

**Superbugs and Super risks: A critical assessment of antibiotic
resistance as a frontier topic in responsible and sustainable
investment**

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ABSTRACT

According to the World Health Organization antimicrobial resistance is one of the biggest threats to society today. The Chief Medical Officer in the United Kingdom, Dame Sally Davies, spoke in 2013 of an apocalyptic scenario in the near future in which people undergoing simple medical procedures die of routine infections “because we have run out of antibiotics”.

Antimicrobial resistance (AMR) is multidimensional by nature with a plenitude of both actors and causes. One aspect that is not adequately understood is the common ground between the issue of AMR and the contribution that might be played by investors. In search of clarity, this dissertation maps out the antimicrobial resistance problem and a potential solution, Responsible investment. The objective is to discover if and how investors resources can be deployed in order to support action to tackle antimicrobial resistance specifically in the pharmaceutical sector.

By interviewing thirty-three experts and contrasting the theory with reality, the research identifies that AMR was a market failure that needs a public policy intervention. *Prima facie*, AMR demonstrates some of the characteristics that may encourage investor action and investors have (or could have) a role to play in the development of appropriate responses, albeit a modest one. This role is a) encouraging public policy interventions on AMR collectively rather than corporate engagement and b) when the funding gap has been defined, by allocating investment towards solutions.

The research confirms the literature, which suggests neither companies nor investors have a compelling business case for investing in new antibiotics. The research supports the literature suggesting the catalysts behind investor attention and action on environmental, social and governance issues and extends the existing body of knowledge on antibiotic economics, which have largely focused on macro-economic implications to date. The research identified a pocket of interest in exploring a conventional bond for funding AMR solutions. This contrasts with the literature, which a) did not appear to recognise the potential role of the private sector and b) tended to emphasise the role of foundations and government financing.

Consequently, the research recommends the creation of a collective initiative for investor policy engagement on antimicrobial resistance. It also calls for further research to define the funding gap and to enable clarity on who should finance it. If the answer includes investors the research helps identify some of the characteristics investors require to allocate capital.

DECLARATIONS AND STATEMENTS

This dissertation is my own work and contains nothing which is the outcome of work done in collaboration with others, except structuring and editing support and other as specified in the text and acknowledgements. It has not been previously submitted, in part or whole, to any university or institution for any degree, diploma or other qualification.

I give consent for the dissertation to be available for entering into the CISL library for photocopying, and for the title and summary to be made publicly available.

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CONTENTS

ABSTRACT
DECLARATIONS AND STATEMENTS
ACKNOWLEDGEMENTS

LIST OF TABLES
LIST OF FIGURES
LIST OF ACRONYMS

CHAPTER 1: INTRODUCTION

1.1. Context
1.2. Scope of research
1.3. Aims and Objectives
1.4 Dissertation structure

CHAPTER 2: LITERATURE REVIEW (1) ANTIMICROBIAL RESISTANCE AND RESPONSIBLE INVESTMENT

2.1. Antimicrobial Resistance

2.1.1 History and context
2.1.2 The problem
2.1.3 The causes
2.1.4 The public policy landscape
2.1.5 Composition of actors
2.1.6 Which companies are relevant and what role do they play?
2.1.7 Which companies does this research focus on?
2.1.8 The commercial implications

2.2 Responsible Investment

2.2.1 Context
2.2.2 Why investors care about responsible investment
2.2.3 Under what circumstances do investors have an interest in taking action on ESG issues?
2.2.4 What are the key areas for investor action to help to address ESG problems?

CHAPTER 3: LITERATURE REVIEW (2) APPLYING THE RESPONSIBLE INVESTMENT LITERATURE TO ANTIMICROBIAL RESISTANCE

3.1. Why would investors care about AMR?
3.2. Do investors have an interest in taking action?
3.3 What actions can investors take to help the AMR problem?

CHAPTER 4: METHODOLOGY

4.1. Literature Reviews
4.2 Interviews
4.3 Questions
4.4 Method of analysis

CHAPTER 5: RESULTS

- 5.1 Research question one
 - 5.1.1 Synopsis of results for research question one
- 5.2 Research question two
 - 5.2.1 Synopsis of results for research question two
- 5.3 Research question three
 - 5.3.3 Synopsis of results for research question three

CHAPTER 6: DISCUSSION

- 6.1 Research question one
 - 6.1.1 Interpretation
 - 6.1.2 Implications
- 6.2 Research question two
 - 6.2.1 Interpretation
 - 6.2.2 Implications
- 6.3 Research question three
 - 6.3.1 Interpretation
 - 6.3.2 Implications
- 6.4 Synopsis
 - 6.4.1 Key findings
 - 6.4.2 Limitations

CHAPTER 7: CONCLUSIONS & RECOMENDATIONS

- 7.1 Context of conclusions
- 7.2 Conclusion by research question
- 7.3 Reflections
- 7.4 Recommendations
- 7.5 Further research
- 7.6 Contribution to scholarly knowledge

CHAPTER 8: REFERENCES

- APPENDIX 1: Causes of antimicrobial resistance
- APPENDIX 2: Push and pull mechanisms

LIST OF TABLES

Table 1: Interview 'heatmap' response coding
Table 2: Results – Why would investors care about AMR?.....
Table 3: Results - Do investors have an interest in taking action on AMR?...
Table 4: Results - What, if anything, can investors do to help the problem?.....
Table 5: Identifying where action could be catalysed.....

LIST OF FIGURES

- Figure 1: Development of antimicrobial resistance.....
- Figure 2: The mechanisms of antimicrobial resistance.....
- Figure 3: Decline in new antibiotic development with increased resistance....
- Figure 4: The antimicrobial resistance risk/opportunity spectrum.....
- Figure 5: Attributes that determine the responsiveness to investor advocacy.....

LIST OF ACRONYMS

AMR	Antimicrobial Resistance
AuM	Asset under Management
BBFAW	Business Benchmark for Farm Animal Welfare
CDC	US Centres for Disease Control and Prevention
DRIVE-AB	Driving Reinvestment in R&D and Responsible Antibiotic Use
ESG	Environmental, Social and Governance
FAIRR	Farm Animal Investment Risk and Return
FAO	Food and Agriculture Organization of the United Nations
GAP	Global Action Plan on Antimicrobial Resistance
LMICs	Low- and middle-income countries
MDR	Multi-drug resistant
MRSA	Methicillin-resistant Staphylococcus aureus
MSCI	Morgan Stanley Composite Index
NAP	National Action Plan
ND4BB	New Drugs for Bad Bugs
OTC	Over-the-counter
ReAct	Action on Antibiotic Resistance
R&D	Research and development
SMEs	Small and medium-sized enterprises
NGO	Non-Governmental Organisation
ODA	Official Development Assistance
PRI	Principles for Responsible Investment
UN	United Nations
WHO	World Health Organisation
WEF	World Economic Forum

CHAPTER 1: INTRODUCTION

1.1 Context

Antibiotics revolutionised the treatment of bacterial diseases following the discovery of Penicillin in 1928 by Alexander Fleming. Their use became widespread by the 1930s and underpin many of the greatest medical advances of the 20th century. On average, antibiotics add twenty years to our lives (Davies, 2015).

However, bacterial diseases have always evolved to resist the actions of new drugs (O’Neil, 2016). This resistance has become a problem in recent years because the pace at which we are discovering new antibiotics has slowed drastically, while antibiotic use and misuse is rising (Farrar, 2014).

Without effective antibiotics, health systems will collapse (Tomson & Vlad, 2014), with commonplace medical interventions, such as hip replacements and chemotherapy becoming too risky to perform due to infections.

Antimicrobial Resistance (AMR) is multidimensional by nature with a plenitude of both actors and causes. One aspect that is not adequately understood is the common ground between AMR and Responsible Investment (RI).

The impact of antibiotic resistance

With resistance on the rise, AMR is important because we stand to lose the major advances in modern medicines including a) progress against pneumonia, tuberculosis and malaria b) chemotherapy c) surgical procedures, including routine operations such as caesarean sections.

As well as the potential costs to human life, the predicted costs to the economy are grave. The O’Neill Review estimates that, without action, by 2050 AMR will cause circa ten million annual deaths globally, reduce gross domestic product (GDP) by 2– 3.5% and cost US\$100 trillion. In 2017, the World Bank estimated that the impact on global GDP may be even greater, with an annual cost of up to US\$ 3.4 trillion by 2030.

At a company level, the food sector is facing increased pressure, from both policy makers and civil society, to phase out the routine use of these drugs in intensive livestock production (Woolhouse and Farrar, 2014).

The healthcare sector is both a user and a producer of antibiotics. Given that the foundations of modern medicine rest on the use of effective antibiotics, the implications are sobering for this industry. In the case of private health insurance companies, Methicillin-resistant Staphylococcus aureus (MRSA) infections incur costs 3 times greater (US\$50,000 more per patient) than the cost with no infection (Antoñanzas et al, 2015).

Investors in all these companies require a financial return. Therefore, if the aforementioned impacts of AMR happen then there are negative consequences for investors too.

The link with responsible investment

RI is an approach to investing that aims to incorporate environmental, social, and governance (ESG) factors into investment decisions, to better manage risk and generate sustainable, long-term returns - Principles of Responsible Investment (PRI) definition.

ESG factors relate to environmental (e.g. water and energy consumption), social (e.g. human rights), and corporate governance factors (e.g. boardroom pay).

Waygood (2011) describes the various reasons for investors to pay attention to ESG issues. From an investment perspective, the analysis of ESG issues is required to make a full assessment of the risks and opportunities associated with particular investments. This should enable investors to make better investment decisions and contribute to a higher quality conversation between companies and their investors on drivers of long-term value creation. These actions should, in turn, result in capital being directed towards better managed companies, and towards companies that are better positioned to contribute to the goals of a sustainable society.

The actors are companies, investors, research and ratings providers, non-governmental organisations (NGOs), policy makers and regulators (Sparkes and Cowton,2004). Research providers offer information that investors use to assess company performance on ESG issues; investment banks analyse how ESG issues impact on the financial fundamentals of a company; governments provide the regulation that determine how companies respond to particular ESG issues; and NGOs scrutinise and challenge the performance of companies and investors on ESG issues. There is a dynamic and interactive relationship between these actors.

For instance, investors can encourage companies to improve their reporting on ESG issues, which can drive improvements in the quality of research generated by investment banks and ESG research providers and can guide the design of public policy.

In turn, the conclusions drawn by investment actors about companies' ESG performance may lead to companies improving their performance or investors changing their investment decisions.

AMR is an emergent ESG issue compared to other concerns, such as climate change. Yet AMR may present a greater danger to humankind than cancer by 2050 and could cut global Gross Domestic Product (GDP) by 3.5%, at a cumulative cost of US\$100bn (O'Neill, 2016).

While there has not been a great deal of academic research specifically looking at AMR as an ESG issue there is the small, but growing, niche of antimicrobial economics, of which the O'Neill Review is the most comprehensive example.

There is also a significant body of scholarly work discussing how investors can influence companies and how investors may have an economic interest in exerting such influence (Hoepner et al, 2018). By probing the RI literature, we can explore this gap in our knowledge and draw an analogy between AMR and other ESG issues. Then we can understand if there is something useful investors can do and if will they take such action.

This willingness to take action is complex. A key aspect is the presence of a market failure. Economists use the term 'market failure' to describe situations where supply and demand do not come together to efficiently or effectively to allocate a good or service. The market failures in the case of AMR are a) externalities and b) an unwillingness to pay for public goods.

An externality is the cost or benefit to a third party for a decision over which they have no say. For instance, if a factory pollutes a river, it may save money, but everyone who relies on the river downstream suffers. Antibiotic consumption is similar – patients may benefit from taking antibiotics, but the resistance which flows from taking antibiotics impacts upon all of society.

At the moment the negative externalities of antibiotic consumption are not regulated strongly and that has led to their overuse in patients and animals (O'Neill, 2016). This is made worse by the fact that antibiotics are often cheap.

Public goods are things that benefit a wide group of people, where that group does not directly pay for their production. For instance, a lighthouse, which benefits ships sailing at night, but where the running costs are not paid for directly by the ship owners. Similarly, a significant majority of the medical industry relies on the ability to manage infections with antibiotics to sell their products.

The fact that the pipeline of new antibiotics is blocked appears to result directly from the two aforementioned market failures and raises a serious problem for those hoping for investor action (O'Neill, 2016). Market failures rarely result in any incentive for investors to demand regulators fix the failure. Therefore, we need to be alive to the possibility that investors could choose not to exercise any of their powers in respect of AMR.

1.2 Scope of research

This dissertation explores the issue the relevance of RI to AMR with specific reference to the pharmaceutical sector.

1.3 Aims and Objectives

This dissertation aims to study the influence UK investors can have on AMR specific to their investments in the pharmaceutical sector.

The objective is to discover if and how investors resources can be deployed in order to support action to tackle AMR. In order to draw conclusions, the motivations, barriers and limitations to investor action have been studied.

Few would argue that industry contributes, either directly or indirectly, to social and environmental problems. According to Mackenzie and Sullivan (2006) these negative outcomes raises two key questions:

- i) *What, if anything can the investors in these companies do to help the problem?*
- ii) *Do Investors have an interest in taking action?*

A third question builds on the above and underpins this dissertation: *Why would investors care?*

This dissertation poses and attempts to give a reply to three core questions of equal importance, inspired by Sullivan and Mackenzie (2006):

The first is why would investors care about AMR?

The second is do investors have an interest in taking action?

The third is what, if anything, can investors do to help the problem?

1.4 Dissertation structure

This section (the introduction), provides an overview to the research. Chapter 2 is the literature review and provides a more detailed background to the a) AMR literature, and b) RI literature. Chapter 3 brings the two literatures together. Insights from Chapters 2 and 3 provide the foundation for the development of a series of questions.

Chapter 4 describes the methods used to select, interview and analyse results. Results from these interviews are detailed in Chapter 5. Chapter 6 discusses the results of the study and the limitations of the research and Chapter 7 contains the conclusions, recommendations and areas for future research. Chapter 8 details the references.

CHAPTER 2: LITERATURE REVIEW

The purpose of this chapter is to describe firstly, the AMR problem in the round and secondly, the RI landscape. At the end of chapter 2 we will have explored AMR as an issue with societal and economic implications. These implications also impact upon companies that use and produce antibiotics as well as their investors. Investors have a set of levers they can deploy on any ESG issue, which are explored in the latter half of Chapter 2.

Chapter 3 then brings the two literatures together to identify the key investor actors to interview, the pertinent questions to ask them and to identify a) if and how investors are relevant to the discussion and b) can and will they take action.

This chapter is divided into two strands; the problem, AMR and a potential solution, RI.

2.1 Antimicrobial Resistance

2.1.1. History and context

The Egyptians and Chinese cultures of old were the first to document the use of microorganisms for the management of microbial infections (Sengupta et al, 2013). However, the golden era of antibiotics started with the infamous discovery of penicillin by Alexander Fleming in 1928. Selman Waksman subsequently coined the term “antibiotics” in 1941 to describe chemical substances produced by microorganisms that demonstrate antagonistic effects on the growth of other microorganisms (Golkar et al, 2014).

Antibiotics have gone on to save millions of lives and underpinned major advances in medicine (Gould and Bal, 2013). They prevent or treat infections that can occur in patients suffering from chronic non-communicable diseases, such as diabetes, and they form an essential part in procedures, such as chemotherapy and organ transplants (Rossolini et al, 2014).

Antibiotics have also contributed toward extending expected life spans globally. In 1920, people in the U.K. were expected to live to be only 56 years old; now the average life span is 80 years (Read and Woods, 2014). In developing countries with sanitation challenges, antibiotics decrease both the morbidity and mortality caused by food-borne and other poverty-related infections (Rossolini et al, 2014).

2.1.2 The problem

Even before its mass introduction, resistance to penicillin was identified. Resistance swiftly became a significant issue and by the 1950's many of the medical breakthroughs of the previous decades were threatened (Spellberg and Gilbert, 2014). In response, microbiologists focused on the discovery of a new family of beta-lactam antibiotics. However, resistance soon followed discovery (see Figure 1).

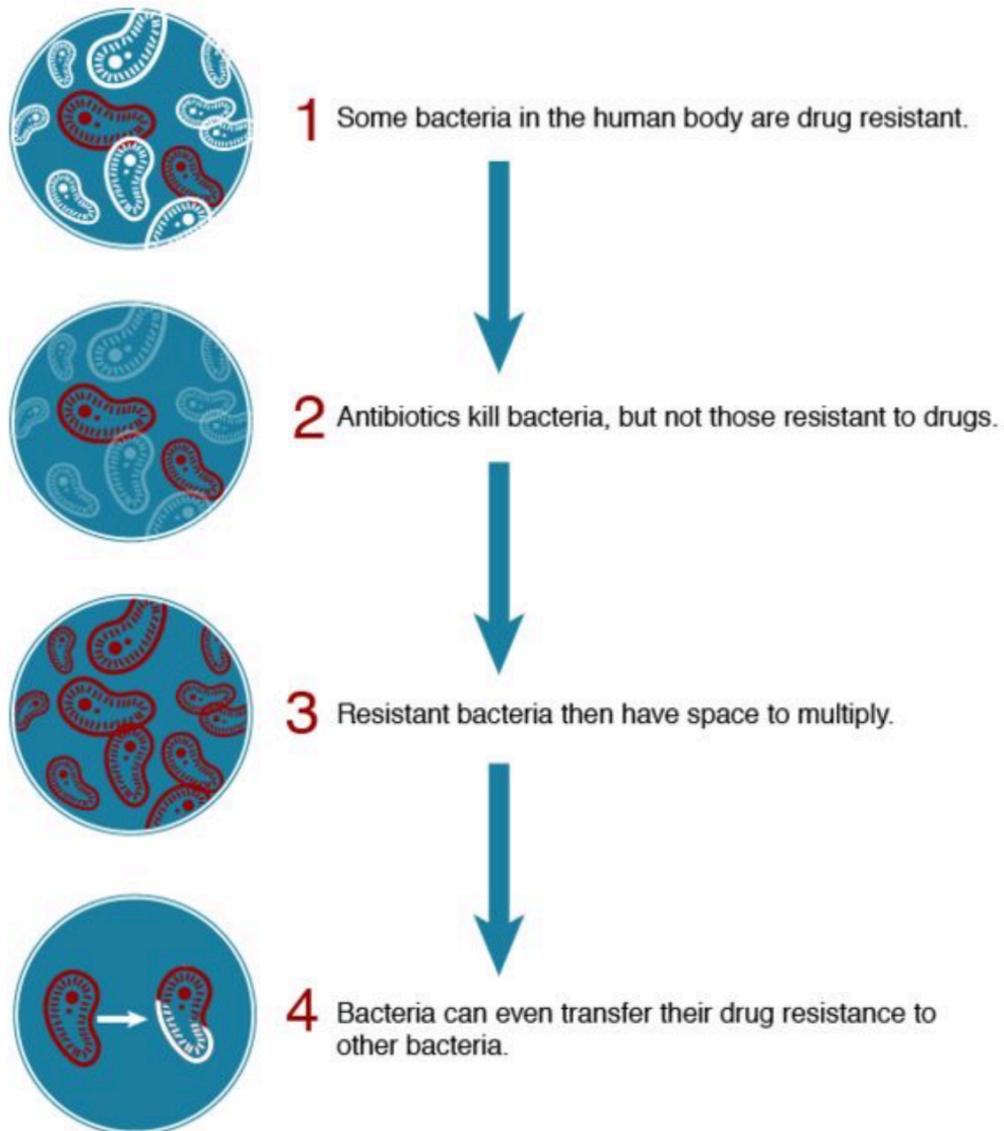
The mechanisms of AMR are explained in Figure 2. In summary, within a bacterial population some cells will be naturally be resistant to an antibiotic. When antibiotics are used, they kill off all the bacteria, except those with natural resistance. Without competition from the other bacteria, these resistant strains are able to multiply with resistance being passed on to their descendants. Resistance is also enhanced by bacteria transferring the genes that allow for resistance directly into other bacteria that may have been previously susceptible to the antibiotics; the more resistant bacteria are, the higher the frequency this transfer occurs.

From the 1960s through to the early 1990s, the pharmaceutical sector discovered many new antibiotics to address resistance, but then the antibiotic pipeline began to dry up.



Figure 1: Development of antimicrobial resistance. (Source: Centre for Disease Control)

How does antibiotic resistance occur?



Source: Public Health England

BBC

Figure 2: The mechanism of antibiotic resistance

2.1.3 The causes of resistance

The 'antibiotic paradox' describes the premise that the misuse of antibiotics destroys their curative powers (Polly; 1993, Levy; 2002).

The three primary causes of AMR are multifaceted and include human behaviour and corporate practice at many levels of society;

- a) overuse and inappropriate prescription in humans;
- b) extensive agricultural use and;
- c) lack of antibiotic research and development (R&D).

Of the three causes of AMR, this dissertation focuses on the lack of R&D (see 2.1.7). For the sake of completeness, the other two causes are summarised below and explored further in Appendix 1.

Overuse and inappropriate prescription in humans

Sir Alexander Fleming predicted that the public demand for penicillin would lead to an era of abuse in its use (Bartlett et al, 2013). Meta-analysis of epidemiological studies shows a direct relationship between antibiotic consumption and the spread of resistant bacteria strains (Brown et al, 2013). Despite warnings regarding their overuse, antibiotics are continually overprescribed worldwide (Gross, 2013).

Extensive Agricultural Use

The practice of administering antibiotics to livestock is extensive; it is estimated that 70% of all antibiotics used in the U.S. and 55% in the EU, are given to farm animals, much of them for non-therapeutic purposes (FAO, 2018).

There are four main reasons to use antibiotics in agriculture: (1) to promote growth, (2) mass disease prevention, (3) selected disease prevention and (4) disease treatment (Boeckel et al, 2017).

Lack of new antibiotic research and development

From 1940 to 1962, more than twenty new classes of antibiotics were marketed, however there had been no successful discovery of any new class of antibiotic since 1987 (Silver, 2011).

Antibiotic development is no longer an attractive area of R&D for the pharmaceutical industry because:

- 1) Antibiotics are priced keenly compared with cancer drugs, that costs tens of thousands of pounds (Wright, 2015). Furthermore, antibiotics are not as profitable as medicines designed for chronic illnesses, such as asthma, because antibiotics are only used for a short period of time and tend to cure the illness. Smaller companies lack the funding to meet the stringent regulations for clinical trials, thus reducing the development of potential new agents (Pidcock, 2012).
- 2) Once a new antibiotic is launched, doctors often keep it in reserve due to fear of accelerating resistance and only deploy it in the most extreme cases. The consequences of this approach are a decrease in the a) use of new antibiotics and b) return on investment (Pidcock, 2012).

A pharmaceutical company that invests large amounts of capital expenditure into R&D can suffer from early dwindling of income when resistance develops (Gould and Bal, 2014).

- 3) Finally, the majority of patents on antibiotics have expired yet here is an expectation that antibiotics, even the new antibiotics, should be priced low (Wright, 2014).

Consequently, only four new classes of antibiotics have been launched in the past 40 years (see Figure 3; Cooper and Shlaes, 2011).

In total, 15 of the 18 largest pharmaceutical companies have abandoned antibiotic R&D (Ventola, 2015b).

Given the resource required to discover a new antibiotic, push it through clinical trials and the finite patent lifespan, the presence of resistance makes investment into new antibiotics unattractive, even though there is a huge demand in the clinical marketplace. Coates et al. (2011) noted that legislation and incentives are required to restart research.

A PERFECT STORM

As bacterial infections grow more resistant to antibiotics, companies are pulling out of antibiotics research and fewer new antibiotics are being approved.

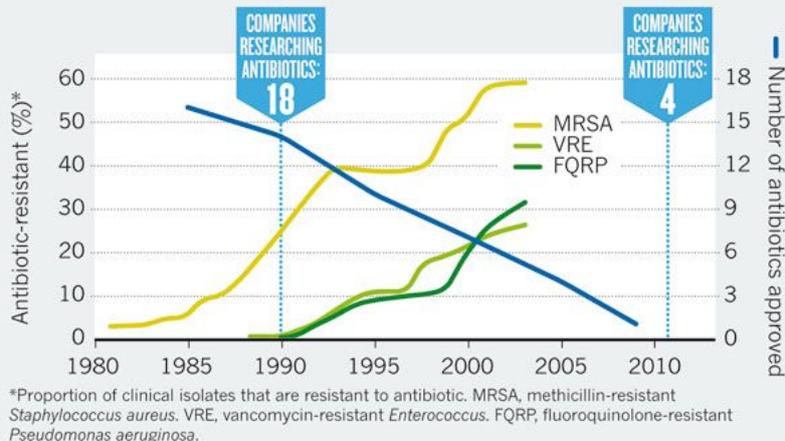


Figure 3: Decline in new antibiotic development with increased resistance

Source: Cooper and Shlaes (2011)

Summary of causes of AMR

The global overuse of antibiotics makes resistant bacteria more common because the more we use antibiotics, the more chances bacteria have to become resistant to them. In parallel to this, there are scant new antibiotics under development to replace those rendered impotent by rising resistance.

The demand for new antibiotics has increased due to resistance but the supply of new antibiotics has dried up leaving us in a precarious position (O'Neill, 2016). By decreasing demand (antibiotic use) and boosting supply (funding R&D) the impact of AMR could be quelled.

2.1.4 The public policy landscape

AMR has risen up the global policy agenda, headlining at the G7, G20, World Economic Forum, and in the United Nation (UN) Agenda for Sustainable Development (Lyer and Mendelson, 2018).

Initial framing of AMR

In 2014, the World Health Organisation (WHO) developed a global template for countries to draft their own national action plans using five objectives:

- To improve awareness and understanding of AMR
- To strengthen knowledge through surveillance and research
- To reduce the incidence of infection
- To optimise the use of antimicrobial agents
- Develop the case for sustainable investment and R&D for new medicines, diagnostic tools, vaccines etc.

The G20 response

In the 2017 G20 Leader's Declaration, the G20 Heads of State made a historic commitment to combatting AMR. The Health Ministers involved expressed their concern regarding the underexplored R&D for new antimicrobial therapies. They highlighted the necessity of new incentive mechanisms to reactivate R&D and stated the lack of R&D was the single biggest contributor to AMR. *This is one of the primary reasons this dissertation focuses on R&D.*

In tandem with the Declaration, G20 Health Ministers committed to extend the voluntary financial support for funding projects, for instance, the Global Antibiotic Research and Development Partnership. The ministers also called on the support of other countries, foundations, academia, and the private sector to help achieve this.

2.1.5 Composition of the actors

The rising importance of AMR is associated with a growing number of parties voicing their concern about the issue (Wernli et al, 2017). The UK Government's five-year national action plan on AMR 2019-2024 (the Action Plan) mapped out the range of such parties as

- National and international governments
- International organisations
- Pharmaceutical professionals
- Businesses
- Investors in the aforementioned businesses
- Civil society
- Academia
- Philanthropy.

2.1.6 Which companies are relevant and what role do they play in AMR?

AMR regulation could dramatically decrease the value of industries tied to conventional antimicrobials such as healthcare and agriculture (Ventola, 2015).

Agriculture

Regulation could lead to farmers seeing a reduction in the availability of antibiotics for veterinary use, which poses challenges for the most intensive farming systems – particularly in the pig and poultry sectors. For those who fail to prepare for this change, the operational disruption could be significant. Unprepared farming businesses may experience disease outbreaks and high mortality rates (Read and Woods, 2014)

Pharmaceuticals

This sector could therefore face restrictions on sales of antibiotic. Other products, for instance oncology drugs which rely on effective antibiotics, could face disruption.

All three causes of AMR, as discussed in 2.1.3, are related to corporate practices, for instance;

- *Overuse* - overprescribing is partly in response to the relationship between health care providers and pharmaceutical companies. This is especially salient in countries where drug sales constitute a major portion of health care providers' incomes (Li et al, 2012).
- *Extensive agricultural use* - agricultural use is driven by market pressures. This tension has significantly increased over the past several decades with the advent of factory farming, which stresses profitability over externalities (Duckenfield, 2013).
- *Lack of R&D* - the scientific talent pool in antibiotic discovery has steadily shrunk with the closure of research centres. This exodus speaks to the fact that the financial justification for developing a novel antibiotic does not reflect its public health value or the investments made into its R&D (Simpkin et al, 2017; Renwick and Mossialos, 2018).

2.1.7 Which companies does this research focus on?

Of all the stakeholder's listed in 2.1.5, this dissertation focuses on the interplay between the pharmaceutical sector and their investors. Specifically, it focuses on what role UK investors in publicly listed pharmaceutical companies could play to address AMR.

Why the pharmaceutical focus?

The Health Care sector, specifically the pharmaceuticals, biotechnology and life sciences industry, discover, develop, and market new antimicrobials (Bax, 1997).

The economic model of antibiotics has resulted in the closure of antibiotic R&D centres, the latest being Novartis in 2018. Only Merck & Co., Roche, GlaxoSmithKline and Pfizer now have active antibiotic programs and only two of these have a novel antibiotic in clinical trials (Jackson et al, 2018).

The O'Neill Report stresses that this corporate trajectory must be reversed in order to deliver sufficient new antimicrobial agents in the future.

Which cause and why?

Of the three causes detailed in 2.1.3, the lack of R&D is deemed the most important within the aforementioned O'Neill Review and the G20 Leaders Declaration. Quite apart from the many infectious diseases, for which we rely on antibiotics to combat, effective antimicrobials underpin our entire modern medicine system (Robinson et al, 2016) by allowing us to carry out common surgical procedures and chemotherapy (Roca et al, 2015).

The O'Neill Review sets out why corporate practice in the pharmaceutical sector is central to the problem:

- pharmaceutical companies have shut their antibiotics research teams steadily, to focus on areas that may not be 'easier', but that have a higher commercial return, e.g. oncology.
- In 2014 there was 800 new oncology products in the pipeline compared to a total antibiotics pipeline of fewer than 50 products. This demonstrates the impact of a sustained industry focus on a scientifically challenging but commercially lucrative disease area.

Why not agriculture?

This research does not wish to purport that agriculture is of lesser importance nor does it wish to assert that addressing issues solely on the pharmaceutical side is sufficient to tackle AMR. Both industries are highly pertinent to the issue however, to date, the pharmaceutical sector has received far less attention from investors (Robinson et al, 2016).

Investors initiatives, for instance, the well-established Business Benchmark on Farm Animal Welfare (BBFAW) and the Farm Animal Investment Risk & Return (FAIRR) Initiative, have promoted attention and action on the use of antibiotics in agriculture since inception, in 2012 and 2014 respectively. A review of the literature indicates the only broadly similar initiative for the pharmaceutical sector is the AMR Benchmark, which was launched in 2018 and provides data but not include any collaborative action platform – see 5.3.

This dissertation only attempts to cover a subsection of the corporate practices relevant to AMR. In Chapter 7 some wider reflections explore if and how the role of investors may be broader if including agricultural companies.

Why institutional investors?

Institutional investors own the majority of the share capital of the pharmaceutical industry.

This research focuses on equity and credit investors because:

- McKinsey Global Institute estimates that 52% of the global investable universe of US\$200 trillion is comprised of equity securities and private debt securities.
- In 2017, of the top twenty-five global pharmaceutical companies involved in antibiotics, twenty-one of them are publicly listed companies (Tacconelli et al, 2018).

Given the quantum of debt and equity investors and their predominant ownership of the largest pharmaceutical companies involved in antibiotics, the focus of this research is on equity and debt investors in listed pharmaceutical companies. The role of investors and the mechanisms of influence for institutional investors upon their investee companies are explored in 2.2.4.

2.1.8 The commercial implications

The costs to develop a new antibiotic therapy are comparable to other drugs, yet the returns on investment for new antibiotics are significantly lower than drugs for chronic conditions. The Office of Health Economics estimated the net present value of a new antibiotic is US\$50 million, compared to approximately US\$1 billion for a drug used to treat a chronic neuromuscular disease. Total antibiotic sales are in the region of US\$500 million (World Economic Forum, 2013). However, companies spend approximately US\$5.2 billion on R&D for each new drug they bring to the market and, even then, 80% fail in clinical trials.

Consequently, neither companies nor investors have a compelling business case for investing in AMR R&D.

2.2. Responsible Investment

2.2.1 Context

The Principles of Responsible Investment define RI as “*an approach to managing assets that sees investors include ESG factors in their decisions about what to invest in and the role they play as owners and creditors.*”

As well as an ingrained expression, RI has become a mature approach

- In 2006, the PRI was launched at the New York Stock Exchange. By 2018, the PRI Progress Report showed 2,232 members, a 21% increase on the previous calendar year.
- In 2015, Friede et al analysed over 2000 academic studies on how ESG factors affects corporate performance and found an overwhelming share of positive results with just one in 10 showing a negative relationship.

RI is also at scale

- In 2019, around a quarter of all professionally managed assets around the world are estimated to take into account RI considerations (PRI Progress Report)

2.2.2 Why investors care about responsible investment?

Sullivan (2011) lists the various reasons for investors to pay attention to ESG topics in their investment practices:

1) Improved investment performance

Investors who devote resources to RI believe that ESG issues affect company earnings through a number of mechanisms, e.g. government intervention, litigation, reputational risk and direct physical risks. Companies who develop effective strategies to counter these issues have the potential to outperform those who do not (Sullivan et al, 2006). If specific ESG issues have not been identified or properly valued by the market, investors alive to this gap may be able to exploit the potential inefficiencies that arise (Waygood, 2006).

2) Reduced portfolio risk

ESG consideration may identify risks that more conventional forms of financial analysis may miss (Pollard et al, 2018).

3) Client demand

Fulfilling the expectations of existing or future clients, based on the rising demand for responsible investment products and approaches (Hoepner & Hebb, 2017). In addition, these clients may have financial and non-financial values at play.

4) Reputational risk and/or benefit

Pressure from stakeholders such as governments and NGOs for investors to play a more active ownership role in investee companies. The inverse to this is the potential brand benefit that may accrue from adopting a leadership position (Kiernan, 2009).

5) Other drivers

Other drivers may include media interest or personal values. Derwall et al. (2011) described investors' values and personal beliefs as a nonpecuniary driver. Trinks and Scholtens (2015) noted that such drivers were increasingly being reflected in investment decisions.

2.2.3 Under what conditions do investors have an interest in acting on ESG issues?

Materiality as a proxy for investor interest

Materiality in this context means the relevance of a sustainability issue to financial performance. The majority of investment research operates on the basis that materiality needs to be proven before an issue will be considered actionable (Eccles et al, 2007).

Consequently, for an ESG topic to be explicitly considered in an investment decision Sullivan (2011) cites three requirements for an investor to determine if a topic is material

- How does the issue impact upon recognised drivers of investment value for the company in question?
- What is the financial impact?
- Is the impact financially material?

What else influences what investors see as material?

The definition of materiality has historically been confined to economic information (Jebe, 2019). However, an issue doesn't need to be financially material for an investor to think its material. Sullivan (2011) further identifies several nuances in the definition of material:

The costs (or benefits) associated with a specific ESG issue is defined by the size, scale and activities of the business.

Time frames are critical with the most interest being paid to how the company will perform over the next 12-24 months. Sullivan (2011) highlighted that investors are likely to be very interested in an ESG issue that has a 10% impact on a key financial indicator over the next 1-2 years, but may have limited interest if the same issue has a 50% impact over the next 5-10 years.

Finally, *the concept* of materiality may be fluid. For instance, if clients ask questions about how an ESG issue is being assessed this may create pressure for the asset manager to explicitly take an interest. Equally, a fund manager may develop an interest in a specific ESG issue, which leads them take action ahead of their peers (Del Guercio & Hawkins, (1999); Rubach & Sebor, (2009); Ryan & Schneider, (2002).

Limitations: Market Failures

A market failure is a situation where free markets fail to allocate resources efficiently (Bator, 1958). There are four basic types of market failure for goods/services or environmental resources: externalities, public goods, common property, and hidden information (Heller and Starrett, 1976).

Sullivan and MacKenzie (2008) explored the economic literature around market failures as relates to corporate responsibility issues. Specifically, they reviewed whether investors were well-placed to intervene in market failure situations where there is no compelling business case for companies to increase their ESG performance and, by extension, no financial reason for investors to encourage companies to do so.

They drew upon the body of knowledge around welfare economics (Coase, 1960), which focuses upon a) externalities and b) depletion of open access to resources owing to overuse. This occurs because no one party has the incentive to concern themselves with the effect of their action on others. Cropper and Oates (1992) cite pollution as an example of (a) and overfishing and deforestation as an example of (b)

Typically, it is left to governments and civil society to deter companies from exploiting market failures, not investors. Not only do investors lack any incentive to intervene, but the economic literature suggests that financial performance actually improves when companies exploit a market failure, leading to benefits for a company's investors.

For the majority of ESG issues with a market failure at their centre, investors are likely to avoid taking action owing to this conflict between the issue and the short-term financial interest of the investor.

2.2.4 What are the key areas for investor action to help address ESG problems?

In section 2.1.7 the rationale for focusing on large, listed companies and their equity and debt investors was justified. This section examines the mechanics of influence that investors have when seeking to influence the corporate behaviour of sizable, listed investee companies.

The mechanics of influence

Investors have a range of options to influence the behaviour of investee companies (Dimson et al, 2015, Becht et al, 2009). Increasing investor activism been widely documented (Benton, 2017; Brav et al, 2008; David, Bloom, & Hillman, 2007; Flammer, 2015).

Waygood (2011) divides the investors influence into two principal categories: (i) financial influence - the buying and selling of equity shares and debt on the capital market influences the cost of capital for listed companies; and, (ii) investor advocacy influence - shareholders can exercise their ownership of the company to the directors, by sending explicit signals regarding the management of the company.

General strategies for investors to exert influence

The following list, inspired by Robins et al (2018), gives an overview of the mechanisms investors have to influence corporate behaviour. Chapter 3 analyses how each mechanism is relevant to the AMR problem.

Mechanism 1: Investment strategy

Explanation: Investors determine how individual ESG issues impact their existing policies, for instance:

Portfolio assessment – A review to identify the performance of companies on ESG metrics that can help investors understand the materiality of the issue and inform action. As seen in section 2.2.3, materiality has a key role to play in determining the level of attention an ESG topic obtains.

Strategic integration - Integrating ESG considerations into investment strategy signals to companies the importance of an issue in the broad list of priorities

Mechanism 2: Capital Allocation

Explanation: Investors can choose to withhold capital (divestment) or allocate capital (investment).

Divestment - Hirschman (1970) famously stated that consumers have two choices if they are unhappy with a company. They can choose either “exit” or “voice”. Exit, in the cases of investors is played out by divesting. Voice refers to investors’ ability to have their concerns heard (see mechanism 3; engagement).

Investment - Recently there has been innovation in financial products, to enable investment directly in projects with ESG impacts (UBS, 2016).

Mechanism 3: Corporate Engagement

Explanation: A conversation between investors and companies (McNulty & Nordberg, 2016) to shape corporate behaviour (Vandekerckhove et al, 2007),

Collier (2004) and Gillan and Starks (2007) both separately outline the two approaches to corporate engagement as a) Individual engagement - dialogue between individual investors and corporate management and b) Collective Action - joining investor networks to engage collectively.

Mechanism 4: Policy Engagement

Explanation: Investors can get involved at various stages in the policy-making process. They can start policy discussions when they notice gaps or weaknesses in regulation, provide information and views that support effective decision-making, facilitate evaluation of policies, and call for the termination or renewal of policy measures (Barton, 2018).

What determines effective influence?

Policy makers and companies cannot focus their attention on all issues simultaneously, and therefore must prioritise stakeholders' claims (Gond and Piani, 2013). The level of focus on an ESG issue may also reflect broader attention on the topic from media interest and NGO scrutiny (Mitnick, 2000).

According to Gifford (2010), effective influence is based on two factors, a) the willingness of investors to put resources towards the engagement process and b) tenacity in engaging over a protracted timeframe with multiple decision makers.

Drivers of investor influence

The saliency of engagement depends on establishing power, legitimacy, and urgency (Mitchell, Agle, and Wood 1997).

Gond and Piani offer a model of how this translates into practice:

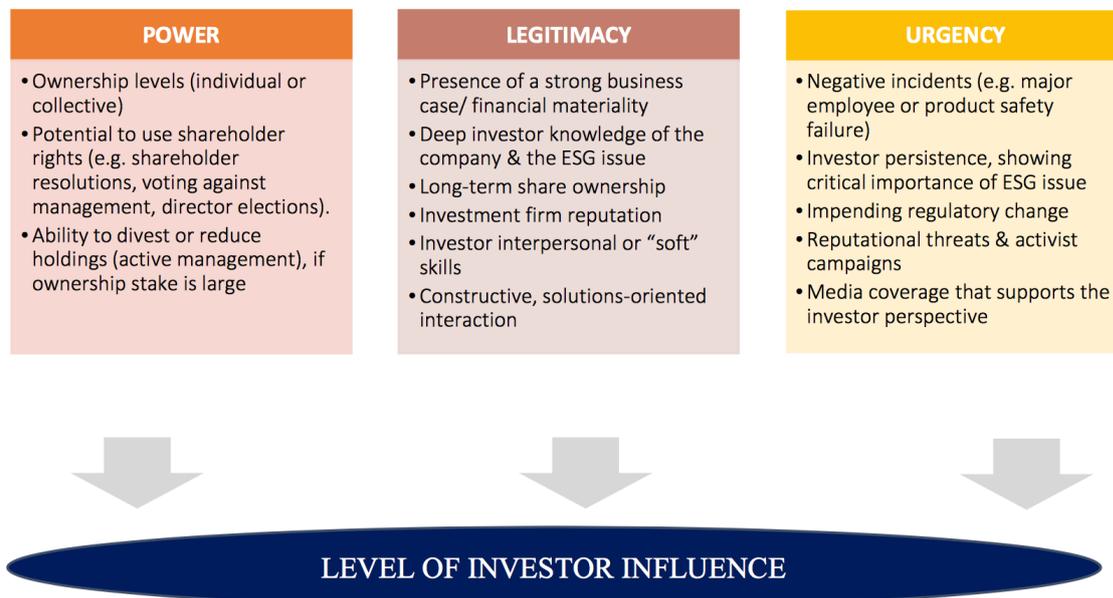


Figure 5: Attributes that determine the responsiveness to investor advocacy

Source Gond and Piani (2013)

Barton (2018) proposed that the more of the above elements that are deployed by investors then the greater likelihood that an ESG issue will be prioritised and addressed. Furthermore, investors can increase their leverage through collaboration (Sullivan 2006).

Engagement strategy for a market failure

Of the mechanisms for influence, policy engagement appears to be the most relevant to AMR in light of the market failure.

Simm (2014) identified the benefits of public policy engagement as:

- Aligning incentives for companies to take significant action on ESG issues
- Creating urgency for companies to respond to new legislation
- Correcting market failures

As the literature demonstrates in 2.2.3, AMR is a market failure that appears to lack urgency or financial incentives so companies lack the incentives to act. Therefore, if investors wish to take action, then public policy engagement is the first mechanism to explore, as opposed to corporate engagement.

How public policy engagement differs from corporate engagement

The PRI and United Nations Environment Program (UNEP) report “*The Case for Investor Engagement in Public Policy*” highlights three areas;

- Longer timeframes;
- Investors are often not the most important stakeholder and;
- Policymakers need to balance a range of factors into their decisions.

What makes engagement effective?

The PRI/UNEP report flags how public policy plays a critical role in framing the relationship between companies and their investors. Essentially, policy sets the rules of the game by promoting economic development, fostering social inclusion and protecting the environment. For long-term investors, effective policies can resolve market failures. The report concludes with a 5C checklist for effective policy engagement;

- Commit resources to public policy engagement.
- Construct a strategic process for policy engagement.
- Clarify public policy positions.
- Collaborate on public policy engagement.
- Communicate to stakeholders regarding public policy engagement.

CHAPTER 3: BRINGING THE TWO LITERATURES TOGETHER

This chapter engages the RI literature and applies it to the AMR problem by framing it around the three research questions introduced in 1.3.

- Why would investors care about antimicrobial resistance?
- Do investors have an interest in taking action?
- What, if anything, can investors do to help the problem?

3.1 Research Question One - Why would investors care about AMR?

The literature suggests a typology of reasons why investors might show interest:

Improved investment performance and reduced portfolio risk

Per section 2.1.3 and 2.1.6 the causes and effects of AMR impact multiple sectors. An HSBC broker note summarised the predicted impacts on food retailers, restaurants and meat producers. However, there does not appear to be a corresponding report focusing on the pharmaceutical sector by any sell-side or academic research.

One of the few industry reports by Schroders on AMR as an ESG issue highlights the opportunities and risks in different healthcare sectors (Figure 4). The veterinary antibiotic producers face the greatest disruption if further restrictions are introduced and offer the best example of financial materiality, as discussed in 2.2.3.

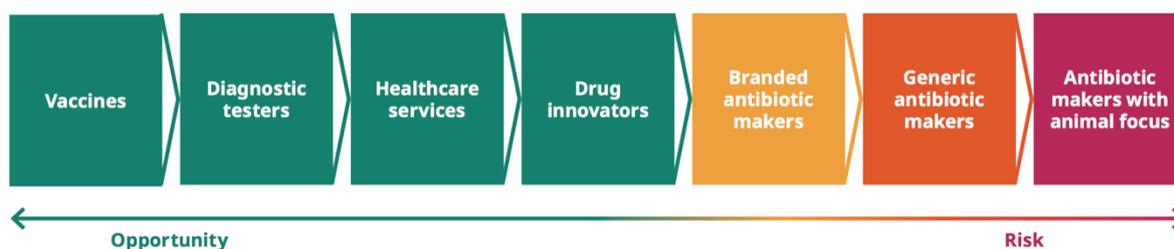


Figure 4: The AMR risk/opportunity spectrum.

Source: Schroders

Investment opportunities in alternatives

HSBC expanded upon the opportunities around alternatives to antibiotics and peripheral services. These include:

Vaccines - Pfizer and Sanofi represent around 80% of global vaccine revenues according to Bloomberg. Pfizer is in the later stages of developing a vaccine against post-surgical infections.

Rapid diagnostic tests – These can be sold on a volume basis without fear that their use will make them ineffective, and benefit from shorter development cycles than antibiotics.

However, some of companies involved in the above may be smaller, private firms and so not an obvious focus for investors.

Client demand

A detailed review of the available information only found one asset owner, the Dutch doctors pension fund Stichting Pensioenfonds Medisch Specialisten asks questions on AMR of their asset managers. However, the FAIRR Initiative's global investor statement on antibiotic stewardship is currently supported by 75 investor signatories collectively managing over US \$3 trillion of assets, indicating some evidence of interest so lends itself to an interview question.

Reputational benefit / risk

There may be some benefits to investors who are perceived as leading on a societal issue (Efimova, 2018).

3.2 Research Question 2 - Do investors have an interest in taking action?

AMR as a market failure

The body of knowledge around welfare economics indicates that if the cost of an externality is not included in the cost of producing goods or services the firm will produce more of the product than is socially optimal, leading to negative outcomes (Hicks, 1939). A key aspect is the depletion of open access of a resource by overuse (Hardin, 1968). The fact that the blocked pipeline of new antibiotics appears to result directly from such market failures raises a serious problem for those hoping for investor action.

Not only do investors lack incentives to intervene, but the economic literature suggests firms perform better when exploiting such a market failure. In this case, the costs to develop a new antibiotic therapy are comparable to other drugs, yet the returns on investment for new antibiotics are significantly lower than drugs for chronic conditions.

Materiality of AMR

Academic literature describing how material AMR is to investors is limited. An industry report from Schroders states that *“AMR is a material topic for investment returns across a range of sectors because regulation is steadily increasing and action on the overuse of antibiotics in food supply chains is a proxy for wider progress on sustainability.”* However, Schroders presents a somewhat oversimplified interpretation of materiality. As discussed in section 2.2.3, materiality is multifaceted, especially at an individual company and investor level.

Schroders further opines that despite large volumes of antibiotic sales, the AMR threat is not yet upon the corporate risk registers or radar. This may be due to AMR not being considered a specific risk for the company, more a sector wide issue. It could also be due to bounded rationality - the idea that decision-making is limited by the information the decision maker has, the cognitive limitations of their minds, and the finite amount of time they have to make that decision.

3.3 Research Question 3: What actions can investors take to help the AMR problem?

This section takes the typology of influencing mechanisms as detailed in 2.2.4 and translates the ones that seem the most relevant to AMR into potential actions. This data is then used to inform the interview questions.

Capital Allocation

The specifics of funding mechanisms for AMR solutions is an area where the theoretical literature is abundant. However, different estimates exist around the amounts of funding needed to stimulate antibiotic innovation and there does not appear to be consensus over a) the amount or b) where this funding should come from.

- The European Union and the European Pharmaceutical Industry Association funded

the DRIVE-AB project, which concluded at least US\$1.2 billion per year will be necessary to fund 18 qualifying antibiotics reaching the market. This does not include investments in AMR surveillance, access initiatives, responsible use, or diagnostics R&D.

- The O'Neill Review estimated US\$16 billion over ten years is needed for promoting the development of new antimicrobials and US\$2 billion over five years for a global innovation fund supporting research in drugs, vaccines and diagnostics.

From the investor's perspective, there does not appear to be any established means for investors to allocate capital towards AMR solutions, even if they were minded to, for instance R&D funds.

The product that most closely resembles a funding mechanism that could be applied to AMR are the vaccine bonds issued by the International Finance Facility for Immunisation (IFFIm). The success of this approach has been highlighted by Clemens et al (2010) as having profound consequences in terms of the funding of research-based innovative efforts to eliminate diseases and raising US\$2.6 billion.

The gap between funding needs and AMR-specific financial instruments

One of the recommendations in the O'Neill Review was the establishment of a Global Innovation Fund for early-stage, non-commercial research. With this in mind, the Dag Hammarskjöld Foundation hosted a meeting in 2018 to discuss how more funds to tackle AMR could be mobilised. This meeting identified five recommendations, two of which relate to the broad investment case.

- Explore what a global mechanism providing catalytic funding could look like.
- Develop stronger investment cases, nationally and internationally.

Unfortunately, the scope of the investment case in the resultant report is limited to two high level paragraphs that relate to investment by countries rather than institutional investors. The case for private sector funding was not explored, perhaps because the funding gap is small enough to be plugged by existing sources. This fuels the recommendation for further research in section 7.5 to quantify the gap. If further research indicates the funding gap needs private

funding too, then for private sector funding to appear the financial returns need to be acceptable to investors. This is explored in section 6.4.

Public health policy makers have traditionally tended to seek push and pull funding (see Appendix 3) from government and foundation grants. Push funding pays for R&D costs, but does not improve the attractiveness of the overall market. The DRIVE-AB project concluded that Pull funding is required to attract private-sector funding, otherwise AMR risks becoming a neglected issue, solely dependent on the public and philanthropic financing of R&D (Årdal et al, 2018). This adds credence to the call for further research on the funding gap and the role the private sector could play.

Where does this leave capital allocation and why does it matter?

As established in 3.2:

- Investors do not have a compelling investment case for investing in companies taking action on antibiotics.
- Organisations tasked with increasing funding for AMR have not set out the precise funding gap and their vision of the role, if any, of private finance.

Corporate Engagement

From a detailed search of three primary sources of RI news¹ it does not appear that there are pharmaceutical centric collaborative engagements in existence.

Policy Engagement

From a detailed review of the literature there does not appear to be any investor activity around the pharmaceutical sector, albeit initiatives exist on the agricultural side per 2.1.7.

The most high-profile industry advocacy tool to date is the Davos Declaration. In 2016, 85 healthcare companies signed the “*Declaration by the Pharmaceutical, Biotechnology and Diagnostics Industries on Combating Antimicrobial Resistance*” (the Davos Declaration) at the

¹ RI.com, SRI-Connect.com and the PRI Website. Accessed September 2019

World Economic Forum. The declaration's signatories have committed to furthering action on drug resistance in three broad areas: reducing the development of resistance; increasing investment in R&D and increasing access to high-quality antibiotics (Patrick, 2016).

CHAPTER 4: METHODOLOGY

A twin pronged approach was applied to this research: a literature review and a survey of experts in the RI arena. This chapter begins with an overview of how the literature research was conducted before detailing the methods used for the interviews.

4.1 Literature review

Bibliographies and references from academic and tertiary journal articles and papers, 'grey' literature comprising practitioner and industry reports and studies, company reports and websites formed the principal research tools.

The RI and AMR literatures provided the foundation for the survey questions.

4.2 Interviews

Given the subjective and emergent nature of the research topic, semi-structured interviews were used to gather and analyse information. This information was used together with literature findings to derive the conclusions provided in Chapter 7.

Selection of interviewees

Chapter 2 led to the focus on pharmaceutical companies and their investors. Interviewees were drawn from both asset managers and asset owners and all were based in the UK, because convenience sampling was used. Some were approached because they had played a prominent role either in the evolution of an emergent ESG. Others were chosen because they were well-known for having been pro-active in taking particular actions on ESG issues. While the interviewees were not necessarily representative of the institutional investor community as a whole (e.g. the interviewees included asset managers who had adopted a pro-active approach to other ESG issues), this potential limitation was, at least in part, addressed through interviews with portfolio managers not usually associated with social or environmental issues.

Interviewees were contacted by email to ask if they would be willing to participate, briefly outlining the intent, the use and security of the information and the process. The majority of the interviews were conducted by telephone and took one hour.

4.3 The Questions

The overarching enquiry is:

- Why would investors care about antimicrobial resistance?
- Do investors have an interest in taking action?
- What, if anything, can investors do to help the problem?

Research Question 1: Why would investors care about antimicrobial resistance?

Predictions based on what the literature tells us

The literature identifies four reasons why investors tend to pay attention to an ESG issue. If investors perceive an ESG topic as fulfilling at least one of these reasons, then they tend to care about it.

The literature identifies these drivers:

- Improved investment performance
- reduced portfolio risk
- client demand and;
- reputational risk or benefit

I will add a question to see if there are any others at play.

Interview Questions

Do you consider factoring in AMR has the potential to improve investment performance?

Do you consider factoring in AMR has the potential to reduced portfolio risk?

Have you had any clients ask you about AMR?

Do you consider factoring in AMR has the potential to mitigate reputational risk?

Do you consider factoring in AMR has the potential to offer reputational benefit to your company?

Are there any other drivers that would encourage you to consider factoring in AMR?

Are you feeling any pressure from civil society to act on AMR?

Research Question 2: Do investors have an interest in taking action?

Predictions based on what the literature tells us

Welfare economics suggests that in situations of market failure investors have less incentives to want the market failure addressed and therefore will be less likely to act.

If investor considers an ESG issue to be material, then they tend to deem it in their interests to act.

In order to determine if an ESG topic is material investors require answers to three key questions:

- How does the issue impact upon recognised drivers of investment value for the company in question?
- What is the financial impact?
- Is the impact financially material?

There are three nuances that drive investors to act, even if they do not deem an issue financially material;

- Time frames,
- Client/fund manager interest
- Costs and benefits

Interview Questions

- Do you consider AMR to be a market failure?
- Are you aware of the O'Neill Report?
- Do you consider AMR to be financially material?

- Are you able to assess;
 - How AMR impacts the recognised drivers of investment value for an investee company?
 - What the financial impact of AMR would be for a investee company?
 - If the aforementioned impact is financially material?

- Do you have sufficient metrics to assess AMR performance in your investee companies?

- Time frames - Do you consider AMR will impact companies in your portfolio within
 - the next 12-24 months
 - 2-5 years
 - beyond 5 years?

- *Clients* - Have any of your clients or potential clients asked questions about how AMR, for instance, in an RFP?

- *Costs/Benefits* - Do you consider AMR could result in significant costs or benefits for companies?

- Do you see any investable opportunities arising from AMR?
- *Open question* – What is your view on why investors are taking action or what's stopping them?

Research Question 3: What, if anything, can investors do to help the problem?

Predictions based on what the literature tells us

If an investor wants to take action to help address an ESG issue, then there are four key ways in which to do so:

- Investment strategy
- Engagement
- Capital allocation
- Policy advocacy

Interview Questions

Investment strategy

- Have you undertaken any portfolio assessment on the basis of AMR or used the AMR benchmark?
- Does AMR appear in your investment strategy?

Engagement

- Do you engage individually with investee companies on AMR?
- Do you engage collectively on AMR?

Capital Allocation

- Have you ever divested on the basis of AMR?
- If you were minded to support funding for R&D for new antibiotics would you expect such funding to come from investee companies balance sheets or from a separate route with separate financing e.g. a AMR bond?
- Are vaccine bonds investible in according to your mandates?
- Are you aware of any financial instruments currently available (or being called for) that relate to the AMR challenge?

Policy advocacy

- Have you conducted any individual or collective lobbying?

Wrap up

- How likely would you be to put resources towards a collective initiative?
- Have you taken any other action on AMR?
- Is there anything you expected me to ask you, that I didn't?

4.4 Method of analysis

Thirty-three interviews were undertaken. Within 48 hours of each interview, recordings were transcribed highlighting any particularly insightful comments. Responses were added into a spreadsheet template using open coding (Strauss and Corbin, 1990) as per Table 1:

Table 1: Interview ‘heatmap’ response coding

Colour	Code	Response
Green	Yes	Positive response, with strong conviction
Orange	Sometimes, yes	Positive response, but with alternative perspectives and exceptions or weak conviction
Yellow	Sometimes, no	Sometimes as an exception, but mostly no
Red	No	Negative response, rejecting the question strongly
Blue	N/A	Not applicable, or no response, or no view.

Once all interviews were complete and the ‘heat-map’ populated, a numeric analysis was created to bring out data analysis and insights.

CHAPTER 5: RESULTS

This section is organised around the three questions used in the interviews. It starts with the table of the overall results, then discusses the themes flowing from the results in order of appearance and concludes with a synopsis.

5.1 Why would investors care about AMR?

	Responses				
	Yes	Somewhat, yes	Somewhat, no	No	N/A
Do you consider factoring in AMR has the potential to improve investment performance?	4 (12%)	0	26 (79%)	3 (9%)	0
Do you consider factoring in AMR has the potential to reduced portfolio risk?	2 (6%)	13 (40%)	15 (45%)	3 (9%)	0
Have you had any clients/trustees/beneficiaries express an interest in AMR?	2 (6%)	0	0	31 (94%)	0
Do you consider factoring in AMR has the potential to mitigate reputational risk or offer reputational benefit to your company?	3 (9%)	3 (9%)	4 (12%)	23 (70%)	0
Are you feeling any pressure from NGOs or civil society to act on AMR?	0	0	4 (12%)	29 (88%)	0

Table 2: Results - Why would investors care about AMR?

Themes

Investment Performance

Seventy nine percent (26/33) of interviewees believed that AMR didn't have the potential to impact investment performance. One interviewee expressed it simply: *"It's too hard in practice to apply AMR thinking to fundamental analysis."* Another thought *"I don't believe any of my key overweight positions are vulnerable."* Another opined *"It's more of a societal issue than a portfolio issue."*

Of the 12% who believed it could impact performance, conviction was strong that this was the case as no one answered 'somewhat, yes'.

Portfolio risk

The results were broadly distributed along a bell curve with a slight skew towards AMR not impacting portfolio risk. Several interviewees believed: *"If the conversation about AMR regulation was more established, then portfolio risk could become relevant, but as it stands, it's too abstract to capture in existing models."*

However, there were also signs that this view is changing because several interviewees were supportive of the creation of a tool to identify potential direct and indirect financial damages and the transformative effect this could have on investors' ability to assess portfolio vulnerabilities. It is noteworthy that, a) a benchmark tool exists, the AMR Benchmark, which is discussed in 5.3 and b) this suggests AMR could be a bounded rationality problem, which is an economic theory with a number of established solutions worthy of further research – see 3.2.

One investor was very clear on the risks to his portfolio *"Failing to take it into account AMR is a massive downside risk. ...it's the foundation of modern medicine, any of our investments in oncology and orthopaedics is based on the premise that antibiotics work, so for me it's about protecting value."* However, this fund manager works for a highly specialised investment firm that only invests in the healthcare sector. Presumably he cares more about AMR than a generalist investor, who invests in everything.

Another thought *"The whole blockbuster drug model is destroyed if we lose the foundations of antibiotics."*

Client interest

A lack of client, trustee or beneficiary interest was a common theme for interviewees. Only six percent (2/33) had been asked about AMR by clients, but in both cases the interest had been very strong. One interviewee sends out a bi-annual survey to all institutional clients. The survey asks for their ESG engagement priorities from a pre-defined list of 29 ESG topics to help them understand their clients' interests and prioritise which ESG issues to focus on. These issues came from the list of ESG topics in the PRI's certificate in ESG Investing syllabus. In 2018 AMR topped the list. The list was skewed alphabetically so AMR

appeared as the first issue which may explain its popularity. However, this is not the only reason as another high profile ESG issue beginning with A (aviation, of concern because of carbon emissions) received only a small percentage.

Reputation

Eighty-two per cent (27/33) believed consideration of AMR has none or very limited ability to mitigate reputational risk or offer reputational benefit.

Civil society pressures

No respondees reported feeling any pressure from NGOs to act, but one mentioned the awareness raising work of the British Society for Antimicrobial Chemotherapy. However, the literature tells us that there is a plenitude of civil society action under the guises of the Antibiotic Resistance Coalition and the Alliance to Save our Antibiotics. It is noteworthy that they have such limited influence on investors. It could be because NGOs in general have an underdeveloped understanding of the full range of actors in the capital markets (Waygood and Wehrmeyer, 2003), so have omitted investors from their scrutiny, to date.

Although respondees gave their answers in terms of the pharmaceutical sector, it was observed that many made unprompted reference to the unfettered use of antimicrobials in agriculture. One interviewee stated simply: *“New agents are coming in at one end and then being flushed down the drain. We need to take care of the ones we have and we’re getting through the new agents very quickly.”*

Another added: *“FAIRR is a very visible investor initiative on the agriculture side”,* and another *“The BBFAW events and briefings are invaluable”*.

Additional drivers

Several interviewees mentioned the role of personal interest which aligns with the literature. *“My child needed antibiotics recently, but they didn’t work at first. I’ll always remember that feeling.”*

5.1.1 Synopsis of results for research question one

- Of the four key factors which cause an investor to care about an ESG issue, only one is resonating in any meaningful sense with the respondees; reducing portfolio risk.
- NGOs are not addressing investors on the pharmaceutical side.
- Client and personal interest are powerful drivers.

5.2 Research Question 2 - Do investors have an interest in taking action on AMR?

	Responses				
	Yes	Somewhat, yes	Somewhat, no	No	N/A
Do you consider AMR to be a market failure?	29 (88%)	4 (12%)	0	0	0
Do you consider AMR to be material?	5(15%)	6 (18%)	14 (43%)	7(21%)	1(3%)
Are you able to assess how AMR impacts the value of a pharmaceutical investee company?	0	0	0	33 (100%)	0
Are you able to assess what the financial impact of AMR would be for a investee company?	0	0	0	33 (100%)	0
Are you able to assess If the aforementioned impact is financially material?	0	0	0	33(100%)	0
Do you have sufficient ESG metrics to assess AMR performance in your investee companies?	0	0	0	33(100%)	0
Do you consider AMR could result in significant costs or benefits for companies in your portfolio?	4 (12%)	19 (58%)	9 (27%)	1 (3%)	0
Do you see any opportunities arising from AMR?	3 (9%)	12 (36%)	11 (33%)	7 (22%)	0
Have any of your potential clients asked questions about how AMR is being addressed?	1 (3%)	0	0	32 (97%)	0

Table 3: Results - Do investors have an interest in taking action on AMR?

Themes

Market Failure

All investors agreed, and eighty-eight per cent (29/33) strongly agreed, that AMR was an example of market failure: *"It's a textbook example of a market failure"*.

Forty-five per cent (15/33) of respondents had heard of the O'Neill Report. Those who had awareness of it had generally encountered it outside of their work-related reading: *"I saw it on the Royal Society Christmas Lectures"*; *"My wife is a doctor - we discussed it over dinner"*. This insight speaks to the demographic of the interviewees - not everyone has a medical spouse.

Materiality

Per 2.2.3 materiality means the relevance of a sustainability issue to a company's financial performance. When asked if AMR was a material issue the majority, sixty-four per cent (21/33), answered somewhat no or no. *"It's important but I can't say it's material"*. Several interviewees believed AMR needs to be tackled as a matter of human survival, but the business case has not yet been articulated sufficiently.

No interviewees recalled seeing any corporate reporting on the matter in response to the three corporate reporting questions nor was there any awareness of any ESG metrics to assess AMR performance.

Clients

Only one interviewee had been asked a question about AMR from a potential client. In this case, a University Endowment Fund.

Timeframes

When asked about the timeframe in which AMRs impacts would be felt, seventy-five per cent (25/33) stated 2-5 years. No one stated it was more urgent.

Costs/benefits

In contrast to the question on materiality, the largest group of interviewees, seventy per cent (23/33), believed AMR could lead to significant costs or benefits for companies in their portfolios. Interviewees recognised the confusion in the industry, agreeing that *“AMR will probably lead to future costs, but I don’t know which companies will be hit.”*

There was considerable discussion around the investment opportunities arising from AMR. One highlighted the recently launched antibiotic-impregnated catheters from Medtronic Inc. Others cited companies positioning themselves to benefit by developing alternatives to antimicrobial agents - specifically the therapeutic use of bacteriophages. *“I’m very interested in [bacterio] phages.”* Phages are viruses that kill bacteria and well-suited to be part of the multidimensional strategies to combat AMR (Altamirano and Barr, 2019). Several other investors cited the potential of phage therapy and another added he was *“overweight on small capitalisation, rapid diagnostic biotech firms”*.

One interviewee flagged why there was little consideration of opportunities: *“Investors are only interested in oncology as an investment theme as investors follow the money. Cancer patients generate more cash flow. If a patient is ill for longer with a chronic condition we can make more money from them. AMR just isn’t as sexy, so it’s eclipsed.”* The theme of oncology presenting the greatest opportunities of all topics in the pharmaceutical sector came up repeatedly.

Motivations and barriers to investor interest

Motivations

When asked an open-ended question about what might help increase investor interest the answers appear to confirm the literature: *“Show me how it will affect the performance of my funds, then I’ll care”* and *“If I thought a big change was imminent, perhaps regulation, then I’d pay attention”* and *“The day a client asks me, then I’ll notice”*.

Barriers

When asked an open-ended question about what is preventing investors taking more of an interest, several respondees noted the demands on investors time by more established ESG

Issues: “*Climate change and plastic have crowded out the attention.*” Another noted that “*ESG fatigue has set in and practitioners are in firefighting mode with no bandwidth to get to grips with yet another problem.*”

Two other respondees said they only understood AMR as they were married to a doctor and a veterinarian respectively, otherwise it would not be on their radar.

Another was inspired but unsure what to do: “*I saw the Chief Medical Officer, Dame Sally Davies, speaking and resolved to do something as soon as I got back in the office. But what?*”.

5.2.1. Synopsis of results for research question two:

- In respect of the economics, there was a clear view that AMR is a market failure.
- In terms of whether investors will act, many of the catalysts for investor action were absent.
- Themes which emerged clearly were a) a lack of investor-centric data b) a lack of urgency c) ESG issue fatigue d) the power of personal interest and e) oncology eclipsing the sector.

5.3. Research Question 3 - What, if anything, can investors do to help the problem?

	Responses				
	Yes	Somewhat, yes	Somewhat, no	No	N/A
Have you undertaken any portfolio assessment or used the AMR benchmark?	0	0	0	33 (100%)	0
Does AMR appear in your investment strategy?	0	0	0	33 (100%)	0
Have you ever engaged individually with investee companies on the topic of AMR?	4 (12%)	12 (36%)	7 (22%)	10 (30%)	0
Do you engage collectively with companies on AMR?	0	0	0	33 (100%)	0
Have you ever undertaken policy advocacy on AMR?	1 (3%)	0	0	32 (97%)	0
How likely are you to put resources towards a collective engagement?	4 (12%)	17 (52%)	7 (21%)	1 (3%)	4 (12%)
Have you ever divested on the basis of AMR?	0	0	0	33 (100%)	0
Are vaccine bonds investible in according to your mandates?	3 (9%)	0	0	1 (3%)	29 (88%)
Are you aware of any financial instruments currently available (or being called for) that relate to the AMR challenge?	0	0	0	33 (100%)	0

Table 4: Results - What, if anything, can investors do to help the problem?

Themes

Investment strategy

No investees included AMR in their investment strategy nor had any undertaken portfolio analysis. One commented “*The topic is far too immature for this level of consideration.*”

AMR Benchmark

Awareness of the AMR Benchmark tool was low – nine per cent (3/33) were familiar with it. Per Chapter 4, a separate interview was conducted with the NGO behind the AMR Benchmark, the ATMI, to understand the aims and progress of the benchmark.

ATMI is a Dutch NGO that aims to advance access to medicine in the poorest countries by stimulating and guiding the pharmaceutical industry.

The AMR Benchmark provides the first independent assessment of how pharmaceutical companies are responding to AMR. The 30 companies in scope include those with the largest R&D divisions and the largest market presence. The goal is to incentivise companies to adopt and implement effective actions for tackling AMR. It highlights where good ideas for limiting AMR are being implemented and where action is still required.

The main finding of the first iteration of the benchmark, launched in 2018, is that *“Every company who committed to the Davos Declaration is doing something to address the problem of appropriate access and resistance but the scale of the interventions vary dramatically.”*

In terms of investor uptake, the AMR Benchmark will *“conduct an independent evaluation of our impact every five years. We know several investors use the benchmark results in their conversations with companies, but we would find it difficult to speculate on the general level of uptake within the investor community.”*

Thinking about the role of investors the spokesperson said: *“We need the [Davos Declaration] commitments from companies, but we also need the commitment from governments to incentivise and de-risk innovation. Investors can support this policy push and keep AMR alive within their company engagements.”*

In terms of barriers to progress *“The investment case needs to be strengthened to help companies and their investors recognise they are not going to be able to sell products such as cancer drugs, unless hospitals are also able to provide antibiotics.”*

Engagement

While none of the respondents had engaged collectively with pharmaceutical companies forty eight percent (16/33) had asked a question about AMR as part of a broader discussion with

investee companies. AMR questions were predominantly phrased to invite comment on the relevance to the company in question, rather than a detailed conversation.

Seventy-two per cent (24/33) were willing to consider putting resources towards a collective engagement. The majority of these respondents thought the engagement should be with public policy makers rather than companies due primarily to the economics of antibiotics. This was echoed by the literature on addressing the underpinning market failure. This is explored further in “*policy advocacy*” below.

Capital allocation

There was considerable discussion about AMR and capital allocation. The consensus was that it wasn't within the gift of any one individual investor or one company to invest sufficiently to remedy AMR because of a) the significant costs of R&D and b) the lack of incentives to pursue such R&D.

The consensus view was that the science to discover new antibiotics is challenging, but it's not the primary barrier to the blocked pipeline, the economic model is. As one interviewee put it “*Non-standard sales models could help. The Government could pay a subscription to have access to antibiotics as and when needed like Netflix, to spread the R&D risk and burden.*”

Another thought: “*Jim [O'Neill] is the big name in economics, but there's no money in fixing resistance for either anyone as things stand.*”

There was recognition of the need to discover and develop new drugs. However, there was also awareness that “*antibiotics are so unpopular that big pharma has essentially pulled out of the market. Some small companies have made progress on discovering new drugs, but face mammoth financial barriers in getting these new antibiotics to market.*” Another thought: “*The science can work, but the economics need fixing.*”

Overall, perspectives typically reflected a lack of faith in the status quo to fix the AMR problem.

One investor put it simply “*Everyone gets the benefits, but no one wants to invest. There's an added complication that you can undermine the effectiveness of a new products just by marketing it.*”

The majority thought the pharmaceutical industry could not be expected to use its balance sheet to fund R&D.

The potential for an AMR bond divided opinion. Some concluded such a product would be too niche to have broad investment appeal. Others indicated interest and sketched out the parameters of what an attractive product would look like:

- A triple-A credit rating;
- A quasi-government bond structure or backing from the UN or the World Bank with the WHO;
- Maturity of between 3 – 7 years;
- Proceeds from the bond would be spent on AMR solutions;
- Euro or US dollar denomination;

One commented that “*The vaccine bond model is a good way of addressing a public health issue, especially in a low interest world*” but eighty-eight per cent (29/33) of respondents did not know if their organisation could invest in vaccine bonds.

Others fundamentally disagreed with any economic incentives and thought AMR was not a private sector problem to solve and the international governments need to respond on this topic.

Policy advocacy

Only three per cent (1/33) had undertaken any public policy lobbying on the topic. Digging deeper, this responder considered attending a UN General Assembly meeting on AMR counted as advocacy, which is rather a stretch. However, the majority of investors expressed (unprompted) support for an industry wide call for government intervention.

One investor suggested an investor driven equivalent to the Davos Declaration might be a well-supported way to demonstrating investors want interventions to address the market failure. Another opined: “*It makes sense to lobby on this rather than engage because what exactly would I be asking a company to do? I’d look amateur and idealistic if I requested capital expenditure on an unprofitable area.*”

5.3.1 Synopsis of results for research question three:

- Of the four areas for investor action only one is being undertaken; corporate engagement.
- Many investors expressed surprise that the AMR Benchmark existed and the benchmark itself did not appear to have detailed knowledge of the level of uptake amongst the investment community yet.
- Another theme that emerged was the lack of faith in the status quo to deliver remedies and the barrier to innovation presented by the current economic model.
- Interviewees indicated a willingness to put resources towards a collective initiative that focused on policy advocacy rather than corporate engagement. Of the other areas for investor action, capital allocation generated the most discussion with a clear view that the pharmaceutical industry could not be expected to fund new R&D in light of the current economic models. The parameters of what an AMR bond could look like were discussed. Investors expressed some interest so long as the bond had conventional features.

CHAPTER 6: DISCUSSION

The discussion is organised around the three research questions, following the same structure as Chapter 5. The aim of this chapter is to demonstrate a) how the results relate to the research objectives and the literature, b) what the results mean and c) why this matters. The limitation section highlights what the results are unable to tell us.

6.1 Research question 1: Why would investors care about AMR?

6.1.1 Interpretation

From the literature, we surmised that if investors perceive an ESG topic as fulfilling at least one of four reasons, then they tend to care about it. The results largely confirmed this argument;

- Of the four key factors, only one is resonating in any meaningful sense with the respondees; reducing portfolio risk.
- The investors who did not perceive any of the catalysts as relevant did not demonstrate intention to investigate the topic further or take action.
- The investors with a strong conviction that consideration of AMR offered a reduction in portfolio risk were correspondingly the ones who had undertaken some action on the topic, predominantly engagement.
- Interestingly, the two investors whose clients had expressed an interest had the most sophisticated understanding of the issues and were taking the most action. Both indicated this was a causal relationship.

A perspective that was present in the literature and brought to life in the interviews was the potential for personal interest to drive investor action. Several investors cited family members who had contracted resistant strains of bacteria as their catalyst for caring and the consequential action undertaken. In addition, two investors cited conversations with their medically trained spouses as piquing their interest.

It is noteworthy that, despite investor initiatives existing for AMR as an agricultural issue, none of the respondees had been approached by any NGOs or investor initiatives on AMR specific to the pharmaceutical sector. Eighty-two percent (27/33) mentioned, without prompting, they had been contacted by investor initiatives active on the food production side of the antibiotics discussion, specifically the FAIRR Initiative and BBFAW.

6.1.2 Implications

These results indicate that, in the current situation:

- A focus on Sullivan's four reasons is key to tracking levels of interest and of the four, clients are (to date) the most important route to get investor attention.
- Stakeholders wishing to advance the topic of AMR in the investment community should focus on a) framing their message around the area current capturing investors' attention, portfolio risk, and b) piquing client and personal interest.

In the future AMR may become higher profile or deemed to be material, in which case these results would need reviewing.

6.2 Research question 2: Do investors have an interest in taking action?

6.2.1 Interpretation

A healthy dose of scepticism should be applied to these results, just because investors can act doesn't mean they will.

Sullivan and Mackenzie (2008) explained why investors rarely felt a compulsion to act in the face of a market failure. The topic of climate change is one example of what was initially a pure market failure where investors felt the macroeconomic implications and the technology opportunities were sufficient to call for short-term pain from corrective regulation to allow long-term gain.

All the interviewees classified AMR as a market failure. However, they also expressed a strong interest in remediation. This could be because AMR echoes some of the attributes of climate change, namely;

- a credible peer reviewed report detailing catastrophic long-term macroeconomic implications of inaction (The Stern Report and the O'Neill Review); and
- investable opportunities around solutions (low carbon technology and rapid diagnostics, vaccine and phage therapies).

In respect of the latter point, the literature speaks to the investable alternatives to antibiotics and the interviews fleshed out those examples with real-life investment positions.

Continuing the climate change analogy, Sullivan and Mackenzie (2008) emphasise that much of the investor action on climate change is business case focused; therefore, the business case for AMR needs to be established. The interviews inform us that the business case is not currently sufficiently articulated, which feeds into the recommendations in 7.4.

The literature tells us that in order to determine if a topic is deemed material, investors need clarity on three key metrics; the impact upon drivers of value; the financial impact and if that impact is financially material. However, the results do not fit with the theory, that is, none of the investors reported seeing any of the three key metrics in corporate reporting yet thirty six per cent (12/33) still classified AMR as material.

One possible explanation for this, as identified by Eccles and Strohle (2016), is the fluid range of interpretations of the term materiality within and between organisations as well as the evolution of the term over time. Other explanations could be that AMR is a) not currently a big enough cost, b) not impacting individual companies at scale and c) lacking any real opportunities to invest.

In addition, respondees may have suggested the topic was material due to 'participatory bias' - the interviewees saying what they think the interviewer wants to hear. This is explored further in section 6.4.2.

Moving onto the nuances of materiality that Sullivan (2011) describes;

The literature tells us that investors are likely to be more interested in ESG issue that will impact performance in the next 12-24 months. The results indicated that none of the investors felt AMR would impact upon investments in that timeframe which may help explain the low levels of activity on the topic overall. Interesting, the consensus was that the impact would be felt in 2-5 years so investors' interest levels may change in the near future.

The interviews confirmed the literature regarding materiality flowing from client or personal interest. Of note is that those who had external client or personal interest were the most engaged overall. However, even if AMR is deemed material that simply means an investor thinks it is relevant – it does not necessarily mean an investor will be compelled to take action.

Despite the above, we must be mindful that the majority of respondees still consider AMR immaterial.

6.2.2 Implications

On the topic of materiality, it would appear investors are determining AMR to be material based on client and personal interest, rather than other measures. This fits with the literature on materiality nuances and personal values. Stakeholders wishing to gain investors' attention may wish to prioritise these avenues in the first instance.

One theme that appeared across several questions was the low level of recognition of an existing pharmaceutical sector specific investor tool to offer selected insights into pharmaceutical company's antibiotic activities; the AMR Benchmark. The results provide a new insight into the relationship between the ATMI, who run the benchmark, and their target audience. This means that the ATMI would do well to rethink how they publicise the next iteration of the benchmark to reach the intended audience. One potential reason why it has not got the traction could be the ESG fatigue mentioned by interviewees.

The literature established the positive impact a client's interest has on investor action, and the interviews confirmed this.

6.3 Research question 3 – What can investors do to help the AMR problem?

6.3.1 Interpretation

There was no mention of any actions outside those identified in the literature. However, there may be other actions available worthy of exploration, for instance, filing a shareholder resolution at a company's annual general meeting.

To help clarify the current state of play, I have developed Table 5 which identifies a) what action could take place, b) where action is taking place and c) where appetite exists to bridge that gap.

RI Strategies	Evidence from interviews that this is happening	Evidence of appetite for taking such action from the interviews
Investment Strategy: portfolio assessment	No	Yes
Investment Strategy: strategic integration	No	No
Corporate Engagement: individual	Yes	Yes
Corporate Engagement: Collective	No	Yes
Capital Allocation: divestment	No	No
Capital Allocation: financial instrument to fund AMR R&D	No	Yes
Policy Advocacy	No	Yes

Table 5: Identifying where action could be catalysed

6.3.2 Implications

The practical implications to help catalyse latent appetite for such action (highlighted in Table 5), include:

Investment Strategy: portfolio assessment

Investors are largely unaware of the existence of a tool to benchmark corporate performance on antibiotic stewardship, the AMR Benchmark. As the only offering to the investment community on this topic it is worth ATMI reviewing their outreach strategy to the investment community before the launch of the next iteration in 2020.

Corporate Engagement: collective

Nearly three quarters of investors expressed an appetite for collective engagement on the topic and willingness to devote resources, but no such vehicle exists. However, while there is latent enthusiasm, a) most interviewees thought it was more a policy issue and b) if corporate

engagement was to be considered, more research is needed to establish to what end the specific engagement asks could focus upon given the current economic models.

Capital Allocation

The interviews identified a significant pocket of interest in exploring a conventional bond for funding AMR solutions. This contrasts with the literature, which a) did not appear to recognise the potential role of the private sector, indicating it is either i) unnecessary or ii) irrelevant and b) tended to emphasise the importance of the role of foundations and government financing.

The literature identified the existence of push and pull mechanisms (Appendix 3). Building on this, the interviews identified that none of the stakeholder involved in such mechanisms are speaking to investors about capturing funding from mainstream investors. The parameters of what such a product would look like mirrored the attributes of a conventional bond.

Policy Advocacy

The literature indicates the presence of a market failure may make investors reluctant to engage with companies. However, the interviews identified a potential solution to this market failure, specifically the latent appetite of investor to engage with policy makers. This enthusiasm for investor lead advocacy work was surprisingly broad especially with investors who had taken no other action, contradicting the welfare model of economics literature and feeds into a recommendation in 7.4.

6.4 Synopsis of discussion

6.4.1 Key Findings

Attention

The interviews suggest that there is a clear link between investors who believe AMR can a) reduce portfolio risk b) meet client needs and c) fulfil their personal interests and those investors who are taking action.

The personal impact aspect is an angle where creativity could be deployed especially as AMR is deemed financially immaterial. Given the human interest aspect, there are more avenues to make AMR resonate personally with the average investor than an ESG topic such as auditor

rotation. This angle could be exploited to address the crowded ESG space that several participants spoke of.

Materiality

The literature indicates that the financial implications of AMR are only defined by peer reviewed papers at a macroeconomic level.

The business case for AMR has not been articulated and AMR is not recognised as material by the majority of interviewees. Furthermore, there is a lack of urgency around the topic.

Solutions

That AMR is a market failure was not in question. The literature indicates this means investors are less likely to press the companies they invest in to take action.

The literature identifies policy engagement as the most effective route towards market failure remediation. Many interviewees expressed an appetite for collective public policy advocacy on AMR as well as citing opportunities for investing in solutions. The implication for policymakers is that stronger policy measures will be necessary to address the market failure inherent in the current economic models for antibiotics. Conversely, the absence of a clear message regarding the impact of AMR from the pharmaceutical industry counts against investors looking at these issues.

Investors agreed policy advocacy trumped corporate engagement especially because it was not clear what action they should be asking companies to take in the face of a market failure. The literature captures the key attributes that determine the success of collaborative investor policy advocacy. These attributes, including increasing saliency and the 5C checklist for effectiveness, are woven into the recommendations section in Chapter 7.

Causes

This research focuses on the pharmaceutical sector implications of AMR. However, the literature relating to the corporate practices fuelling the causes of AMR (in Chapter 2 and Appendix 1) and the results both speak to the interplay between the demand and supply side of AMR. Several investors highlighted the futility of researching new antibiotics only to squander away their efficacy by overuse in agriculture. This highlights a wider question ripe

for further research, namely what is the relative weighting of the different causes of AMR acceleration - agricultural use verses human clinical use.

Funding

Questions remain over the precise mechanics of funding needed to generate AMR solutions and the size of the funding gap. Foundations and governments have provided the majority of funding to date. Until we have clarity on the gap then there will be ambiguity over the role that institutional investors can play, likely to compound investor inertia. The funding gap may be anywhere from negligible to circa US\$16 billion, as estimated by the O'Neill Review.

To date, research has focused on the loss of GDP not on how to bridge the funding gap (Thorpe et al, 2018). There is investor interest in exploring a conventional bond with conventional characteristics for funding AMR solutions. However, bonds are only one funding option and the bigger question is the size of the funding gap and if the government wants or needs private sector finance.

6.4.2 Limitations of the research

Geographic bias

There was a deliberate interviewee bias towards UK investors, as I have a developed network in that region. This interview biases could have been removed by having representative of the other investment hubs, but is somewhat mitigated by the fact that many of the interviewees invest globally

Sample size

The reliability of this data is impacted by the limited number of interviews (33x). Moreover, interviews were held across two different interviewee groups, asset managers and asset owners, each with different perspectives on the industry. The positive aspect of this is the diverse perspectives captured.

Participatory bias

Given my acquaintance with the majority of interviewees, the responses given may be subject to the 'halo effect', where participants may distort their answers to present themselves in the best light, rather than give an honest answer (Norris, 1997).

Quality of responses

The interviewees knowledge ranged significantly resulting in a wide range in the quality of their responses. Some claimed deep expertise in the issue, while others had limited knowledge. This may be indicative of the reality of AMR knowledge in the investment industry. A larger sample size across asset managers and asset owners, and an initial screening of interviewees would help mitigate this limitation and/or confirm the state of play around AMR knowledge.

Interpretation of data

The generalisability of the results is limited by the interpretation of the interview style of collecting data by the interviewer, leading to the potential for misinterpretation. This could have been mitigated by engaging a support researcher to confer the accuracy of interpretations. The interviewees could also have confirmed the interpretation and coding of the results ex-post.

Lack of academic literature and data collection consistency

Given that antibiotic economics and AMR as relates to ESG are both relatively embryonic fields of research, much of the literature used was 'grey literature', namely, industry reports and websites. The lack of peer review of such sources reduces their credibility. However, there is an established body of academic literature around ESG, from which analogies were drawn, which mitigates this limitation somewhat.

In addition, the emergent stage of the topic created definition and data collection issues including: (i) a lack of a common language, which reduced the consistency with which respondents interpreted and answered questions and (ii) determining the current and future risks and opportunities with accuracy. While this limitation could erode the robustness of the findings it could also be considered an opportunity to identify new gaps in the literature, per 7.5.

CHAPTER 7: CONCLUSIONS & RECOMMENDATIONS

7.1 Context of conclusions

This dissertation builds on work in the field of RI and antimicrobial economics. I drew upon the work of Mackenzie and Sullivan (2006) to frame my research around three questions

a) Why would investors care about antimicrobial resistance;

b) Do investors have an interest in taking action: and

c) What, if anything, can investors do to help the problem?

Mackenzie and Sullivan's emphasis on the catalysts for investors to care, as well as the drivers of investor action, are especially useful to my analysis as it allows me to a) think through the reasons driving current action/inaction, b) what is missing that could attract investors' attention and c) the limitations investors are subject to.

Few would argue that companies contribute, either directly or indirectly, to social and environmental problems, in this case the interplay between corporate practice and the causes of AMR. To this end, the literature's conceptualisation of the tenants of investor action is generative for grasping how investors' resources could be deployed in order to support action to tackle the AMR problem.

This is primarily by using their investments in pharmaceutical companies and their ability to influence policy makers as an important stakeholder group. The literature on effective collaborate investment policy advocacy shapes part of the recommendations in 7.5.

Prima facie, AMR has some of the characteristics that may encourage investor action. The literature on ESG and market failures offered some insight into barriers to investor action and how best to frame investor action – specifically focusing on collective policy engagement as a remedy rather than corporate engagement.

This research owes a factual and interpretative debt to O'Neill's work on the economics of AMR, which is of value for quantifying the financial consequences of runaway resistance. The

dissertation differs from other studies of antibiotic economics by identifying interest and motivations as pertains to the RI lens.

7.2 Conclusions by research question

The findings contrast what we know about investor motivations and actions with the reality of investors' views on AMR in 2019. More broadly, the research blends the literature and the results to provide some insight into the pathways as to how to fast track investor consideration of the topic.

I found in answer to question 1, of the four key factors which cause an investor to care about an ESG issue identified in the literature, only one resonated in any meaningful sense; reducing portfolio risk. Client and personal interest were the most powerful catalysts to get investor attention. In the absences of these factors, stakeholders wishing to advance the topic of AMR with investors should focus on framing their message around portfolio risk. As things currently stand, the majority of investors surveyed did not currently care about the topic sufficiently to take action.

I found in answer to question 2, many of the indicators which would give investors an interest in taking action are absent. Also missing are credible investor-centric sources of data and knowledge, a sense of urgency and a tool to promulgate widespread knowledge of stock specific winners and losers. The only existing project that focuses solely on the pharmaceutical sector, the AMR Benchmark, was largely unknown. The organisation behind the benchmark only had anecdotal evidence regarding the uptake of the benchmark within the investment community.

I found in answer to question 3, gaps between what action could be taken and what action is current being taken. The interviews identified a pocket of interest in a) collective policy engagement and b) exploring a mainstream bond to help fund AMR solutions, whilst the literature tended to emphasise the importance of the roles of foundations and government financing.

7.3 Overall reflections

The question is whether investors have (or could have) a role to play in the development of appropriate responses to AMR? The prima facie answer is yes, albeit a modest one, with an emphasis on a public policy engagement in the first instance.

The literature and interviews concur that;

- Neither companies nor investors have a compelling business case for investing in AMR R&D.
- AMR is a market failure that needs a public policy intervention. Therefore, Governments have the primary power to remedy the issue.
- Investors may have a small role to play in encouraging public policy action on AMR and, when the funding gap has been defined, by allocating capital towards solutions. However, no one investor can allocate funds sufficiently to fix AMR.

There is presently a lack of data, urgency and knowledge around AMR. It is not currently considered material. Given the presence of ESG fatigue, as identified in the interviews, even proving materiality may be insufficient to make investors care. The role of personal values and interest came through as a pertinent way of catalysing action.

There was a clear view that the pharmaceutical companies cannot be expected to fund new R&D from their balance sheets in light of the current economic models. Therefore, the most effective avenue for investors who wish to take action is to engage with public policy makers to address the economic models, rather than engage with companies.

Once the funding gap is comprehensively defined we can have clarity on who should finance it. If the answer includes investors this research helps identify some of the characteristics investors would need.

While the primary focus of this research is on the pharmaceutical sector, both the literature around the causes of AMR and the interviews agreed that the agricultural use of antimicrobials was a fundamental issue. It would be helpful for further research to be conducted to identify what proportion of the problem flows from the different causes of AMR.

Some care is required with this conclusion as it may do a disservice to other actions investors could or are currently taking, for instance, supporting the AMR Benchmark. However, the literature on AMR as a market failure underpins the conclusion that, without addressing the inherent broken economic model, other investors actions face a fundamental and potentially

insurmountable headwind. Investors should also recognise that their role on public policy is only part of the picture and they are only one of the stakeholders.

7.4 Recommendations

Influencing initiative

Tapping into the latent interest identified, an influencing initiative should be launched to aid investors in advocating at a public policy level for the economic model to be fixed as opposed to a corporate engagement initiative.

Drawing from the body of literature on what makes an effective public policy initiative (2.2.4) and the public policy response to AMR (2.1.4), the initiative should

- a) Use the 2017 G20 Leader's Declaration on AMR as a framing mechanism
- b) Be collaborative and focus on establishing the power and legitimacy of the collaborators and the urgency of AMR.
- c) Establish commitments from investors to dedicate resources to the initiative and prepare investors for such engagement to span a protracted time period
- d) Frequently calibrate adherence to the PRI's 5C checklist for effective policy engagement.
- e) Explore the potential for an investor version of the Davos Declaration

The Business Case

To compliment the policy initiative and garner the aforementioned commitment from additional investors, production of a report to plug the gap between the macroeconomic outlooks of the O'Neill Report and investee company and sector specific implications.

Such a report could draw inspiration from what the literature tells us on what makes investors care as a starting point and include opportunities around solutions e.g. phage therapies.

Essentially this report would translate the O'Neill Review into a report to drive buy-side buy-in. To harvest the results from this research, the report should also

- explore the impact on investment performance and portfolio risk;
- articulating materiality, for instance in the veterinary pharmaceutical sector;
- highlight case studies of companies who have significant costs and benefits;
- demonstrate the reliance of the investor *topic du jour*, oncology, on effective antibiotics
- detail the regulations appearing internationally including potential impacts and timeframes.

Awareness

The research highlighted the ability of the personal interest aspect of AMR to catalyse awareness in investors. In order to stimulate action those with an interest in increasing investor attention to AMR should:

- *Reframe and make it personal* - Cut through the ESG practitioners issue fatigue by a) framing AMR as a sub topic of established ESG pharmaceutical issues rather than a brand new issue to digest and b) using novel personal interest stories to highlight impact of AMR e.g. doctors or survivors of AMR at investment conferences.
- *Roadshow* - ATMI to rethink the launch of the second iteration of the AMR Benchmark to increase awareness of it amongst target audience.
- *Civil Society* – Expand campaigns to include investors. The literature tells us that there is a plenitude of civil society action yet only very limited focus on investors. The interviews tell us that investor initiatives can impact on AMR, as evidenced by the awareness of FAIRR and BBFAW and their targeting towards investors. However, there is not an equivalent investor initiative in the pharmaceutical sector, although the AMR Benchmark shares some of the characteristics of FAIRR and BBFAW, specifically the offering of a benchmark.

7.5 Further Research and wider reflections

To calibrate the recommendations further research is needed to:

- Define what the funding gap is for AMR innovation and consequently; a) if investors could help plug the funding gap on AMR and b) how this sits with the creation of a bond that is attractive to investors. If it is concluded that the funding gap requires

injection from investors, then further research is required to identify the parameters of what one solution, namely a bond, would look like including a) who could issue it and b) how it fits with existing public-private partnerships in this space. My research provides a starting point for the parameters needed to appeal to investors.

- Many investors made unprompted remarks regarding the demand side of the antimicrobial conundrum; the overuse of antibiotics in agriculture. This highlights a wider question for further research, namely a) what is the relative weighting of the different causes of AMR acceleration - agricultural use verses human clinical use and b) how the role of investors may be broader if investments in agricultural companies are included.

7.6 Contribution to scholarly body of knowledge

The main way in which my work has contributed to the field of antimicrobial economics and RI is that it has provided readers with the first academic research piece that applies the body of knowledge around RI to the emergent topic of AMR.

The findings support the current academic thinking of the catalysts behind investor attention and action on ESG issues. The finding extends the existing body of knowledge on antibiotic economics, which have largely focused on macro-economic implications to date.

These findings identified latent interest by investors in engaging with policy makers to address a market failure and a current absence of any activity in this area. These findings could be of interest to stakeholders wishing to build such coalitions for collaborative action on AMR, for instance civil society, industry, think tanks and investors. Civil society may wish to press investors to take action; the research indicated that currently investors are feeling no pressure to take action.

Why was it important to do this research?

The main way in which readers should think differently as a result of this research is:

Firstly, not to assume that investors will take action AMR simply because the O'Neill Review has estimated the catastrophic macroeconomic implications.

Secondly, to comprehend the barriers to investor action on the topic and what can be done to surmount them.

Thirdly, to understand why it is strategically more effective to engage with policy makers rather than companies.

CHAPTER 8: REFERENCES

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GLOSSARY

Antibiotic - A drug that kills or stops the growth of bacteria. Antibiotics are a type of antimicrobial. Penicillin and ciprofloxacin are examples of antibiotics.

Antibiotic resistance - Antimicrobial resistance is the result of microbes changing in ways that reduce or eliminate the effectiveness of drugs, chemicals, or other agents to cure or prevent infections.

Antimicrobial – A substance, such as an antibiotic, that kills or stops the growth of microbes, including bacteria, fungi, or viruses

Asset Managers - Financial company that manages investments on behalf of others. These include, for example, investment managers that manage the assets of a pension fund.

Asset Owners - Asset owners include pension funds, insurance companies, official institutions, sovereign wealth funds, banks, foundations, endowments, family offices, and individual investors.

Bacteria - Bacteria are single-celled organisms that live in and around us. Bacteria are necessary for us to function normally, but in some conditions may cause sickness such as strep throat, ear infections, or pneumonia.

Bacteriophage - A virus that selectively infects bacteria.

Bond - A bond is a loan that is tradable, a so-called debt security that can be sold to investors.

Corporate engagement - This strategy employs shareholder power to influence corporate behaviour including through direct corporate engagement (i.e. communicating with senior management and/or boards of companies), filing or co-filing shareholder proposals and proxy voting.

Externalities - A positive or negative consequence of an economic activity experienced by unrelated third parties. Pollution emitted by a factory that spoils the surrounding environment and affects the health of nearby residents is an example of a negative externality.

Financial actor - A diverse set of actors operating in financial markets. These include financial institutions, institutional investors, investment banks, pension funds, and others

Institutional investor - Investor who pools large sums of money and invests those sums in equities, bonds, property, or other investment assets.

Institutional Investors - A non-bank investors that trade securities in large quantities that qualifies it for preferential treatment and lower commissions. Institutional investors face fewer protective regulations because it is assumed they are more knowledgeable and better able to protect themselves e.g. Sovereign Wealth Funds, pension funds and insurance funds.

Investment portfolio - A collection of investments, for example, equity securities in different companies.

Market failure - A market failure occurs whenever the individuals in a group end up worse off than if they had not acted in perfectly rational self-interest. Such a group either incurs too many costs or receives too few benefits. Commonly cited market failures include externalities, monopoly privileges and information asymmetries. Where there is market failure, markets do not operate to provide a price to provide the good or service.

Materiality - The relevance of a factor to a company's financial performance.

Mortality rate - The number of deaths per units of time in a defined population.

Multi-drug resistance - Resistance to at least one agent in three or more antimicrobial categories.

Phage - See "bacteriophage".

Pipeline - The set of drug candidates that are researched and undergo clinical tests at a specific point of time.

Principles of Responsible Investment -The United Nations-supported Principles for Responsible Investment (PRI) initiative is an international network of investors working together to put the group's six Principles for Responsible Investment into practice.

Public goods - A 'product' consumed by a society, not necessarily by an individual consumer, without reducing its availability to another society or individual, and from which no one is excluded. Public goods are financed by public revenues and cannot be withheld from people

who do not directly pay for them. Public goods are those where there is no market and therefore provided by governments such as national defence, sewer systems, public parks.

Push and pull mechanisms - In the context of Antibiotic R&D, a pull mechanism is generally outcome-based, and typically it offers a reward that is granted only after a product (i.e., a new antibiotic) has been fully developed. A push mechanism is generally a way to subsidize research activities in a given scientific area (e.g., certain types of antibiotics). It is typically used to start new research and it is not related to the results of such activities.

Responsible investment - Responsible investment refers to an array of investment approaches including the following investment strategies; impact investing, positive and best-in-class investing, sustainability thematic investing, norms-based screening, negative screened investing, ESG integration and corporate engagement.

Zoonosis - A disease that can be transmitted from animals to humans and/or vice versa.

APPENDIX 1: Causes of antimicrobial resistance

Overuse and inappropriate prescription in humans

High Income Countries are coordinating efforts to limit the use of antibiotics, however, there is concern that a reverse trend has been occurring in low- and middle-income countries. Klein et al, 2018, conducted a large-scale observational study using national quarterly antibiotic consumption data. They found that between 2000 and 2015, antibiotic consumption increased by 65%. The primary driver of this increase in global use was the increased consumption in LMICs where antibiotics are often freely available over the counter. Consequently, this lack of oversight results in easily accessible, plentiful, and low-cost access to antibiotics which promotes overuse. Antibiotics may also be purchased online through less reputable e-commerce websites which has also made antibiotics freely obtainable in high income countries where antibiotics are regulated. (Michael et al, 2014).

The injudicious prescribing of antibiotics is a key contributor to resistance, has questionable therapeutic benefit, save for the placebo effect, and expose patients to potential complications of antibiotic therapy (Lushniak, 2014). Yet, Public Health England found that more than 20% of all antibiotic prescriptions in primary care in England are inappropriate. Furthermore, 30% - 60% of antibiotics prescribed in intensive care units (ICUs) have been found to be unnecessary or inappropriate (Luyt et al, 2014).

Much of the inappropriate prescription of antimicrobials is linked with the absence of rapid diagnostic biotechnology that can isolate the precise diseases causing microbe (O'Neill, 2015). Medics and veterinarians rely on treatment using broad-spectrum antibiotics that may or may not remedy the disease but still expose microbes to a variety of antibiotics, thus increasing the likelihood of resistance forming.

In addition to the above the online sale of antimicrobials without prescription and the supply of poor-quality and falsified antimicrobial drugs compound the problem (O'Neill, 2016).

Extensive agricultural use

Giving antibiotics to livestock is said to producing larger carcass yields and a higher-quality product however, the routine administration of subtherapeutic quantities of antibiotics for growth promotion has been banned, but only in the European Union (Lushniak, 2014).

The antibiotics used on livestock impact upon humans via:

- a) Consumption of animal products - resistant bacteria in farm animals reach consumers through meat products (Golkar, 2014);
- b) Working on farms - higher rates of antibiotic resistance were found in the intestinal flora of farmers (Bartlett et al, 2013);
- c) Through the watercourse - Up to 90% of antibiotics administered are excreted in urine and stools, then widely dispersed through slurry, groundwater and surface runoff (Ventola, 2015). In some instances, antibiotics are sprayed on fruit trees as pesticides.

The global increase in demand for animal-based protein and associated intensification of livestock production has led to greater use of antibiotics, since they were first introduced as growth promoters (Dibner and Richards, 2005; Anonye, 2016).

Concerns around antibiotic usage in agriculture are not new. In 1960, the UK Government set up the Netherthorpe Committee to investigate the danger to humans from the use of antimicrobials in animal feed. This was followed by the Swann Committee in 1968, which concluded that the use of antibiotics in animal feed did pose a danger to human health, due to increase in antibiotic-resistant bacteria.

A review of more recent evidence is outlined in the UK government commissioned O'Neil Review in 2015. The review acknowledges that the link between animal and human resistance is more controversial than evidence solely on antibiotic resistance in human bacteria. However, the report reviews the literature and finds the evidence compelling for a link.

The review looked at 139 academic papers on the link between antibiotic use in agriculture and rising antibiotic resistant bacteria in humans – 100 papers found there is a link, while only 7 argued there was not. The WHO also commissioned a review of all evidence on this topic when it produced its WHO guidelines on use of medically important antimicrobials in food-producing animals (2017). The review covered 111 studies and concluded the following:

“Limiting the use of antimicrobial supplementation for food animals is likely to reduce the presence of antimicrobial resistance in other food animals and humans. This may extend beyond the antimicrobial used to other antimicrobial classes.”

A recent review by Hoelzer et al, 2017 reached a similar conclusion, stating:

“The review clearly demonstrates that there is compelling scientific evidence available to support each step in the causal pathway, from antimicrobial use on farms to a public health burden caused by infections with resistant pathogens.”

APPENDIX 2: Push and pull mechanisms

Push mechanisms reduce a firm's R&D costs by distributing the expenditures across multiple parties, for instance, research grants and offering tax incentives.

The InnovFin Infectious Diseases is a risk-sharing financial instrument jointly developed as a push mechanism by the European Commission and the European Investment Bank. It offers loans up to €75 million for the development of innovative vaccines, drugs and diagnostic devices, and novel research infrastructures for combatting infectious diseases (Eichberg, 2015).

On paper, this late-stage push funding is available to all research providers. In practice, smaller participants are blocked as eligible projects must have surpassed the initial basic research and preclinical phases of development.

In isolation, push funding is insufficient to stimulate a functioning antimicrobials market therefore pull funding has emerged (Perfect, 2017)

Pull mechanisms reward successful development of a drug by increasing or ensuring future revenue, for instance, cash prizes, accelerating the market approval and extending patents.

Pull mechanisms could address the fundamental unattractiveness of funding new antibiotic R&D, for instance, decoupling the cost of R&D from volume-based sales and prices of antibiotics as GSK, Shionogi, Pfizer and Novartis report that they have done (Outterson, et al, 2016).

However, there are scant pull incentives to transition new antibiotics from early clinical phases, through the market approval stages towards commercialisation or attract large pharmaceutical companies to invest in the market. Those, that do exist, include:

- i) The United States' Generating Antibiotic Incentives Now (GAIN) Act grants an additional 5 years of market exclusivity to companies developing antibacterials that target a selected group of pathogens.

- ii) The Antimicrobial Resistance Diagnostic Challenge awards a US\$20 million for AMR innovation but it remains to be seen whether this is a large enough incentive, especially when compared to the lucrative nature of designing new drugs for chronic diseases.

A critical assessment of 47 incentives has been compiled by Renwick et al, 2016, and updated by Simpkin et al, 2017, detailing the major push and pull initiatives directed at AMR research; the majority are push based.