Law, Medicine & Ethics*, 2013, 41(3): 688–96.

[22] Outterson, K., Powers, J.H., Daniel, G.W. and McClellan, M., 'Repairing the broken market for antibiotic innovation', *Health Affairs*, 2015, 34(2): 277–285.

independent joint venture or as a strong collaborative network concentrating on common objectives, strategic direction and priorities. We refer to a PPP for collaboration on pooling resources as the Global Antibiotics Private–Public Partnership (GAPPP).

The Workshop discussions suggested a number of ways in which the GAPPP could be created. One of the strong messages was that a collaboration/consortium/joint venture is needed to bring about wholesale change. As well as for change of infrastructure, investment is needed to increase R&D funding. This is essential for attaining a 'critical mass' in discovery and development that will deliver results in early-stage work sufficient to overcome the high attrition rate that each organization currently faces on its own and to minimize the risk exposure of individual companies.

As with the Knowledge Unlatched model, this would bring together all the providers to jointly deliver against set needs/profiles that customers (governments and healthcare systems) identify as priorities. This powerful independent collaboration of private, academic and public-body partners would combine all the necessary skills, expertise and resources with a clear, coordinated focus on who within the collaboration is delivering against which profile. The defence industry 's experience further supports this.

The key research groups and companies involved are relatively few. Robust global coordination is essential, and the proposal discussed above could be built from the current New Drugs 4 Bad Bugs (ND4BB) collaborations under the IMI.

Working groups in the EU, the US, the WHO and elsewhere should not limit their vision to a national or regional approach but should explore a global PPP for antibiotics R&D (as now being discussed by the WHO). The exact nature of this needs to be explored further with an understanding of the how this organizational model would drive the changes needed and achieve the desired impact.

2. Creating a global antibiotics fund to manage the funding programmes

Besides the GAPPP collaboration, the Workshop stimulated thinking on the possibility of establishing a global antibiotics fund (GAF). Many stakeholders support the generation of a GAF, administered by an independent third party and accessible to many companies, academic institutions and public bodies, in order to fund the appropriate research, early development and good stewardship of antibiotics.

Alongside the major national funds such as the IMI, BARDA and key targeted research council funds, a GAF would be set up as an overarching fund to bring together all the small existing funds in the sector. It would also generate the additional finances needed.

It is envisioned that much of the financing from a GAF would support research efforts up to early phase I, but a GAF could also offer grants for early-stage development, underpinned by the concept of 'no strings attached to failure'. This would mitigate risk for venture capitalists and companies, especially for small biotechs, as they face more uncertainty than large

companies. It would mean that if companies fail to produce a new antibiotic, they do not have to give the money back. BARDA is a model for this, and could be built on. Its funding is 100 per cent non-dilutive, with almost no strings attached, and there is no repayment, whether there is failure or success. Some of the existing funds have some strings attached, which should be evaluated in due course.

It is important that such a fund should be financed sustainably. This could include one or more of the various funding mechanisms proposed in previous sections of this report, as well as existing funding sources. Funding could relate to both pre-launch and post-launch incentives for new antibiotics. The challenges to address are:

- Ensuring that a GAF generates sufficient external funds to help drive a transformational change to the delivery of innovative antibiotics
- Whether or not a GAF should hold and license antibiotics patents, akin to the Medicines Patent Pool[23]
- Setting up an appropriate model for governance of a GAF, including transparency and accountability

Further work by the IMI DRIVE-AB consortium, the US CARB, the WHO and the UK's Review on AMR could test how a GAF could be established and operated.

The models put forward at the Workshop highlighted that various funding and procurement models could also work in collaboration. For antibiotics, it is important to explore how independent funding from bodies such as the Wellcome Trust, the IMI and BARDA could coexist with funding and administration from a GAPPP and a GAF. All these groups could collaborate around a common framework besides participating in pooled funding.

Additionally, it is proposed that consideration should be given to setting up an EU BARDA-type fund.

3. An independent third party becoming the procurer and distributor of antibiotics

As mentioned above, a further evolution of this model could be that the global, central funding body (such as a GAF) also becomes the global procurer and provider of the antibiotics. This would be analogous to the model used by Gavi, the Vaccine Alliance. Gavi is an international organization bringing together public and private sectors with the shared goal of creating equal access to new and underused vaccines for children living in the world's poorest countries. It not only pays for vaccines but also stimulates their development and expanded production. By pooling the demand from developing countries for new vaccines and providing long-term, predictable financing to meet this demand, Gavi's business model influences the market for vaccines. It has secured, among other things, long-term commitments from donors for national immunization programmes and an innovative

[23] The Medicines Patent Pool, established by UNITAID, seeks to improve access to HIV treatments by licensing patents from originator companies and making them available non-exclusively to generic companies for sale in developing countries. This is designed to reduce prices in developing countries and also to enable the development of new fixed-dose combinations.

advance market commitment pilot programme for pneumococcal vaccines. The AMC is a form of delinked reward whereby the companies supplying the vaccine are rewarded separately for their investment in R&D in return for supplying products at close to their production cost. There has evolved both a predictable finance stream (both pre-launch and post-launch) and a commitment from companies to supply the vaccines at a predefined price. Some challenges will need to be overcome in order to apply this model to antibiotics: AMCs have been criticized as inefficient,[24] and antibiotics, unlike vaccines, can have harmful effects for others when used inappropriately.

The Knowledge Unlatched model stimulated thinking about ways in which an independent third party could act as a broker to connect public health payers with industries in an efficient way, e.g. to prioritize funding, delivery and focus against public health needs. It also instigated thinking about how the industry can work together to agree on cost ranges for a particular product (based on agreed criteria). That would enable simpler consistent pricing arrangements so as to help cover costs.

Further work is needed in order to understand how a third-party independent broker could have the desired impact and to determine how it ought to be set up, run and governed.

Another question that must be explored is whether or not a GAF should also be the global procurer and provider of antibiotics to customers.

4. A global treaty or framework to support appropriate access and use

Even successful research efforts will ultimately be futile unless global society takes better care of new antibiotics brought to the market. We need to ensure appropriate access to these lifesaving drugs while dramatically reducing inappropriate use. National efforts can delay resistance but resistant pathogens know no borders, and failure in one country threatens the health of everyone. Thus we need a global treaty or framework agreement that will articulate measurable goals for disease surveillance and antibiotics stewardship in every country. Some countries may require financial support in order to improve national laboratory capacity and to strengthen access, stewardship and appropriate use.

In the energy sector, EDF Energy was unable to convince its customers to buy less energy without direct financial incentives, and no one energy company can take that step without a clear agreement from government to share conservation costs fairly among the companies. For antibiotics, we face a similar problem of collective action. A global agreement can support national efforts to conserve antibiotics, with countries appropriately sharing the risks and benefits.

[24] Light, Donald W., Advanced Market Commitments: Current Realities and Alternate Approaches, Health Action International, 2009. Available at http://www.haiweb.org/31032009/27%20Mar%202009%20AMC%20Current%20Realities%20&%20Alternate%20Approaches%20FINAL.pdf.

Moving from selling products to 'option-to-use'/'availability' agreements

Moving towards 'availability' contracts requires agreement between relevant parties in advance about what should be included and the nature of any collaboration. In the defence industry, companies simultaneously collaborate with their competitors and compete with their collaborators. Many of the contracts have a prime contractor, but it then subcontracts with most of the industry. There is a long-standing understanding about this in defence, as individual companies are not able to develop the type of products required and to deliver value-adding services on their own. Thus although contracts are to be competed for, laws, waivers and systems allow for the collaboration needed in order to serve the government's defence needs and to ensure that any competition does not hinder its ability to act rapidly if necessary.

In the field of antibiotics, the need for collaboration is great, rooted in the biology of resistance. Resistance can be expressed across different pathogens and drugs both within and across classes. As a result, much of the collaborative effort to preserve antibiotics' effectiveness would be needed after regulatory approval. This would be a change from current practice.

Collaboration among antibiotics companies is already happening, e.g. in the IMI's ND4BB programme. However, these collaborations tend to be at the pre-competition stage. They may need to be expanded to the development and post-approval of antibiotics. For the types of collaboration being proposed, and especially when related to joint clinical and/or post-launch programmes, there may be a need for specific governmental guidance in order to ensure that anti-competition laws do not hinder the activities of PPPs.

As with the 'availability' contract and the proposals for collaboration discussed above, there is a need to test and explore the ways for companies to collaborate more effectively in the clinical phases of R&D and in the delivery of antibiotics after approval. As a further lesson from the defence sector, groups such as DRIVE-AB and the UK's Review on AMR would be well placed to explore all the conditions required to make collaboration successful.

Building trust

Without trust among key stakeholders, no change will take place. The EDF Energy experience underlines that customer trust, as well as trust between companies and government, is essential. In the energy sector, the government's role is to oversee the competition process and to ensure that incentives and policies are aligned in order to achieve efficiency targets. EDF Energy undertook background research to understand the government's priorities so as to work collaboratively. As part of this trust-building exercise, and given the competitive nature of the energy sector, it was important for companies that the framework set up by government allowed them a degree of flexibility and independence. Similar trust-building steps may be needed for all stakeholders in antibiotics.

In the defence sector, the commitment between the company and the customer is made many years before the service is expected to be needed. For this reason, there must be real clarity about what will need to be delivered. Trust is built by transparency about each partners' needs and also by being held accountable (and regularly checked against this) to deliver against the details of a contract. There are clear mechanisms for changing orders over the extended period of the contract and clear dispute-resolution processes are in place.

BAE Systems seeks to engender trust through key performance indicators. Once the product is available, the defence contractor is held accountable to very clear KPIs. They include the turnaround time for provision of the product and the degree of availability. A simple example of a KPI would be the number of aircraft in a fleet that is ready for service at any one time. KPIs can be tailored for many different forms of availability.

Dun & Bradstreet works to improve trust through greater transparency and by offering options. It changed from a 'price-per-report' model to an annual payment model for its intelligence in order to add value for its customers, thereby delinking from the unit–volume model.
An additional option in the pricing model that D&B offered was a fee based on a per cent (e.g. 10, 5 or 1 per cent) of customers' savings made thanks to information provided by it. Most of the time that would be significantly more than the cost of the Dun & Bradstreet contract. No one took that option, but it meant that customers were far more willing to pay the price that was being quoted for the annual service fee. Customers are still offered the choice to pay for individual reports; but with prices increasing regularly, they are incentivized to move to the new model.

Drivers and facilitators for change

Each of the business models had one of three strong drivers for change relevant for antibiotics: market drivers, societal drivers and financial drivers.

Market drivers
Market forces required change. This was the result of different causes, such as a burning platform or customer or government needs (sometimes government is the customer). In the defence sector, for instance, the government as the client wanted to ensure that companies could provide the required service arrangements and better manage their own expenditure. The Knowledge Unlatched initiative came about because of a desire to change the market, to use the internet and to extend to books and monographs the concept of open access successfully pioneered in the market for some academic journals by the Public Library of

Science (PLOS). Dun & Bradstreet realized that clients were requesting a change in its service for greater focus on reduction of risks (such as credit risks), and it had to take into account new competition from internet-based data providers.

In antibiotics, if the market environment does not change, life sciences companies with a broad portfolio will continue to switch their investment and work to other disease areas. And SMEs focusing only on antibiotics could face extinction.

Societal drivers
In some sectors, such as the energy industry, there was a 'societal need' for change. The prospect of climate change was the driver for enhanced energy efficiency, but it requires collective action, at the global level, followed up by governments implementing different relevant policies to achieve their national targets within a global framework. This global 'societal need' is evident also in relation to resistance to antibiotics, and any actions may need to follow a similar pattern in which international challenges/agreements are then addressed by national or regional initiatives.

Financial drivers
Financial drivers of change were very important. There was a need for a steady revenue stream, but the existing business model was becoming unviable as a result of external factors. This was particularly the case for Dun & Bradstreet and Knowledge Unlatched. Clearly, this is a critical driver for antibiotics too.

The Workshop also drew attention to important factors in catalysing change. These included:

- **The importance of effective 'champions'.** Creating Knowledge Unlatched required a 'champion' who could see and push forward an alternative vision and envisage how it could be made operational. The new proposal needed to encompass practical considerations, such as reducing waste in the supply chain, reducing the risk to publishers, covering origination costs, achieving open access and making the purchasing process easier. *We already have some 'AMR champions', mostly at the national level (e.g. Dame Sally Davies, currently Chief Medical Officer in England), but they need to be heard and to be able to take action at the international level in order to drive forward the necessary changes*.
- **The importance of generating a steady revenue stream, with increased transparency.** BAE Systems' experience shows how providing a service rather than just a 'product' can generate steadier revenue streams. Moving towards that model increased the understanding and transparency of the variability and complexity of all in-service support costs, enabling all parties to benefit. 'Risk-sharing' ('gain-share' and 'pain-share' mechanisms) can be seen as a facilitator, by reducing uncertainty about future expenditure and revenues, should actual costs markedly exceed expected costs. *In the antibiotics scenario, sustainable and predictable costs for healthcare systems and revenues for companies are essential.*

- **The importance of governments partnering and providing clear direction.** Government involvement is relevant for only some of the models, but the EDF Energy example shows the importance of governments providing strong direction and a regulatory framework. It is also important this is done in partnership with the relevant companies and civil society and with sufficient flexibility in the way targets can be achieved. This keeps competitive pressures on companies, ensuring that targets are met at the least possible cost. *It is clearly important that leading governments involved with antibiotics R&D should provide both this direction and the framework within which companies and other actors can move towards common goals.*

- **Meeting client expectations.** The Dun & Bradstreet example shows that as technologies change, consumers expect that the service provided to them will adapt accordingly in order to meet their needs. In these circumstances, competition is a powerful force to deliver the changes consumers want. Companies need to change rapidly and adapt or competition will drive them out of business. In a fast-moving environment, people are more open to considering new business-model ideas, including the risks associated with them.

What is missing in the drivers for change in the antibiotics market

We need to understand the drivers of the antibiotics market more clearly. We also need to engage the correct individuals globally in order to test the future-option proposals and to ensure a clear understanding of the type and magnitude of market changes needed to achieve the desired result.

Unlike in most examples, there are many 'customers' for antibiotics (and medicines in general): patient, payer, pharmacist, hospital and doctor, all of whom may need different incentives to manage antibiotics appropriately. Because there is no single driver of change, bringing it about is particularly complex. There are currently no incentives that target each of the various customer groups. Incentives, both financial and non-financial, may help in finding new ways to preserve the effectiveness of existing antibiotics and any new ones developed. The solutions should address the related issues of overuse of existing drugs and access to antibiotics in lower-income settings. In essence, such incentives relate to social and behavioural interventions.

The ultimate customer, i.e. the patient, does not have an effective voice in bringing about the change needed. To the extent that the consumer has any voice, it will not generally be informed by the need to limit resistance. Patients must be educated about when an antibiotic should or should not be used and be involved in bringing about the changes needed to manage the use of antibiotics appropriately.

This recognition highlights that there is a further need to address how patients and their civil society groups can gain a voice in the major global discussions to design policy responses to the crisis of AMR (such as DRIVE-AB, the WHO Global Action Plan, the UK's Review on AMR and the US CARB). In addition, incentives for all 'customers' should be aligned to ensure a rational use of antibiotics in every setting around the globe.

Barriers to change

There are always barriers to change in any industry, ecosystem or organization. The participants from the other industries discussed some of the barriers they faced and how they got past those challenges.

Insufficient trust

Establishing trust is very important in effecting change. In the energy sector, customers often do not trust companies. This means that any action driven by companies that requires customer engagement can be difficult to implement. To overcome this barrier, companies need to come up with imaginative ideas about how to build and sustain trust based on a realistic understanding of customer motivations. The experience of EDF Energy was that customers accepted investments in energy efficiency when they were not required to make a contribution under the Energy Company Obligation. But it was less successful in the Green Deal scheme in which consumers, although recipients of a significant subsidy, are required to make a contribution.

For antibiotics, patients have not responded strongly enough to warnings about creating resistance in, for example, *clostridium difficile* and methicillin-resistant *staphylococcus aureus*. Increased cooperation and coordination between the industry, government and media could help in raising customer awareness of resistance by focusing future stories on a possible lack of hygiene at hospitals and also on the difficulty in treating the infection as a result of resistance.

Mutual trust and understanding of the needs of both healthcare systems and private companies in antibiotics has been growing in recent years. Otherwise, all the engagement seen recently would not have been possible. There is a need, however, to bring down any further barriers that would block future developments.

Infrastructural/organizational change

Adopting new business models usually involves changing internal structures and incentives – not always an easy process. For example, Dun & Bradstreet required strong leadership throughout the organization in order to make the transition to revenue streams delinked from physical-product sales.

One of the crucial challenges for Dun & Bradstreet was that radical changes in its sales model necessitated wholesale revision in the training and compensation of its sales force. Different skills were needed, as was a willingness of the team to learn and adapt quickly. Where this did not happen, Dun & Bradstreet had to change the sales team and its leaders. Similarly, ‘delinkage’ in antibiotics will require strong leadership and fundamental changes in sales forces’ behaviour.

As it has not been tested before on this scale, departure from the traditional ‘price–volume’ model is not straightforward, and there is a need to ensure that several options are available for companies. Larger pharmaceutical companies might have more resources to adapt to big changes; but SMEs, with more limited resources, can face greater uncertainties. These need to be taken into account.

Hospitals, pharmacies and providers will not be motivated to change their antibiotics business model without leadership. As change costs time and money, there may be a need for upfront incentives to embrace and embed a change of business model along the antibiotics supply chain, including hospitals, clinics, healthcare providers and patients. This issue is acute both in wealthy countries and in low- and middle-income countries.

Additional research is needed to investigate which drivers will ensure that change happens. For good stewardship, a coordinated approach is required between numerous actors supported by government; and appropriate incentives, both financial and non-financial, are required for the entire supply chain. The UK's Review on AMR, the DRIVE-AB group, the US CARB and the WHO are well placed to explore these issues and how they can contribute best to good stewardship.

Timelines for change

The industries that went through significant business model changes emphasized that change does not happen overnight; it can take a long time. *But for antibiotics, time is of the essence*. There is strong evidence that the important changes required must begin immediately; otherwise it will be too late. The global political momentum supporting these changes has never been greater. Thus there is an urgent need to make use of it.

The Knowledge Unlatched model is a small-scale change in comparison to the challenge posed by antibiotics, and yet it took 18 months to convince stakeholders before a pilot scheme could be designed and run. The time from inception to execution was about four years. But once the pilot scheme began, there was significant momentum.

For BAE Systems, there has been a progressive evolution over the past 10 to 15 years, with several stages and with enhancements to the business model made over that time.

For Dun & Bradstreet, the initial transformation began about seven years ago. It took about three to four years to embed it in the business. Owing to the major change that was required, a staged approach was taken. Retraining staff took approximately 6 to 12 months. Implementation took another 12 months, and further adaptation and enhancements were needed in the years after that.

As an illustration of the lags in implementing changes in the AMR field, 'delinkage' models for antibiotics were first discussed seriously in 2009 at a conference organized by the Swedish government, which then held the EU presidency. Since that time, very little has been done to improve the commercial environment. The only notable exception is the GAIN Act in the US, which many observers consider will have only a limited impact.[25]

[25] Outterson, K., Powers, J.H., Daniels, G.W. and McClellan, M.B., 'Repairing the broken market for antibiotic innovation', *Health Affairs*, 2015, 35(2): 277–285.

Because we need a new business model to be embedded in the healthcare industry in 5 to 10 years' time, we must move fast to determine the business model options that we want to test. Even setting up and executing small pilot schemes take time.

Initiatives to re-engineer antibiotics business models should also assess the time taken to deliver and implement any new ideas proposed. Some initiatives can begin immediately, such as increased funding for basic research, monitoring and infection control. But in view of the time lags expected while the macro changes are put in place and start to have effect, interim solutions will be needed.

5 How Could This All Work as a System?

The problems of increasing resistance and a thin R&D effort are complex, and a menu of incentives and funding mechanisms will be required throughout the life cycle of an antibiotic. In this section, we draw on the analysis presented in previous sections of this report and provide examples of how some of these mechanisms could be linked together to create a holistic system.
As stated earlier on, it may be appropriate that different funding mechanisms and different collaborative partnerships/infrastructures are put in place for the R&D stage and for the post-approval and marketing stages.

Below are three illustrations of how several mechanisms could be combined together.

Illustration 1: A combined approach that includes both pre-approval and post-approval incentives

There are three aspects to this approach:

a) Creation of a global antibiotics public–private partnership (GAPPP)

Pharmaceutical companies have sometimes come together to create an independent entity, for example the HIV company ViiV, as a joint venture between three companies. The proposal here is that besides companies coming together, public bodies should join with companies to create a new PPP to focus on collaborative research on antibiotics and their clinical development.

A global antibiotics private–public partnership/consortium of private companies, academic institutions and public bodies should be established. A GAPPP should be sustainable, independent and self-funding from operations. Preferably it would be independent, although it could be made to work as a virtual PPP. It would be a collaboration of resources and science focused on the research and early development of antibiotics in line with

predefined public health-need profiles. This partnership is more likely to reach a 'critical mass' of compounds in early R&D than are companies and institutions working alone.

b) Creation of a global antibiotics fund coordinating with key national targeted funds

Alongside the major national funds such as the IMI, BARDA and key targeted research council funds, a global antibiotics fund would be set up to bring together all the small existing funds in this area as well as to generate additional finances in order to deliver the greater funding needed. A GAF would provide monetary support to a GAPPP so as to enable the R&D needed in response to identified public health needs globally. It would work with existing funds for awareness of the work each is supporting and would collaborate with them in agreeing the priorities and direction for funding and determining courses of action.

In this illustration, access to grant-funding could be gained by making a precommitment to accept that after approval of the new antibiotic, the organization would have to agree to a 'delinkage' regime. It could not commercialize the antibiotic in the standard 'price–volume' model; the antibiotic would be used and targeted only where and when needed.

c) Funding and administration

A GAF should aim to be self-sustaining, and therefore funding needs to be available in advance of antibiotics' development and approval. Besides the funding coming from the amalgamation of the small currently existing funds for antibiotics research, one option is a 'premium' payment by governments at a set percentage of national expenditure on antibiotics. A level of 10–20 per cent in wealthy countries could be sufficient. Other options include a user fee on non-human uses of antibiotics.[26] Barclays also proposed financing and replenishing funding with models such as the ACB–PEC mechanism. Other funding mechanisms should also be explored.

As part of the ACB–PEC model put forward by Barclays, it is proposed that an agency (possibly a GAF itself) should be created that administers the whole ACB generation, the investment of funds, the sale of the PECs that are awarded and the subsequent distribution of funds from the sales. Some of these funds would be given back to the organization that developed and licensed the new antibiotic.

Rather than as a one-off payment by this agency to the organization that developed the antibiotic (potentially a GAPPP), this payment could be set up as a 'service-availability' contract and be spread over 5–10 years and linked to KPIs agreed on by the main customers for the antibiotic. It is important to ensure that it is attractive for the organizations not only to develop the new antibiotic but also to be incentivized to support delivery, good stewardship and appropriate use when needed. The payment method to the developing organization should adequately compensate for any services that the organization would be asked to deliver and should be large enough to ensure that it incentivizes organizations to develop the antibiotics and to set up these 'service-availability' agreements. The annual

[26] Hollis, A. and Ahmed, Z., 'Preserving antibiotics, rationally', *The New England Journal of Medicine*, 2013, 369(26): 2474–76.

payments could be determined so as to include an appropriate return on investment for organizations. The KPIs to trigger payments could include:

- Keeping the antibiotic registered globally
- Keeping manufacturing capabilities and capacity current and at an appropriate level of preparedness
- Ensuring, setting up and maintaining the ability to distribute and deliver the antibiotic when needed
- Providing the professional education required to ensure appropriate use of the antibiotic
- Potentially providing a continuous monitoring programme

But trying to create one mechanism that covers all phases of the research, development and marketing of an antibiotic could overcomplicate matters.

Illustration 2: Separate pre-approval and post-approval-funding schemes

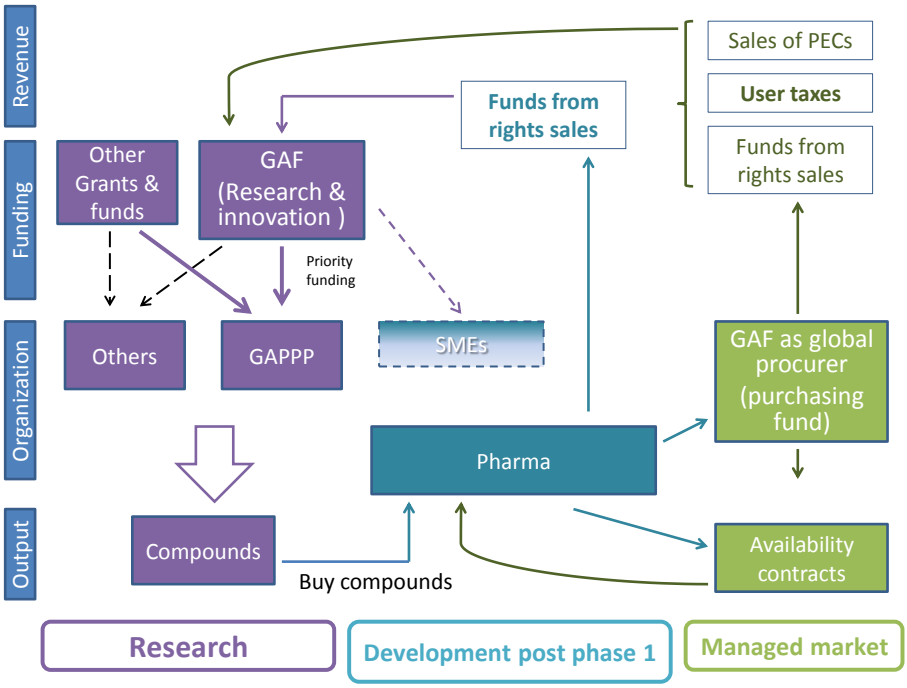
As with Illustration 1, consideration should be given to a GAPPP of private companies, academic institutions and public bodies established to pool resources and science in order to address R&D for antibiotics. Separate funding mechanisms can be put in place to create the finances needed to a) fund innovation and research to enable getting a compound to phase 1 of development, b) pay for development and then c) fund all the services needed to keep the antibiotic available for use, i.e. to maintain, manufacture, distribute and deliver it as needed.

Lessons from BAE Systems' 'service-availability' contracting model and Allianz' catastrophe insurance model indicate how this could be applied to the antibiotics sector.

In the pre-approval stage, funding could be provided by the national and regional funds that already exist, in parallel with a newly formed GAF.

This illustration suggests two options. The first option assumes that large pharma could do the development from the phase 2 clinical trial to approval and assume the risk and funding. The assumption would be that any post-approval agreed payments would compensate for these costs and bring an appropriate return on investment. The second option is that SMEs could take on the development from phase 2 and find ways to secure investment and funding.

Figure 1: Holistic application of all proposals in to one system



a) '*Service-availability' agreements/insurance-type policies*

Large organizations. In the event that a large organization has developed a new antibiotic and it is approved, a separate funding mechanism would come into operation. This post-approval system would consist of 'service-availability'/'option-for-use' agreements between the developer/deliverer of the antibiotic and the governments and healthcare systems in need of it (or an independent body acting on their behalf). During development, the organization would look to secure contracts with its customers, i.e. to gain agreement that governments would pay an annual fee (for the commitment to provide the product and the services to deliver it) delinked from the volume of sales.

'Service availability' would cover the supply chain (manufacturing capacity and delivery of product), maintenance of regulatory approvals, post-approval pharmacovigilance, adverse-event reporting, education of healthcare professionals on how to use the antibiotic and similar requirements. It would also focus on issues specific to antibiotics, for example delaying resistance and building better surveillance datasets to guide policy and the health impact of the programme.[27] The annual premium paid to the developer would ensure covering the costs of developing the antibiotic and providing the post-approval availability service and would factor in an appropriate profit. This profit margin is needed to ensure that developers are enticed back to developing antibiotics and that they stay in the field.

Small and medium-sized enterprises. If SMEs were to take on the development of a new antibiotic from phase 2 onwards, they would probably need to look for further investment

[27] Outterson, K., Pogge, T. and Hollis, A., 'Combating Antibiotic Resistance Through The Health Impact Fund', in *The Globalization of Health Care: Legal and Ethical Issues*, Glenn I. Cohen, ed., Oxford University Press, 2013, Ch. 18.

and funding in order to reduce their risk. It is expected that like large organizations, SMEs would early on in development come to an agreement with their customers on 'service availability'. Agreement on 'service-availability' contracts should then enable the SMEs to secure further finance from investors in relation to expected returns from customers once the antibiotic is approved. Additionally they may look to the GAF and other national and regional funds to help with funding through to development and not just through the research phase.

b) Insurance-type schemes supporting a focus on pandemics and regional resistance

For agreements made with governments about services needed in the event of a pandemic, additional steps could be taken. Owing to the unpredictable nature of a pandemic, the annual 'service-availability' premium charged to governments would need to be higher. This would ensure that sufficient funds are built up in years with no pandemic in order to cover the cost of supplying services when a pandemic does arise.

The contracted organization needs to work out the costs to it of responding rapidly to a pandemic, for example for quickly manufacturing the antibiotic and delivering it to the affected regions. As with insurance premium calculations, the total estimated cost is then divided by the number of years expected between events, i.e. from when the contract is signed to when modelling shows that a pandemic may arise.

Insurance companies' catastrophe policies show that calculated premiums would need to be frontloaded and raised by 30–50 per cent so that companies can amass the funds needed to cover all the costs of responding when a pandemic occurs and of the risk element relating to its unpredictable size and timing. But owing to the regulatory process, developing a new antibiotic from scratch will take time. Additional changes to streamline regulations might be needed, as in the recent case of Ebola; and that was possible only because governments had invested in basic Ebola research for more than a decade.

It is expected that several governments would establish these policies with the various companies/organizations or the GAPPP that has developed the antibiotic and that, as a result, the full costs would be covered and the companies would make a profit (i.e. they would have an incentive to make and deliver the antibiotic). Alternatively the companies could license the drug to the global agency and turn the production and delivery functions over to a global agency, as discussed below in Illustration 3.

Additional information from the defence industry is needed about how these models work in practice, and the government's perspective is necessary too. The UK's Review on AMR would be well placed to investigate this further with the aim of making proposals to governments. The IMI DRIVE-AB groups could model and test the impact of these potential changes.

Illustration 3: Buy-out option of approved antibiotics to a delivery company

A further evolution would be to consider whether or not the registered antibiotic should then be licensed for the full term to a global agency akin to the Medicines Patent Pool. This delivery entity (possibly a GAF) would eventually own several new antibiotics and would be the body that works with governments/healthcare systems to generate and deliver against the appropriate 'service-availability' contracts. It would be responsible for service tasks such as maintaining registration and ensuring production and distribution.

The pros and cons of these various illustrated options need to be tested. It is suggested that the IMI DRIVE-AB consortium work plan and the US CARB programme could most appropriately explore them.

6 Areas to Explore Further and Recommendations for Further Programmes

In the antibiotics sector, governments and health services are the customers. They can determine the profile of the antibiotic, the diagnostic and the vaccine required to address the public need.

The case studies of models from other industries presented at the Workshop raised a number of areas in which further modelling, research and testing are needed in order to determine whether or not these models could be applied to the antibiotics sector, could work robustly and could achieve the aims we are looking for.

a) Funding-model considerations

Several further matters, set out below, must be addressed as these various funding models are explored further.

- How can the various funding-model proposals generate sufficient external funds to drive a transformational change in the delivery of innovative antibiotics.
- What volume of additional funding is needed? What is the process for determining this global budget?

'Service-availability' agreements/insurance-type premiums

- If 'service-availability' agreements with annual insurance-type premium payments were put in place, what level of payment could governments afford and what level of funding could be raised from this 'annual premium' paid by governments?

National and regional funds plus creating a global antibiotics fund

- How can existing regional and national funds be better coordinated?
- How could a GAF be established and administered by an independent third party, and be accessible to companies, academic institutions and public bodies, in order to fund the appropriate R&D and good stewardship of antibiotics?

    - What would be needed to get governments to endorse and support such an approach?
    - How would an independent agency (possibly a GAF) arrange with all the governments and health services involved what the requirements are for given products?
    - How would that agency work with the various companies to ensure that the requirements for a product are provided and that companies receive an appropriate reward for delivering the product?
    - How would various funding and procurement models exist in parallel? How could funding from bodies such as the Wellcome Trust, IMI or BARDA coexist with funding and administration from a GAF?
- Should a GAF also be the global procurer and provider of a product to customers?

Creation of a government-backed antibiotic corporate bond

- How should be evaluated the efficiency, fairness and unintended consequences of schemes such as the antibiotic corporate bond for various repayment mechanisms (including PECs)?
- What are the modifications needed in the ACB–PEC scheme to make it work for all stakeholders?
- How should be tested the economics of an ACB and whether or not it can function with or without a PEC?

User fees for non-human uses

- How would the feasibility of a user fee for non-human uses of antibiotics be established?

b) Environmental/process considerations

Public–private partnerships

- How could a global antibiotics PPP focused on the research and early development of antibiotics be established? How could different industry, academic and public-body players be involved so as to generate a 'critical mass' in discovery and development and fill the supply pipeline while minimizing the risk exposure of individual companies?
- What is the best way to identify the potential collaborations needed to make these various business models a success and for them to be effective and efficient?
- How should be expanded collaboration between companies and research organizations after approval of antibiotics as well as for R&D?

Working with governments to promote access, conservation and innovation

- Global efforts on access, conservation and innovation may require a global treaty or framework agreement.
- Political momentum is necessary; and as key AMR stakeholders are already talking to each other, this momentum should be appropriately used. Along with it, there needs

to be clarity about the measures and targets that are communicated publicly and about who is accountable for delivering these measures.

- In energy, customer trust is essential. But trust is also crucial between companies and government. EDF Energy did background research to help shape the government effort. It is important that governments set a framework for what the industry needs to deliver in addressing the AMR challenge, but a framework must also be created that allows companies and organizations to provide input in the design phase and also affords some independence for implementation within the framework.

Competition law

- It is necessary to explore what is needed (waivers, new guidance from governments etc.) to ensure that competition policy does not hinder the necessary collaborative actions required in the antibiotics sector.

Incentivizing all the appropriate points in the entire supply chain

- If companies are expected to lead on conservation measures with their customers, there must be a clear understanding of what incentives are needed for hospitals, GPs, dentists, pharmacists and patients in order to embed and sustain the changes needed.
- These changes must be global but must also be painstakingly adapted to the unique conditions in each country.

7 Summary and Conclusions

Learning from other industries has been a very fruitful exercise. They have offered a different perspective on how to tackle the AMR issue, and provide relevant analogies to consider. This report has highlighted a number of key lessons about how these industries have adapted to diverse challenges in their external environment. For them, it was a matter of adaptation and flexibility to ensure success. And the report has shown that although change is difficult and requires substantial effort, cost and time, it is more than possible when all the necessary stakeholders are aligned.

Based on these lessons and on our own review over the past few months, we now articulate three essential messages:

1. There is a need for global collaboration on a scale not seen before in relation to AMR. Many independent initiatives are under way nationally and regionally, but these need to be brought together to engage on a global scale. This report is designed to help bridge these various efforts and move towards consensus for global action. The proposals for a GAPPP and a GAF are a possible way forward for pooling skills, resources and funding in order to ensure a long-term, sustainable solution. A global treaty or

framework agreement might be needed to ensure access to antibiotics and their appropriate use, including surveillance.

2. There is a need to start thinking about 'service-availability'/'option-to-use' agreements/contracts between developers/manufacturers and healthcare systems as a means to support the 'delinkage' concept. As in defence, products are developed but kept on the shelf, maintained and ready when needed, including all the services to deliver them effectively and efficiently. Long-term contracts with customers ensure that the services they require are available when needed. Innovators of new antibiotics should not be rewarded with the traditional 'price x volume' model; they should focus more on delivering the product, resources and services when needed. In the life sciences sector, there is already a move beyond the traditional 'price-per-pill' model. But the idea of a 'service-availability'/'option-to-use' model goes beyond that. Governments would pay an annual 'service-availability' fee/premium delinked from the volume of sales. Enough resources need to be available to guarantee that new antibiotics can reach a patient in any place as soon as they are needed, but only when needed. Lessons from the insurance industry indicated how these annual 'premiums' could be calculated.

3. Customers (in the broadest sense) must be engaged in order to ensure that the right incentives, both financial and non-financial, are aligned from bench to bedside. We should not focus on incentives just for companies but must include prescribers, health systems, patients and all other stakeholders.

We very much hope that the ongoing initiatives and programmes in the antibiotics field will actively consider our ideas and recommendations. It is important that the most is made of the current political momentum across the globe to tackle resistance to antibiotics. This is the time to move, and we need to move quickly.

Appendices available at:
www.biginnovationcentre.com/publications

Acknowledgments

Research and authoring contribution

Office of Health Economics Research & Consulting

BU School of Law

Supported and sponsored by

wellcome trust

Technology Strategy Board
Driving Innovation

MRC Medical Research Council

Contributing companies

Allianz

BAE SYSTEMS

BARCLAYS

D&B

eDF ENERGY

Knowledge Unlatched

Additional research support

KPMG Global

About the Authors

Ella Jaczynska

Ella Jaczynska is Vice President in GlaxoSmithKline's (GSK) Corporate Strategy Group. She is seconded, as an innovation leader, to the Big Innovation Centre and leads the Health Plus Action Group, devising and driving projects in the health sector that cannot be resolved by the health industry on its own. She is a physiologist and pharmacologist by training with 23 years' experience in pharmaceutical R&D. Most recently, she directed the Infectious Diseases Global Regulatory Group in GSK. She was responsible for leading the regulatory support in GSK's discovery and development portfolio for antibacterials, antivirals, HIV and diseases of the developing world. She was an active member of the Association of the British Pharmaceutical Industry and the pharma antibacterials working parties that collaborated with the European Medicines Agency, the Medicines and Healthcare Products Regulatory Agency and the US Food and Drug Agency to bring necessary changes and updates to the regulations for the development and licensing of antibacterials.

Kevin Outterson

Kevin Outterson is Professor of Law and N. Neal Pike Scholar in Health and Disability Law at Boston University. He is an associate fellow at Chatham House and a founding member of the Antimicrobial Resistance Working Group at the Centers for Disease Control and Prevention in the US. For the past decade, his academic research has focused on the legal ecology of antimicrobial resistance. At Boston University, Professor Outterson co-directs the Health Law Program and is Editor-in-Chief of the *Journal of Law, Medicine and Ethics*.

Jorge Mestre-Ferrandiz

Jorge Mestre-Ferrandiz is Director of Consulting at the Office of Health Economics (OHE), which he joined in 2001. He spent 2005 at Farmaindustria, the Spanish pharmaceutical trade association. He rejoined the OHE in 2006 as a senior economist, becoming Director of Consulting in July 2012. He is a well-known economist in the economics of the life sciences industry, with more than 20 publications on the subject, and is regularly invited to international conferences, both academic and more commercially orientated. Mr Mestre-Ferrandiz has a PhD from the Universidad Autónoma de Barcelona, is an honorary visiting lecturer in the Department of Economics at City University London and is an honorary research fellow with RAND Europe.

The Royal Institute of International Affairs
Chatham House
10 St James's Square, London SW1Y 4LE
T +44 (0)20 7957 5700
F +44 (0)20 7957 5710
contact@chathamhouse.org
www.chathamhouse.org
Charity Registration Number: 208223

Big Innovation Centre
Ergon House
Horseferry Road
London SW1P 2AL
T +44 (0)20 3713 4036
h.lawrence@biginnovationcentre.com
www.biginnovationcentre.com