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Proposals for a Novel UK Antimicrobial Subscription Model: The Investor Perspective

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Matthias Hofer
Grace Hampson

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Matthias Hofer
Office of Health Economics, London

Grace Hampson
Office of Health Economics, London

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Corresponding Author:
Grace Hampson
ghampson@ohe.org

OFFICE OF HEALTH ECONOMICS
CONTRACT RESEARCH

For further information please contact:

Professor Graham Cookson
Chief Executive, OHE
Honorary Visiting Professor in Economics at City, University of London

Tel +44 (0)207 747 1408
Email gcookson@ohe.org

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Executive Summary

Antibiotics are essential for modern medicine, but antimicrobial resistance (AMR) is reducing their effectiveness, causing thousands of deaths annually. New antibiotics are urgently needed, but their development is hindered by a market failure largely due to limited sales and competition from cheaper generics. A 'volume-delinked model' subscription approach has been suggested to overcome this market failure, providing compensation regardless of sales volume.

The UK is the first country in the world to publish proposals for a subscription model to stimulate investment in the research and development of novel antibiotics. The proposals were under consultation between July-October 2023. The proposed scheme involves annual invitations for novel antibiotic tenders. A two-step process is proposed that first assesses eligibility based on pathogen targeting, environmental compliance, financial standing, and social value commitment. Once eligibility is established, the value of antimicrobials will be assessed across 17 criteria to calculate a score. Based on their score, they may be placed into one of four payment bands, representing volume-delinked payments to the manufacturer of £5M to £20M per year from England. The subscription contract spans 3 years in the first instance, and may extendable up to 15 years or patent expiry, whichever is sooner.

This report examines the likely success of the proposed pull incentive for antibiotic development by seeking the perspectives of (potential) investors in the antibiotics space. Investors are key stakeholders in the development of new antibiotics, as their buy-in is critical to unlock the required funds and expertise for the development of novel antibiotics. Nine interviews were conducted, involving financial investors, and biopharma executives. Among the financial investors, we distinguished between institutional financial investors and mission-led investors; the latter having a clear societal goal or mission for their investment decisions.

The interviews have provided valuable insights into investor views on the subscription model and its potential impact on antibiotic R&D investment.

The key insights from the interviews were as follows:

- All investors agreed that the UK proposals are hugely significant. They are novel, the first of their kind, and will send signals to other key countries regarding the importance of such a scheme and how it can be actioned.
- Pull incentives are considered to be a key mechanism for incentivising the development of novel antibiotics by mission-led investors and biopharma executives. Institutional investors are less likely to take public policy, including but not restricted to pull incentives, into account in investment decision making.
- Some elements of the eligibility criteria may be a barrier to participation, particularly for smaller companies, thereby undermining the pull incentive.
- The upper bands (£15m, £20m) are deemed sufficient to be effective as England's proportion of a global pull incentive, but the lower bands (£5m, £10m) are not.
- The scheme as proposed is not sufficiently predictable to support investment. This is due to the existence of multiple value bands, a scoring system which is likely to change over time (therefore representing a moving target), uncertainty over contract length, the option to unilaterally cancel contracts, and/or the potential for abolition of the incentive scheme part

way through development. Clearer signposting for investors over what they can expect to receive is required.

- While the UK effort in isolation will not represent an effective pull incentive, combined action from the EU and the USA would be expected to provide a sufficient minimum pull incentive.
- Substantial harmonisation on the target products supported across schemes will be required for global sums to add up to a sufficient incentive.
- A combination of different types of incentive would generate the most powerful stimulus for investment.

Based on these insights, we provide suggestions for strengthening the UK proposals from an investor perspective. Key suggestions include:

- **Consider whether the initial contract length could be extended beyond 3 years.** Investors would prefer a 10-year term but accepted that five years may be a reasonable compromise.
- **Provide clarity and potentially higher flexibility in the application of eligibility criteria,** particularly around financial standing, environmental and societal commitments for smaller companies.
- **Implement a transparent collaborative process for the review of scoring criteria and contract conditions over time.** Changes should be made gradually, with adequate warning to allow investors and innovators adapt. Major changes should be consulted upon with external stakeholders.
- **Clarify the long-term commitment to the scheme.** Investors require assurance that the scheme will still be in action at the time of market entry. As investments are made early in the development process, investors will require a long-term commitment to the scheme (or a similar replacement).
- **Share best practices and encourage the development of streamlined and harmonised subscription systems internationally.** The UK scheme will not be sufficient on its own.

Given the key role investors (could) play in the development of novel antimicrobials, we believe these suggestions will i) support the proposed UK scheme in achieving its aim of stimulating investment in novel antibiotics and ii) provide useful learnings for establishing effective pull incentives in other jurisdictions.

1. Introduction

Antibiotics, a sub-group of all antimicrobials, are fundamental for modern medicine. Antimicrobial resistance (AMR) is characterised by bacteria developing resistance to existing antibiotics, reducing the ability of these antibiotics to treat infections. AMR is a significant problem in Europe, with an estimated 670,000 infections and 33,000 deaths a year due to resistant bacteria (European Centre for Disease Prevention and Control and WHO Regional Office for Europe, 2022), and globally, with an estimated 1.27 million premature deaths in 2019 (Antimicrobial Resistance Collaborators, 2022).

There is an urgent need for novel antibiotics, but the current pipeline has been described as underdeveloped in terms of novelty of product and target pathogen(s), resulting in few promising antibiotics in late-stage development (Wellcome Trust, 2020; Butler et al., 2022).

The main reasons for this under development are: i) persistent market failure caused by higher failure rate of antibiotic development due to clinical safety concerns, ii) limitations of sales in line with antimicrobial stewardship practices, iii) short treatment durations, iv) high competition from existing, often cheaper and generic antibiotics, and v) lack of adequate HTA methodologies to capture their full value (Prasad et al., 2022; Leonard et al., 2023). As a result, many large pharmaceutical companies have left the antibiotics space while smaller players have gone bankrupt (Årdal et al., 2020).

Policy solutions for this market failure have been proposed in the form of both push and pull incentives. Push incentives are usually public or philanthropic funds that provide upfront funding for research and development (R&D). In contrast, pull incentives represent rewards for products at the time of market entry (Dutescu and Hillier, 2021). For AMR, a 'volume-delinked' pull incentive has been proposed that would take the form of a subscription, allowing products to be compensated independent of the volume of sales (Rex and Outterson, 2016).

For a successful subscription model, health economists have highlighted that the aggregated global monetary reward must be sufficient to attract research and development investment in antibacterial drug development, while delivering value for money, with rewards being targeted at the type of new antibiotic needed. Such a system should also be predictable and sustainable, with consistency of the reward and rules over time, as well as consistency of eligibility and reward criteria across jurisdictions (Rex and Outterson, 2016; Outterson, 2021; Brassel et al., 2023; Hampson, Steuten and Towse, 2023).

1.1. The UK proposals under consultation

In England, the NICE-NHS England Antimicrobial Resistance (AMR) Pilot (NICE, 2023) tested the application of this type of pull incentive for two antibiotics, with the maximum subscription payment capped at £10M/year. The funding arrangements under the pilot commenced in July 2022 and will last for three years, with the option of extending up to 10 years (Leonard et al., 2023).

NHS England have now initiated a public consultation (open July-October 2023) on new UK-wide proposals for a more long-term follow-up scheme (NHS England, 2023). Under the scheme, an invitation to tender for novel antibiotics will be issued approximately once a year. All products receiving a marketing authorisation in the period since the previous tender will be able to apply, as will products with a high probability of receiving a marketing authorisation within 12 months.

In a first step, eligibility for the scheme will be assessed in an "administrative" procedure according to set criteria, with the eligibility criteria reviewed every 12 months. The criteria are detailed in Table 1. The population(s) to be included within the scope of the award may also be defined at this stage.

TABLE 1: ELIGIBILITY CRITERIA FOR UK PROPOSALS UNDER CONSULTATION

Target pathogens	Products must be active against pathogens on the WHO Priority List
Agreement with contract terms on surety of supply, antimicrobial stewardship, and performance	Agreement to surety of supply, antimicrobial stewardship (including sales and promotional activities), key performance measures and payment terms
Environmental Standards	Companies must demonstrate compliance with specified antibiotic manufacturing standards
Economic and Financial Standing	Companies must demonstrate they have a sufficient economic and financial standing to justify award of the proposed contract
Probity	Companies must demonstrate they do not trigger any of the requirements that would make them ineligible to be awarded a public contract
Social Value	Companies must demonstrate their commitment to specified social value requirement, e.g. achieving net zero emissions

Adapted from NHS England (2023)

In a second step, eligible antimicrobials will be assessed in terms of value across 17 criteria that cover aspects of clinical effectiveness, global and national needs, pharmacological benefits, and health system benefits. Each criterion is associated with scores and a weight that will aid the evaluation of total value. A proposed product can achieve a total value score between 0 and 100 (further details of the scoring system are provided in the Appendix). Assuming a minimum score (50%) is achieved, the scoring system will be used to categorise the new antimicrobial into one of four bands. Each band corresponds to a payment value. For England, the values are: £5 million, £10 million, £15 million, or £20 million per year respectively (Figure 1). NHS England and the devolved governments, at their discretion, will offer a contract in the relevant value band. If the minimum score is not achieved, the new antimicrobial will not qualify for the incentive.

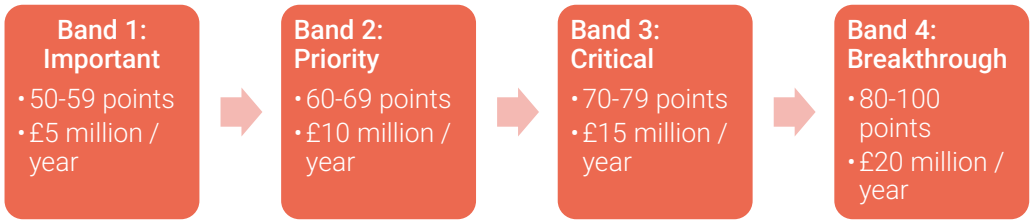

FIGURE 1: PROPOSED VALUE BANDS FOR ENGLAND
Adapted from NHS England (2023)

The proposed subscription contract is for an initial three-year period and is extendable to cover the patent exclusivity period of the product (to a maximum of 15 years). The product could be moved between value bands over time if the value of the product to the NHS changes, and the NHS reserve the right to cancel the contract if it is determined that the product no longer warrants a subscription contract. The contract will include key performance indicators on surety of supply.

1.2. This report

While the global policy community has highlighted the potential benefits of a subscription style payment mechanism that is delinked from sales, the mechanism is so far largely untested. It remains unclear if the proposed mechanism will be effective in attracting private investment into the R&D and marketing of novel antibiotics.

Investors are a key stakeholder in the development of new antibiotics, as their buy-in is critical to unlock the required funds and expertise for the development of novel antibiotics. Investors' perceptions of any such pull incentive are therefore a critical indication of its likelihood of success. The aim of this report is therefore to seek the perspective of investors on the proposed UK subscription model.

We conducted nine interviews across three types of investors:

1. **Institutional financial investors (n=2):** major collectors of savings and suppliers of funds to financial markets including investment funds, insurance companies and pension funds (OECD, 2020).
2. **Mission-led investors (n=4):** institutional investors with a clear societal goal or mission for investment decisions.
3. **Biopharma executives and decision makers (n=3):** Biopharma industry representatives that make decisions about R&D spending, pipeline or asset acquisition/licensing.

Interviews were semi-structured and contained a mixture of closed and open-ended questions that allowed the participants to express their opinions on the current investment environment, the UK proposals, and the wider international policy context. Interviewees were spread across USA, Europe and the UK, but they all shared a global perspective on investment (see appendix for the geographical breakdown). All interviews were undertaken in July and August 2023.

Through the interviews we identified areas of clear consensus and areas of diverging opinion. In this report we set out the themes that emerged from the interviews, alongside individual insights of key relevance to the consultation.

2. Investor insights

This chapter details the results of the interviews across three areas: the interviewees' experience and awareness of AMR and related policies, their perceptions of the implications of the UK proposals, and reflections on what the UK proposals mean in a global context.

2.1. Experience, awareness and interest

Key insight: Pull incentives are considered to be a key mechanism for incentivising the development of novel antibiotics by mission-led investors and biopharma executives. Institutional investors are less likely to take (unestablished) public policy into account in investment decision making.

All nine investors were in roles where they had influence on investment decision making. They all had previous exposure to AMR investments, however we generally found more experience of AMR investments in the mission-led investor and biopharma leadership sub-groups.

All investors agreed that that from a public health perspective, antimicrobials are of high priority and there should be initiatives to promote, value and pay for novel antimicrobials. They confirmed that there has been a broken value chain for antimicrobial pharmaceuticals over the long term, which has been characterised by little R&D activity into novel antibiotics, shortage of talent and skill, absence of entrepreneurial activity, and lack of sustainable financing solutions. As a result, there was little activity across all investor groups in terms of de novo investments.

All biopharma decision makers and mission-led investors were aware of the public policy agenda of the UK and of the consultation. This was in contrast to the institutional investors who were not following the policy agenda (Figure 2).

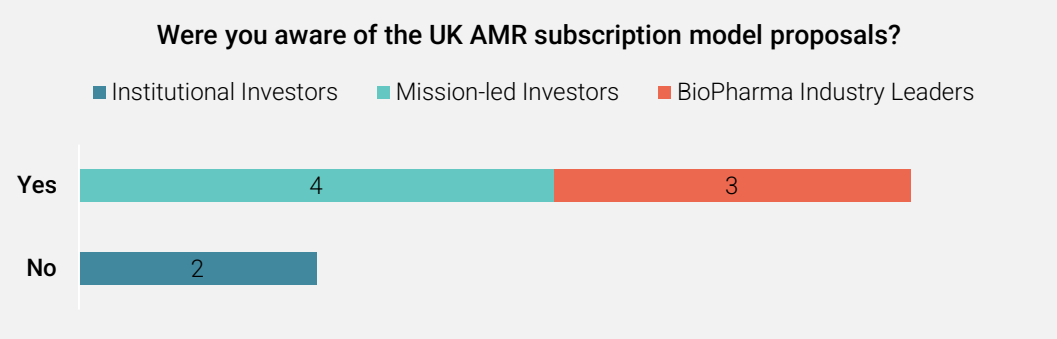

FIGURE 2: AWARENESS OF THE UK AMR SUBSCRIPTION MODEL PROPOSALS

The majority of mission-led investors and biopharma leaders believe in the power of public policy and take it into account for investment decision making (Figure 3). Specifically with regard to pull incentives, mission-led investors pointed out the benefit of the pull system is that it allows governments or healthcare systems to incentivise novel antibiotics whilst only paying for success, without taking development risks.

In contrast, the two institutional investors were generally less influenced by public policy in general and reported that they would not routinely take pull incentives into account when taking investment

decisions. This is partly as they are more opportunistic in nature, and partly due to the nature of a market-based pull incentive and the limited window of opportunity in which they have to realise their return on investment. Typically, investors are required to deliver a return within ten years, but payback via the proposed revenue guarantee would fall outside of this time horizon. Any benefits to the investor would therefore be 'indirect' via an effect on their exit strategy[1] (e.g. the 'exit' (sale price) would include consideration of future revenue). This is less appealing to investors than direct rewards. There are potential solutions that might help mitigate this issue, including front-loading the revenue guarantee early over the contract length, or via milestone payments, which would be payable at earlier phases in the products lifecycle (prior to product launch).

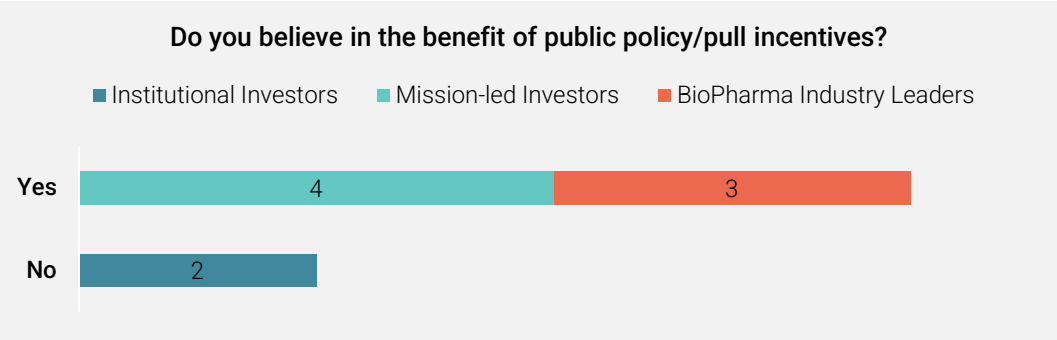

FIGURE 3: INVESTOR PERSPECTIVE ON PUBLIC POLICY/ PULL INCENTIVES IN AMR

2.2. The UK proposals

Eligibility criteria and contractual requirements

Key insight: Some elements of the eligibility criteria may be a barrier to participation, particularly for smaller companies, thereby undermining the pull incentive.

All investors expressed concerns that the criteria on economic standing might not be achievable for smaller companies, especially when considering potential applications from companies before the generation of revenue. Furthermore, environmental standards and net zero emissions are also hard to achieve for the smaller companies, particularly when manufacturing and packing is outsourced and not under direct control of the applicant. Even when a commitment to net zero emissions can be made, this would be associated with additional costs that would diminish the return of investment through the guaranteed revenue model.

While investors acknowledged that it makes sense to demand surety of supply, there was concern that over time this is difficult to predict and prepare in terms of supply and manufacturing chains. For the pull incentive to be effective, investors require assurances on this aspect.

One biopharma leader commented that a commitment to supply is an insufficient condition, as quick (i.e. overnight) access to products may be required. They suggested this condition should be amended to include consideration of the envisaged demand for stockpiling and renewal of stock over the contract length.

[1] *The exit is how the investor realises their return on investment. In this type of scenario exit would usually be via acquisition (often by big Pharma) or less frequently via initial public offering (IPO).*

Finally, one biopharma executive argued that the application and assessment for the scheme should not be subject to fees for the applicant, as this may prelude some smaller firms from entering into the scheme.

Monetary value

Key insights:

- **The upper bands (£15m, £20m) are sufficient to be effective as England's proportion of a global pull incentive, but the lower bands (£5m, £10m) are not.**
- **Payment values should be based on smaller bands or a linear scale, rather than the points scored at the bottom of the band. The 'rounding down' as currently proposed will lead to systematic undervaluation of the products included.**

When asked about the monetary values offered via the UK proposals, many of the interviewees referenced the global estimates of the amount required for a cost-based pull incentive as calculated by Outterson (Outterson, 2021)[2]. There were mixed opinions about the size of the published estimate ($4.2bn), as some thought it was too high and others thought it was too low.

Nevertheless, two thirds of the interviewees (see Figure 4) believed that the monetary values that are currently proposed for NHS-England are overall sufficient, i.e. they approximately represent England's fair share[3] for monetary contribution to a global subscription model, at least when considering the £15m and £20m value bands. This was particularly the case for mission-led investors and biopharma decision makers.

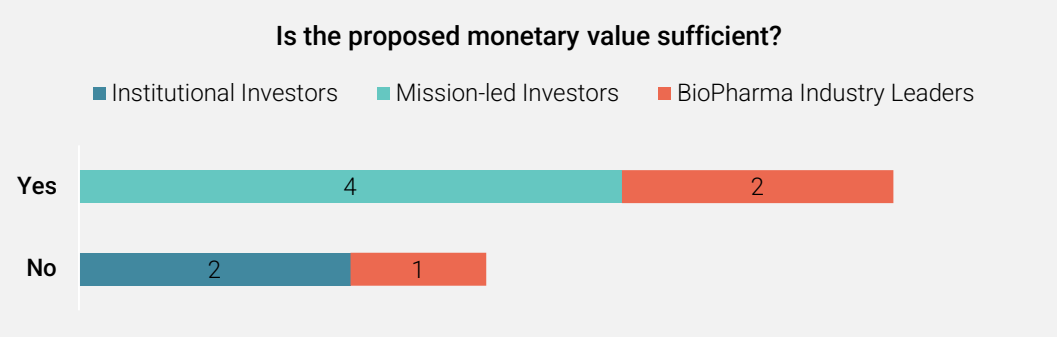

FIGURE 4: INVESTOR PERSPECTIVE ON THE PROPOSED MONETARY VALUE

While the majority believed that the higher value bands would be overall in line with England's fair share, they expressed concern that the lower bands would be insufficient to draw investment in antibiotics. This is because the lower bands would not deliver a substantial return on investment for investors, nor incentivise new investment into novel innovation for biopharma companies. The lower bands may however be sufficient to stimulate companies to supply to the UK, which is a decision made much later in the lifecycle of the product than any investment decision.

Institutional investors feared that the proposed revenue guarantee, even if combined with other global incentives providing their fair share, would not provide a return on their investment plus

[2] For a fully delinked subscription model, the estimate is $4.2 billion over 10 years globally (Outterson, 2021).
[3] Assuming a country's fair share towards such an incentive should be based on its relative wealth and, therefore, its ability to pay (as proxied by its gross domestic product, GDP), the UK's fair should be around £12million per year for ten years. This is based on the assumption that all G20 countries (and remaining EU countries) also contribute to the global incentive. If only the G7 countries contribute, the UK's fair share would be £23M/year for ten years (Brassel et al., 2023).

sufficient 'upside' to make the investment worthwhile. This is partly due to the indirect nature of a market-based incentive on an institutional investor's return on investment. Higher contract values would provide a stronger (albeit still indirect) incentive.

Whilst most investors were not concerned with the details of the proposals, one mission-led investor expressed concern regarding how the monetary values of the bands were determined. Our understanding is that they have been extrapolated from the pilots, with points from the scoring system somehow mapped to quality adjusted life years (QALYs). Further detail on how this mapping has been conducted is required to allow critique.

Investors highlighted that the scheme must allow for the value of the bands to increase over time to allow for increasing costs of development (i.e., with inflation) and the expected higher need for novel antibiotics. Whilst the bands are intended to represent value rather than cost, they will not be effective if they (on aggregate) are lower than development costs.

Furthermore, it was pointed out that the embedded option to unilaterally change criteria and value bands over time creates substantial uncertainty for investors and biopharma companies. Investors require more clarity around the intentions and commitments for the scheme in the long-run if the proposed subscription model is to be effective.

Predictability and sustainability

Key insight: The scheme as proposed is not sufficiently predictable to support investment. This is due to the existence of multiple value bands, a scoring system which is likely to change over time (therefore representing a moving target), uncertainty over contract length, and/or the potential for abolition of the scheme part way through development. Clearer signposting for investors over what they can expect to receive is required.

Investors are used to handling uncertainty, however, many reported that the proposed scheme is not sufficiently predictable to support investment. Uncertainty and predictability were discussed over multiple dimensions, as set out below.

Multiple bands and time of value assessment: Some investors stated that they are used to taking risks and therefore feel sufficiently comfortable not knowing which of the multiple bands will be applicable to their antibiotic. This would not be a barrier to their investment. Moreover, mission-led investors were more likely to actively support the use of multiple value bands to tailor the reward to the value offered by the new product. Specifically, they believe that greater levels of novelty and innovation should receive a higher revenue guarantee compared to adapting existing antimicrobials.

However, other investors believed that not knowing which of the multiple bands will be applicable to their product will stifle investment. The latter group suggested they would be more likely to invest if the system allowed the value to be evaluated and designated at an early stage in development with a guaranteed amount awarded upon approval (a form of advanced market commitment). Alternatively, they suggested the tendering of target product profiles with an associated monetary value. This would allow for predictability in early development and guaranteed returns when the target product profile is fulfilled.

Changes to the scoring or contract conditions (i.e. change in value band or cancellation): All investors agreed that there should be little change to the contract, with fair warning and engagement with the industry partner in case any changes to the contract are foreseen. Changes move the goalposts, thereby undermining the incentive.

Contract length: All investors agreed that the three-year contract duration is shorter than desirable. There was consensus that a 10-year incentive would be much more powerful in drawing investment

in this space, but many of the interviewees also accepted that this may be unrealistic in practice. Indeed, more typical products (non-antibiotics) face competition and other factors that affect their markets post-launch, so some level of uncertainty is normal. The challenge with the current proposals is that the UK's fair share is calculated based on the assumption that the payment will be made for 10 years, thus if the payment is not made for the full 10 years, the UK is not paying enough to cover their fair share and this undermines the pull incentive. Investors commented that a minimum of five years may represent a reasonable compromise.

Longevity of the scheme: All investors stated they would require a long-term commitment to the scheme (or something similar) in order for it to influence investment decisions. At the point of investment, there must be a commitment that the scheme (or a similar scheme) will be in place upon market entry, otherwise it cannot be factored into investment decision making.

2.3. International efforts

Key insights:

- **The UK effort in isolation will not represent an effective pull incentive. Action from the EU and the USA is also required at minimum.**
- **Substantial harmonisation across schemes (particularly in eligibility criteria) will be required for global sums to add up to a sufficient incentive.**

All investors agreed that the UK proposals are hugely significant. They are novel, the first of their kind, and will send signals to other key countries regarding the importance of such a scheme and how it can be actioned.

However, investors also agreed that a subscription model in the UK in isolation is insufficient to be a pull incentive for investment into novel antimicrobials. Most investors believed that similar subscription models across the EU nations and most importantly the USA would be the minimum pull factor. The EU should commit to a similar subscription-based scheme, rather than transferable data exclusivity vouchers as has been proposed[4]. Most investors also stressed the importance of the implementation of the US PASTEUR ACT[5] as significant additional value and as a strong signal for the global incentive to gain momentum. A smaller number of investors felt that a wide range of G7 and G20 countries would need to commit in order to create a critical mass and pull for novel antimicrobials (Figure 5).

[4] In the EU, the European Commission has recently proposed transferable (data) exclusivity vouchers (TEVs) as part of its major revision to Pharmaceutical Legislation (European Commission, 2023b). The TEVs will grant an additional year of regulatory data protection to the developer of the priority antimicrobial, which the developer can either use for any product in their own product portfolio or sell it to another marketing authorisation holder. Furthermore, the European Commission has started the discussion for a complementary EU multi-country pull incentive scheme in the longer term to further stimulate the pipeline for antibiotics, including the possibility of a revenue guarantee amongst other options (European Commission, 2023a).

[5] In the USA, the PASTEUR ACT, which was originally introduced in 2021 and reintroduced in Congress in 2023, also aims to stablish a delinked subscription program. If passed, medicines would be assessed within 5 years after FDA approval, with contracts ranging from $750 million to $3 billion over a period of up to 10 or through the length of patent exclusivity (Michael Bennet, 2021, 2023b; a).

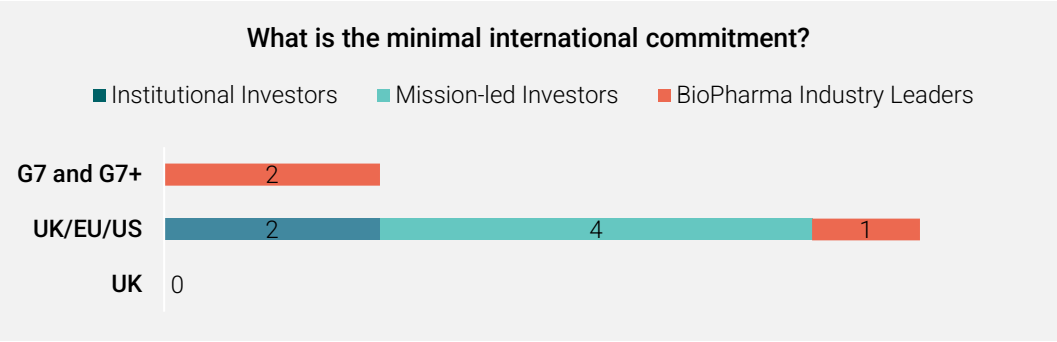

FIGURE 5: INVESTOR PERSPECTIVE ON INTERNATIONAL COMMITMENT

With regard to the transferrable data exclusivity vouchers, one mission-led investor suggested the vouchers may provide a quicker monetisation of investment at time of marketing authorisation as compared to a subscription model.[4] They also acknowledged though that these schemes are difficult predict or value, especially in UK and Europe where there are no experiences with this type of incentive. This lack of predictability is a disincentive for investors.

When it comes to global implementation, there would need to be a substantial level of harmonisation across the different models for the global sums to add up for investors. Investors accepted that the level of harmonisation would be unlikely to be complete, as is the case with other medicines (non-antibiotics). It is, however, important that the level of harmonisation is sufficient to allow global sums to add up to the minimum required for an effective pull incentive. In practice, harmonisation may be most critical in the eligibility criteria for a scheme, as this will determine whether a pull incentive will be applicable, as opposed to any scoring or valuation which may determine the size.

It is also a requirement that all countries that opt in pay at least their 'fair share' (calculated based on GDP), even though this might be complicated to assess.

Finally, investors believed that there should be a more harmonised regulatory framework and roadmap for antibiotics. This would help to create a single evidentiary standard and to substantially reduce administrative costs and uncertainty. For example, there should be agreement amongst regulators and payers if non-inferiority trials or superiority trials should be considered for the demonstration of value.

2.4. Alternative or additional policy options

Key insight: A combination of different types of incentive would generate the most powerful stimulus for investment.

The investors also discussed alternative or additional policy initiatives. Most investors welcomed a combination of incentives to generate a more powerful stimulus for investment.

Push incentives: Investors pointed out that push incentives must be used in combination with proposed pull incentives to bridge from R&D phase to marketing phase.

Transferrable exclusivity vouchers: See section 2.3.

Regulatory harmonisation roadmap: See section 2.3.

Orphan policy initiatives: Some investors suggested that incentives used for orphan drugs (such as more flexible evidence requirements for regulatory and health technology assessment and acceptance of higher prices) could be used for the stimulation of antibiotic development and the creation of a more functional antibiotic market that can generate higher process and returns.

Milestone payments: Some investors highlighted that milestone payments could provide a more direct ways of return of investment at earlier time of development. See section 0.

Acceptance of higher prices for novel antibiotics: Many investors stressed that the reason for a failed antibiotics market is over-reliance of the health system on cheap antibiotics that can drive resistance without the willingness or opportunity to procure novel antibiotics with higher prices. Often, antibiotics are bundled for procurement and novel antibiotics will not make it into the formulary amid high prices that are not compatible with hospital economics. Investors argued for reform of procurement practices and for higher prices to be accepted by healthcare systems, independent of the introduction of the delinked revenue guarantee.

Tendering of target product profiles: Many investors expressed their preference for a system that would tender detailed target product profiles with an associated value. This would allow for predictability in early development and guaranteed rewards when the target product profile is fulfilled. This would serve as an alternative to the proposed scoring system but would retain the pull incentive mechanism (the delinked revenue guarantee).

3. Summary and way forwards

3.1. Summary

To summarise, we found that most investors (7/9) were generally optimistic that a pull incentive could be a useful policy tool if it provides a sufficient monetary incentive globally (which will require high levels of consistency on eligibility and award/scoring criteria between jurisdictions) and is sufficiently predictable for investors and innovators.

We present a SWOT analysis in Table 2 to summarise the key insights and themes on the UK proposals from the perspective of investors. The analysis highlights that key strengths and opportunities of the UK proposal are considered to be its novelty and the signal it will send internationally. However, the scheme as proposed (either on its own or if replicated internationally) may still be insufficient to stimulate investment in antibiotics. Key challenges are the monetary values of the lower bands, and the lack of predictability across several dimensions, both of which are a strong deterrent for potential investors in the antibiotics space. Moreover, the UK incentive will not be effective in isolation, so further international action is required.

TABLE 2: SWOT ANALYSIS ON UK AMR PROPOSALS FROM THE INVESTOR PERSPECTIVE

Strengths	Weaknesses
1. The proposal is the first of its kind globally 2. It is built on a successful pilot programme 3. The monetary value of higher bands (£15m and £20m) has the potential to match the UK's fair share 4. The scheme will likely attract companies to launch products in the UK, thereby ensuring supply for UK citizens	1. The monetary value of lower bands (£5m or £10m) will not be sufficient to generate substantial return or stimulate further R&D 2. There is a low level of predictability across eligibility criteria, contract length and scoring, which will deter investment 3. Wide value bands will lead to systematic undervaluation of eligible antibiotics
Opportunities	**Threats**
1. The proposal sends a signal to the rest of the world which may support the establishment of other schemes internationally 2. It suggests a potential harmonised way of value assessment worldwide 3. It can coexist with other pull and/or push incentives to create a full package to support investment in new antibiotics	1. UK in isolation is not sufficient. A global aggregated revenue guarantee is needed 2. Institutional investors have doubts if they can achieve a significant return of investment through the current proposals amid low level of predictability and reward, and a lack of direct financial returns

3.2. Strengthening the UK proposals

Investors are key stakeholders in the development of new antibiotics, as their buy-in is critical to unlock the required funds and expertise for the development of novel antibiotics. The results of the interviews with investors indicate that there are several areas in which current UK proposals could be strengthened, enabling them to become a more convincing and effective policy tool for investors:

- **Consider whether the initial contract length could be extended beyond three years.** Investors would prefer a 10-year term but accepted that five years may be a reasonable compromise.
- **Provide clarity and potentially higher flexibility in the application of eligibility criteria,** particularly around financial standing, environmental and societal commitments for smaller companies.
- **Implement a transparent collaborative process for the review of scoring criteria and contract conditions over time.** Changes should be made gradually, with adequate warning to allow investors and innovators to adapt. Major changes should be consulted upon with external stakeholders.
- **Consider some form of early advice or dialogue to enable developers (and thus investors) to predict how their product may perform against the scoring criteria.** Mechanisms that increase the predictability of the scheme would serve to increase investor confidence and thus investment in the development of novel antibiotics[6].
- **Replace wide value bands with smaller more incremental value bands** to mitigate the proposed systematic undervaluation of eligible products.
- **Clarify the long-term commitment to the scheme.** Investors require assurance that the scheme will still be in action at the time of market entry. As investments are made early in the development process, investors will require a long-term commitment to the scheme (or a similar replacement).
- **Share best practices and encourage the development of streamlined and harmonised subscription systems internationally.** The UK scheme will not be sufficient on its own.
- **Maintain a package of additional national and international pull and push incentives to help mitigating potential weaknesses of and gaps in the proposed subscription system.** Investors agreed that a combination of different types of incentive would generate the most powerful stimulus for investment.

Based on the insights collected via nine interviews with investors, we believe these suggestions will aid the UK scheme in attracting investors and support the design of effective pull incentives in other jurisdictions. Ultimately, they will help NHS England and international policy makers to achieve the aim of the pull incentive in stimulating investment in novel antibiotics.

[6] Alternatives favoured by the investors were designation of value earlier in the development process or tendering of target product profiles. We see these as more fundamental changes to the proposals, perhaps less likely to be adopted by NHS England and NICE, and therefore suggest some form of early dialogue as a compromise.

Annex

Proposed scoring criteria and weights

Figure 6 below details the scoring criteria and the criteria weights towards the total score. Each criterion contains a range of levels, with each level associated a set number of points (not shown here, for full details see NHS England, 2023). In scoring the product, it is assessed against the levels to produce the score for each criterion. The points associated with each level are then weighted according to the weight for that criterion and summed to produce the total score. If a score of at least 50 is achieved, the antibiotic will qualify for one of the four value bands.

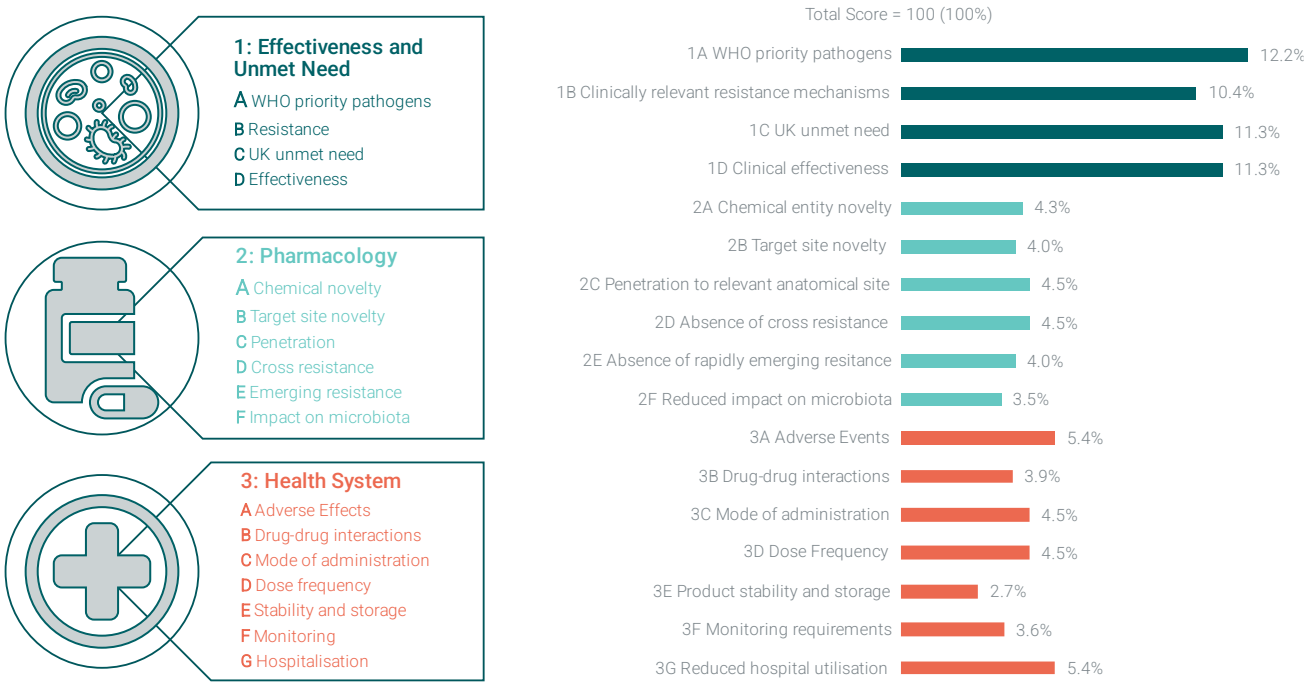

FIGURE 6: OVERVIEW OF SCORING CRITERIA AND WEIGHTS

Adapted from NHS England (2023)

Investor profiles

TABLE 3: INVESTOR PROFILES

	Institutional Investor	Mission-led Investor	Biopharma Exec	Total
USA	1	3	1	5
Europe	-	1	-	1
UK	1	1	1	3

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