Alphinity Investment Management

What's new in ESG – August 2023

Antimicrobial Resistance | An emerging ESG consideration

When used correctly, antimicrobials play a key role in treating human and animal health. Antibiotics in particular have saved millions of lives since the 1940s and have contributed significantly to the life expectancy we see today. But microorganisms are becoming more resistant to contemporary medicine. Without responsible antimicrobial use, disease prevention and research into alternatives, the systemic risk posed by antimicrobial resistance (AMR) could be extremely disruptive. This has brought awareness from policymakers, industry bodies and investors of late. This report explores the ESG considerations related to AMR and the importance of stewardship and company engagement in the healthcare and food sectors to address this risk.

Introduction

Antimicrobials – antibiotics, antivirals, antifungals and antiparasitics – are widely used to prevent and treat infections in humans, aquaculture, livestock, and crop production. These agents have transformed modern healthcare, enabling the treatment of diseases that were once uncurable. Antibiotics in particular have played a vital role in the success of medical procedures such as organ transplants and cancer treatment.

However, the misuse of antimicrobials could lead to a considerable economic cost and financial risk for investors. If antimicrobials are not prescribed and used for their intended purposes, disease-causing microorganisms, or microbes, can become immune to the medication that once suppressed them. This worsens the spread of disease, severe illness and associated deaths, a phenomenon referred to as AMR.[1]

In general terms, AMR is about the survival of the fittest. By introducing antimicrobials into a system, an environment is created whereby the strongest microbes can survive and multiply. The impact is essentially two-fold. Firstly, diseases can become more severe and secondly, infections are increasingly difficult to treat as medicines lose their potency.

While these impacts are relatively straightforward to understand and manage at the individual or group level, the systemic risks are more complex and coming to the attention of stakeholders. The threat of antibiotics becoming ineffective, and even one day obsolete, has prompted policymakers to acknowledge AMR as a serious danger to human health, food security and economic stability. The United Nations has openly called for more robust management of AMR, with the World Health Organization (WHO) listing AMR among the top ten threats to global health.[2] Shareholders too are voicing their concerns in the area of animal agriculture.

This report offers perspectives on the systemic risk posed by AMR and key ESG considerations for investors. This research has an emphasis on the healthcare and food sectors as we believe they are exposed to the most significant risks, and equally, can influence the system-wide impacts of AMR. We outline examples of good management of the risks, and questions that can be asked of companies to delve deeper into their AMR strategies.

Key terms

Antimicrobials: Medicines that kill or slow the growth of microbes (bacteria, virus, fungus, parasites) that cause diseases. Antibiotics are the most commonly prescribed antimicrobial.

Antibiotic: Medicine used to treat bacterial infections by directly eliminating the underlying bacteria.

Antimicrobial resistance: The ability of microbes to grow in the presence of an antimicrobial substance (a medicine) that would normally kill or limit their growth.

[1] Antimicrobial Resistance | WHO (2021)

[2] Antimicrobial resistance: A global threat | UNEP (2023)

Why AMR is relevant for investors

In early 2021, we identified AMR as an emerging research area. AMR is considered a systemic risk that holds implications for specific sectors in the shorter term, such as healthcare and food. But, left unmanaged, AMR could impact the productivity and resilience of companies across industries and affect the global economy. We believe that the market's understanding of AMR and its implications is relatively nascent compared to other ESG topics. However, AMR has started to gain investor attention.

In 2023, we saw shareholders submit proposals at the AGMs of major food industry players such as Tyson Foods and McDonald's, urging them to prioritise AMR-related issues. Since AMR and ecosystem health are interrelated, the focus on nature and biodiversity as an investment risk will likely elevate awareness of AMR.

Regulation too is evolving. The European Union (EU) was an early mover in 2006, banning antibiotic growth promoters from being added to livestock feed (European Commission). Similar regulations followed in the United States in 2017 (Food and Drug Administration) and China in 2020 (WHO). Last year, the EU also banned routine antibiotics in animal farming meaning that antibiotics could only be used for targeted treatment and not for mass application to prevent disease.[3] In June 2023, the EU adopted 2030 targets[4] to step up the fight against AMR:

- 20% reduction of antibiotic consumption in humans;
- At least 65% of antibiotic consumption in humans should be effective (use of the right antibiotic);
- Reduce infections of three key antibiotic-resistant bacteria, which will apply mainly to hospitals.

In Australia, essential antibiotics used in human health are not permitted for use in animals in order to slow resistance from developing and to preserve treatment success (Australian Government).

Back to basics: What is AMR?

It is important to acknowledge that AMR is a naturally occurring phenomenon. However, it is accelerated through the misuse and overuse of antibiotics in human health, animal health and agriculture. Human interference has introduced selective pressures at a faster rate than those existing in a natural environment.

Emergence

AMR occurs when disease-causing microbes no longer respond to antimicrobials, adapting and growing immune to medication that once suppressed them. As resistant microbes survive, the proportion of so-called 'super' bugs in an ecosystem multiply and increase. These microbes can also transfer resistant DNA to others.

The types of microorganisms that can develop resistance to antimicrobials include:

- **Bacteria** – develop resistance to antibiotics;
- **Viruses** – develop resistance to antiviral medicines;
- **Fungi** – develop resistance to antifungal medicines;
- **Parasites** – develop resistance to antiparasitics.

Drivers

Over-prescription and misuse of antimicrobials, particularly antibiotics, are considered to be the main drivers of AMR. The use of antibiotics is commonplace in agriculture, not just for the treatment of disease but also misused on occasion for growth promotion and preventative purposes. Discharge of waste and contaminated water through pharmaceutical (or medicine) production and agriculture also contribute to AMR.

Impact

Intensive use and overuse of antimicrobials in human and veterinary medicine has resulted in the occurrence of resistant disease in both clinical and natural environments. Resistant microbes can spread between people and animals, are harder to treat than non-resistant microbes and can lead to serious illness. Resistant infections require more second-line/reserve medication that rely on access to quality healthcare and can be costly.

The impacts of AMR are essentially two-fold:

1) Disease severity: AMR increases disease severity as the strongest microbes often survive and multiply.

2) Ineffective treatment: AMR reduces the success of treatment as microbes become resistant to multiple medicines and cannot effectively be suppressed.

Antibiotic resistance is considered to be the most critical subset of AMR by researchers and medical practitioners. Antibiotics play a crucial role in treating disease and supporting medical procedures. But with the broad application and potential misuse of antibiotics, resistance is developing at concerning rates.

Some bacteria are now so resistant that no common antibiotics can treat the infections they cause. For example, Staphylococcus aureus ('golden staph' or MRSA) is now almost always resistant to benzyl penicillin. In the past, these infections had been effectively treated by this medicine.

[3] Ending routine farm antibiotic use in Europe | European Public Health (2022)

[4] EU action against AMR | European Commission (2023)

Example: Antibiotic resistance

A patient who does not complete a full course of antibiotics could inadvertently create a condition whereby the strongest bacteria survive.

Emergence: A patient with a bacterial infection is prescribed a ten-day course of antibiotics. Typically, there is a rapid reduction of bacteria within the first few days. While the weakest are eliminated first, there can remain a group of persistent bacteria that still survive.

Driver: The patient may feel better after a few days and not finish the full antibiotic course. But halting treatment early can leave the remaining 'strong' bacteria in the system.

Impact: As the strongest bacteria survive there is a greater risk of recurrent or severe reinfection. Resistant bacteria might not impact the patient but could spread to vulnerable groups that are prone to infection: for example, the elderly, infants or immune compromised.

The same principle can be applied to animals. If the wrong antibiotic or a weak dose is prescribed, or a full course is not taken, an environment can be created where the strongest bacteria tend to survive. While the infection can be seen as 'treated', resistant bacteria could grow and reinfect the animal, or transfer to other animals or people.

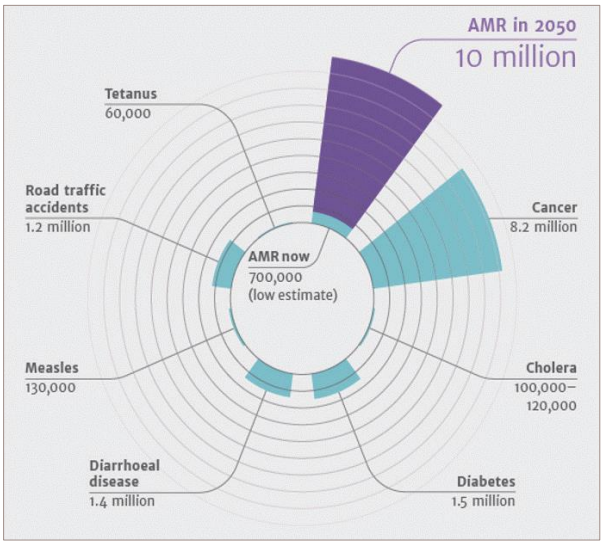
AMR as a systemic risk

Covid-19 demonstrated the scale of global disruptions that can be caused by infectious diseases. Without mitigation, AMR could reach epidemic, or even pandemic, proportions and has the potential to impact the global economy and increase sector or company-specific ESG risks.

The implications are far-reaching, not only confined to human health but extending to the resilience of food systems and development of emerging countries. The World Bank suggests the cost of AMR could reach $US100 trillion by 2050 as a result of lost productivity, decreased livestock output, reduced trade and additional healthcare expenses.[5]

The first comprehensive global AMR analysis estimated that resistance itself caused 1.27 million deaths in 2019 – more deaths than HIV/AIDS or malaria combined – and that antimicrobial resistant infections played a role in 4.95 million deaths.[6] A study commissioned by the UK Government estimated that this number could rise to 10 million people by 2050.[7]

Attributable AMR deaths in 2050 compared to other major causes of mortality[8]



As the world stands today, we are a long way off from achieving a reduction in antibiotics use. According to the research institute One Health Trust, antibiotic consumption in humans increased by 65% between 2000 and 2015.[9] Without a change in behaviour, overall antibiotic consumption would increase by 200% between 2015 and 2030.[10]

Demand for animal products could also accelerate AMR. The animal antibiotics and antimicrobials market grew 8% from $4.7 billion in 2022 to $5 billion in 2023 and is forecast to grow to almost $7 billion in 2027.[11] Consumption in animals is expected to increase by more than 10% between 2017 and 2030.[12] There are concerns that antibiotic-resistant foodborne infections, such as E Coli, could become more common and worsen severe illnesses.

Example: AMR in developing countries

The implications of AMR are relevant worldwide but likely to be more pronounced in the "Global South". Broadly speaking, developing or underdeveloped countries. A study from the World Economic Forum illustrates the downside scenarios from waterborne AMR using an example of resistant cholera affecting Bangladesh. The study found that an adverse outbreak could cause 700,000 infections and 140,000 directly attributable deaths. These numbers come from high population density, poor sanitation and water treatment systems, inadequate healthcare infrastructure and limited access to healthcare services. Supply chain impacts are also foreseeable in this circumstance, whereby production and/or distribution of key commodities such as garments and food could be disrupted.

Source: Costs and risks of AMR water pollution (WEF)

[5] Drug-Resistant Infections: A Threat to Our Economic Future | World Bank (2016)
[6] Global burden of bacterial antimicrobial resistance in 2019 | The Lancet
[7] Antimicrobial resistance review: Government response | Gov.UK (2016)
[8] Figure recreated by the New Zealand Medical Association, statistics from UNEP (2023)
[9] State of the World's Antibiotics 2021 | CDDEP (2022)
[10] Global increase and geographic convergence in antibiotic consumption between 2000 and 2015 | PNAS (2018)
[11] Animal Antibiotics and Antimicrobials Global Market Report | Research and Markets (2023)
[12] The State of the World's Antibiotics 2021 | Centre for Disease Dynamics, Economics & Policy (2021)

AMR could hinder the achievement of the Sustainable Development Goals (SDGs)

Interestingly, AMR was not mentioned in the original SDGs. Through various advocacy measures over the years, AMR has been recognised as a threat to people's health, livelihoods and the environment. In March 2020, two SDG indicators addressing AMR were introduced to bring about better AMR management and stronger surveillance systems:

- **SDG 3.d.2:** Percentage of bloodstream infections due to selected antimicrobial-resistant organisms; and
- **SDG 3.d.3:** Proportion of health facilities that have a core set of relevant essential medicines available and affordable on a sustainable basis (where antibiotics will be disaggregated from the core set of data used in the metadata).

While these indicators sit within SDG3, AMR could impact many of the other SDGs.

	AMR could cause an additional 28.3 million people to be pushed into extreme poverty by 2050 due to high treatment costs, chronic infections and inaccessible or high-cost medication.
	Animals effected by AMR impacts farmers' income, productivity and broader food security. There is a risk that current, affordable medication to treat animal disease loses efficacy.
	Reducing child and infant mortality relies on effective antibiotics. 200,000 newborns die each year from drug-resistant infections.
	AMR-related morbidity and mortality can disrupt labor supply and could cause a 1-3% decrease in economic output by 2030, a potential $US3.4 trillion loss.
	AMR is likely to disproportionately impact lower income countries, increasing treatment cost and health coverage, especially where sanitation systems are less advanced.

Source: Alphinity, UN's Antimicrobial Resistance Threatens Development Report

Key ESG considerations of AMR

AMR is a broad and complex issue. AMR is challenging to monitor and emerges across a range of environments and regions. As such, the management of AMR is not confined to one industry but requires a holistic strategy across supply chains and end markets. This is often referred to by regulators and research institutes as the 'One Health' approach that balances the interests of the planet, people and economy.

From an investment perspective however, we believe AMR can be distilled into a subset of core ESG considerations and that the materiality of a company's AMR exposure can be assessed. The following graphic aims to illustrate the various drivers of AMR, the systemic risks and the different industry-level considerations as we understand them.

We anticipate that the highest AMR exposures sit within **pharmaceuticals** (animals and human), **food production** and **food retail**. This conclusion is based on preliminary research and a materiality matrix that accounts for:

- **Maturity** - level of AMR knowledge or understanding; and
- **Influence** - degree of control to manage AMR.

The subsequent sections in the report explore the specific threats and opportunities for companies in these industries, questions to guide engagement and examples of good management.

ESG considerations: External system-wide considerations and industry exposure

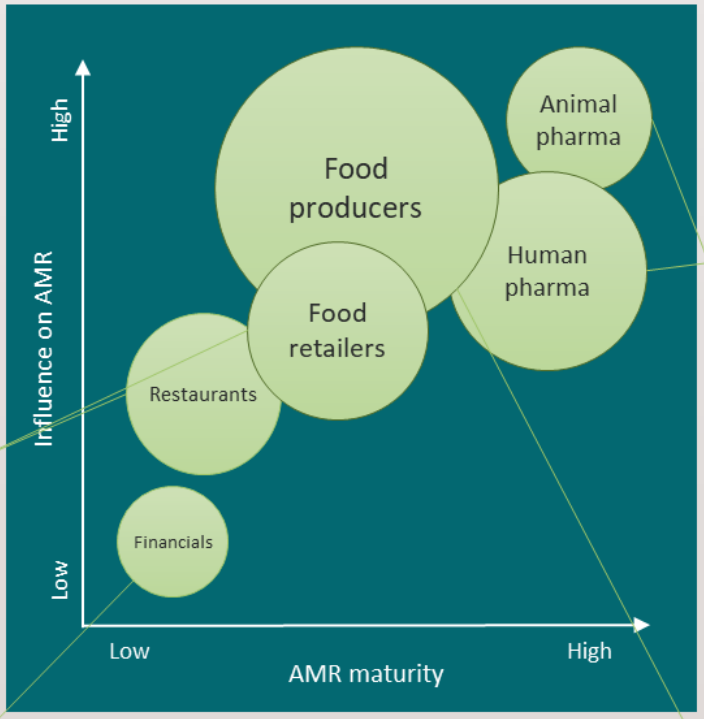
DRIVERS

- Discharge of waste and water from healthcare and agriculture
- Misuse and over prescription of antibiotics* in human health and animal agriculture
- Insufficient research & development (R&D) into new, effective antimicrobials or alternatives
- Lack of AMR regulation, surveillance and stewardship

SYSTEMIC RISKS

Antimicrobials lose efficacy	Disease severity and incidence	Food security	Supply chain stability
Increasing health burden on society and impacting the success of medical procedures and treatments	Severe infections are harder to treat and transmissible between humans, animals and the natural environment	Resistant disease in animals disrupt farming production and elevates food safety risks	Resistant disease outbreaks in emerging markets disrupt production and supply chains

KEY INDUSTRY CONSIDERATIONS



Food retailers & restaurants
Product quality, regulatory and reputational risks from resistant disease in the supply chain; Procurement and cost implications from food producers managing hard-to-treat disease, or animal farming changes to tightening regulation.

Animal and human pharmaceuticals
Impacts on the effectiveness of medicine and R&D spend; Changing regulation and awareness could affect downstream demand for antimicrobials, or requirements for stronger oversight and training to support responsible prescription and application.

Financials
Banks and insurers are exposed to the agricultural and health sectors and may be exposed to AMR risks. Health insurers could face customer challenges with a rise in hard-to-treat diseases.

Food producers
Resistant diseases and decreased availability of effective medicine impacts animal protein production; Emphasis on safety & quality systems to manage diseases; Growing regulation and awareness changes antimicrobial use practices, impacting farming conditions and output.

*Antibiotics are the focus given their importance in treatment, scale of use and accordingly, rising rates of antibiotic resistant bacteria. Comparable systemic risks, industry considerations and company questions are relevant to other antimicrobials (antiparasitics, antivirals, antifungals), but generally to a lesser degree.

Industry and company-specific considerations

AMR is a universal issue that has the potential to impact many sectors and companies around the world. Relevance from an investment perspective, however, is more material to some sectors than others. We have summarised the internal business considerations related to AMR for three key industries: **Pharmaceuticals** (humans and animal), **Food Production**, **Food Retail**. As highlighted in the materiality matrix, we consider companies in these industries to have the highest overall exposure to AMR and the greatest influence in mitigating AMR impacts. AMR risks identified in the table could be a threat and/or an opportunity, subject to company management of the issue.

Materiality	Internal business considerations*
Pharmaceuticals - [H] Human, [A] Animal	
Maturity: High Advanced knowledge of AMR and the current state, and impacts, of resistant disease and regulation. **Influence: Medium-High** Reasonable degree of influence through oversight and training around antibiotic prescription, overseeing counterfeit production, investing in new drug research, and developing alternative treatments.	**Risks** • **[H/A]** Increased R&D requirements into new antibiotic development • **[H/A]** Decreased revenue as available antibiotic treatment become less effective • **[H/A]** AMR awareness and a shift towards prevention/alternative treatments decrease antibiotic demand • **[H/A]** Regulatory focus and surveillance systems presents liability for irresponsible manufacture, or insufficient downstream oversight and training • **[H]** Stronger government initiatives to reduce human antibiotic use • **[A]** Increasing regulatory restrictions on agricultural antibiotic use **Opportunity** Increased demand for new lines of non-antimicrobial business: • **[H]** For example, preventative supplements, early intervention through disease diagnostics, vaccines • **[A]** For example, preventative supplements, disease diagnostics, vaccines, genetic profiling to improve healthier food-animals
Food production	
Maturity: Medium Moderate knowledge of AMR and the possible impacts of resistant disease, or regulation, on farming practices and productivity. **Influence: High** Strong degree of influence by decreasing antibiotic use in animal agriculture and improving farming conditions to reduce disease prevalence.	**Risks** • Decreased effectiveness of medicine for animal treatment impacts food-animal volume, and limits the availability of cost-effective treatment • Increased frequency and severity of disease disrupts food-animal volume and impacts food quality requirements • Tightening regulation restricts antibiotics in preventative treatment and growth promotion, requiring operational changes and investments to prevent (for example, less crowding, more hygienic farming conditions, stronger focus on animal welfare) in turn impacting production volume **Opportunity** Renewed focus on preventing disease and improving animal welfare practices decreases risks of hard-to-treat disease outbreaks, strengthens reputation and resilience to changing regulation.
Food retail	
Maturity: Low Outside of food quality risk management, responsibility for AMR risk management in the supply chain is less advanced. **Influence: Medium** Moderate degree of influence to encourage AMR management practices in the supply chain.	**Risks** • Procurement and cost implications from food producers managing hard-to-treat disease, or animal farming changes due to tightening regulation • Food safety is impacted by resistant disease in the supply chain, resulting in operational, reputational and regulatory risks **Opportunity** The extent of impact is lower than food producers. However, advocating for stronger AMR management along the supply chain indirectly supports a secure and resilient food system and also mitigates the systemic risks posed by AMR.

Managing AMR risks

Importantly, managing inappropriate and unnecessary use of antimicrobials is critical to slow the progression of AMR over the longer term. Expanding research and development into new antimicrobial medicines, vaccines and diagnostic tools to prevent disease will combat rising rates of resistant disease. Infection control and prevention, and clean water and sanitation reduce the need for antibiotics. Industry bodies have also called for stronger oversight to prevent counterfeit antimicrobial production and antimicrobials sales on the informal market.

These interventions are well recognised but data collection would also enhance risk monitoring and attribution of AMR to its sources. As AMR regulation and awareness grows, this could potentially create liabilities for irresponsible antimicrobial users and manufacturers.

As investors, we believe that healthcare and food companies are exposed to the most significant risks, and equally, can influence the system-wide impacts of AMR. In order to stay informed, we have collaborated with FAIRR to expand our knowledge in these industries. Alphinity joined FAIRR in 2021 and is taking part in two collaborative engagements with Global companies (Zoetis Inc and McDonald's Corp) aimed at addressing AMR-related concerns.

Given that corporate disclosures on AMR tend to be limited, we believe dialogue with investee companies is likely to be a valuable tool to better understand this risk and promote better management of the issue. As such, we have outlined example of what we see as good management of the issue, and questions to help guide company engagement below.

Healthcare

Expanding into non-antimicrobial alternatives, vaccines and diagnostic tools to prevent disease will combat rising rates of resistant disease. For example, **Zoetis Inc** is a global animal health company taking an active role in advancing alternatives to antimicrobials. The company's antibiotic revenues have decreased over recent years and replaced with alternative products. The company is a strong proponent of veterinary oversight and responsible application of antibiotics and is monitoring its outstanding antimicrobial portfolio.

Pharmaceutical manufacturers can support stewardship by investing in R&D into new treatments to compensate for any loss of effective antimicrobials. Rates of resistance can be slowed by advocating for the responsible prescription and application of antibiotics, supported by physician and veterinary training. This is especially important in developing countries where there is weaker AMR regulation, awareness and problems around counterfeit antimicrobials.

Healthcare companies have a role in preventing active pharmaceutical ingredients being released into wastewater, and manage this in outsourced manufacturing also.

Questions for pharmaceuticals

- Is there an AMR strategy in place?
- What is current revenue from antibiotics, how has this changed recently and what is the trajectory?
- Have the potential impacts of AMR to the business been assessed?
- Has there been a change in R&D expenditure to compensate for potential AMR? Is there a chance this needs to increase in the future?
- How is the product portfolio shifting towards non-antimicrobial alternatives?
- What kind of downstream, AMR training and stewardship strategy is made available?

Food production and retail

Managing antimicrobial use in animal agriculture is an important focus area from regulators and industry bodies. Disease can be prevented through better animal welfare practices, hygiene and sanitation systems and breeding of healthier animals. Regulators banning antibiotic growth promotion was an early step in some regions. Other regions may follow Europe's lead and restrict antibiotics being used for preventative purposes, and more responsibly in human health.

Questions for food producers

- What metrics does management follow to measure progress in the AMR strategy?
- How has the use of antibiotics been trending over time?
- Has the prevalence of resistant disease in operations been assessed? How has this changed?
- Is there a policy position on responsible antibiotic use?

Food retail exposure to AMR is contingent on the management of the issue in the supply chain. However, retailers can promote AMR management in their own supply chains by demanding producers restrict antibiotics for use in growth promotion and setting expectations around prudent antibiotic use for treatment rather than prevention. For example, **Woolworths** has clearly set out its position on antibiotics for use in free range chicken, beef and seafood in its Animal Welfare Policy.

Questions for food retailers and restaurants

- What measures are in place to support AMR management in the supply chain?
- Is there a supplier engagement program to manage AMR for key animal protein suppliers?
- Have the impacts of AMR been assessed as a risk to the business?

Summary

There is growing awareness of the impacts of AMR to economies, people and planet. To date, the benefits of antimicrobials have far outweighed the system level costs. However, increasing antibiotic use and growing rates of disease resistance could tilt this balance in the wrong direction over time.

This report outlines the systemic risks posed by AMR and the related business threats and opportunities for the healthcare and food industries. Companies outside of these key industries could also hold a level of exposure due to the systemic nature of AMR. The implications of AMR span restaurants, banks, insurers and healthcare providers (as examples).

We have identified two primary mechanisms by which AMR risks can be addressed. Firstly, by reducing antimicrobial use and promoting responsible application and oversight will decrease the drivers of AMR. Secondly, by investment in research into new antimicrobials and a focus on alternatives and prevention will help to mitigate its impacts.

As stronger regulations emerge and the financial impacts of AMR on investee companies become more pronounced, we anticipate that industry engagements on AMR will become more targeted and sophisticated. Improving investor knowledge will enable detailed, and therefore more credible, dialogue with companies going forward. With this in mind, we hope that investors consider engaging with companies using the risk assessment and questions outlined as guidance.

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