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NHS England

Antimicrobial Products Subscription Model: Guidance on Commercial Arrangements

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Contents

Introduction

Antimicrobial resistance (AMR) is one of the most pressing global challenges we face this century. Already, AMR infections are estimated to cause 700,000 deaths each year globally. That figure is predicted to rise to 10 million, alongside a cumulative cost of $100 trillion, by 2050 if no action is taken[1]. The World Bank estimates that an extra 28 million people will be forced into extreme poverty by 2050 unless AMR is contained[2].

The UK Government has recognised AMR as a global problem and committed international action to tackle it as a priority issue. The global approach is based on antibiotic stewardship and infection prevention and control. The global action plan on antimicrobial resistance sets out the World Health Organization's (WHO) priorities for tackling AMR. The scale of the AMR threat, and the need to contain and control it, is widely acknowledged by governments globally, international agencies, researchers and private companies alike.

In the United Kingdom (UK), rising AMR and suffering attributable to infectious diseases will increase overtime as they become more difficult to treat, the number of human deaths will subsequently increase as will the socio-economic costs associated with treating ill health in humans.

No new classes of antibiotic have been discovered since the 1980s3. This, together with the increased and inappropriate use of the drugs already in circulation, means we are heading rapidly towards a world in which these current antibiotics are no longer effective.

For most antimicrobial products, there are few replacements or alternative products in development and even fewer that target priority pathogens. Investment in novel antimicrobials is widely seen as commercially unattractive, because high research and development costs and low returns (due to restrictions in usage to reduce resistance patterns) have led to market failure, i.e. companies do not see the return

[1] https://www.who.int/docs/default-source/documents/no-time-to-wait-securing-the-future-from-drug-resistant-infections-en.pdf
[2] https://www.worldbank.org/en/topic/health/brief/antimicrobial-resistance-amr#:~:text=Each%20year%2C%20700%2C000%20people%20die,Threat%20to%20Our%20Economic%20Future'
[3] https://www.nature.com/articles/d41586-020-02884-3

on investment seen with other innovative products where uptake is encouraged rather than restricted.

The ideal scenario would be for companies to develop and manufacture new antimicrobials which are not released into circulation until needed. However, this is not a viable commercial model for companies.

The UK Government's national action plan for antimicrobial resistance includes the commitment to lead the way in testing solutions that address this market failure of companies not investing in the development of new antimicrobials. The UK is the first country in the world to have tested an innovative model, through a pilot, that pays companies a fixed annual fee for antimicrobials based primarily on a health technology assessment of their value to the National Health Service (NHS), as opposed to the volumes used.

Following the success of the pilot, the NHS will use a subscription style contract to pay for antimicrobial products that offer value to patients and the NHS. These contracts delink payments from the volume used while having appropriate contractual requirements to guarantee supply.

Section 1: Aims and Purpose

The purpose of this document is to set out the routes to evaluate and commission antimicrobial products through the antimicrobial product subscription model. The procurement process for the subscription model has been designed to allow all four nations of the UK to take part in a single procurement process. To minimise repetition, through the document the term contracting authorities is used to mean NHS England; NHS Scotland; NHS Wales; Northern Ireland Department for Health, Social Services and Public Safety; Department of Health and Social Care where those bodies have chosen to take part in the procurement.

The intention is to give clarity to the roles of contracting authorities and the National Institute for Health and Care Excellence (NICE). This guidance supports the introduction of clinically effective antimicrobial treatments into the NHS in order to maximise health outcomes and value for the taxpayer.

The contracting authorities recognise that the characteristics of the market for antimicrobial products – specifically the need for clinical stewardship – undermine the normal business model for pharmaceutical companies. While good stewardship means prescribing the right antimicrobial to treat the right pathogen at the right time, strategies to preserve the effectiveness of new products often means that they are used very little in the first few years after they have received marketing authorisation.

Low usage means low sales revenue for companies in the early years and mainstream use may only be achieved many years later when the patent protection and marketing exclusivity period may have expired. As a result, many large pharmaceutical companies have scaled back their research and development programmes for antimicrobial products and small companies find it difficult to raise finance for product development, further contributing to a reduced pipeline of new products coming to market.

The UK Government and the NHS are committed to evaluating and paying for selected antimicrobial products in a different way from other medicines. This document sets out the commissioning route for antimicrobials that offer exceptional value based on meeting a set of clear clinical criteria, where payments are delinked from volumes used and contractual requirements guarantee surety of supply – ensuring antimicrobial product availability at the right time and right place to meet

need and demand. The contract evaluation will attribute different scores for antimicrobial products depending on the value they offer to the NHS and place them into one of four value bands. Not all products will qualify for a subscription style contract. For products that do not qualify, the standard routes to market for launching a medicine in the UK should be followed. More information on this in Section 4.

Section 2: Roles and Responsibilities

This section sets out the roles and responsibilities of different organisations within the UK health system. This includes NICE, NHS England, NHS Scotland, NHS Wales and Northern Ireland Department for Health, Social Services and Public Safety.

NHS England, NHS Scotland, NHS Wales and Northern Ireland Department for Health, Social Services and Public Safety

The national bodies for the NHS in each devolved nation set out the commissioning strategy and clinical priorities for the health systems in their jurisdiction. For the commissioning of antimicrobial products, where each nation of the UK choses to participate in the subscription model, these organisations will be the contracting authorities of the procurement process through which subscription styled contracts will be tendered.

Initially NHS England will act as the lead authority running the procurement process and issuing the invitations to tender. The devolved administration will be listed as contracting authorities within the tender documents and will be responsible for the decision to issue a contract for their nation and for the payments within their respective jurisdictions.

National Institute for Health and Care Excellence

NICE has a world-leading role in producing independent evidence-based guidance, advice and quality standards for health, public health and social care. This is an important mechanism for ensuring medicines and other interventions used by the NHS offer both clinical- and cost- effectiveness to patients and taxpayers.

Within the subscription model for antimicrobials, contracting authorities will have overall responsibility for the process to award subscription style contracts, however the authorities will commission NICE to support key clinical input to the process:

- To provide representatives for the eligibility panel, established by the authorities, to assess the suitability of an organisation and its product for a contract award based on clinical and non-clinical criteria before it progresses to the evaluation stage. The representatives provided by NICE will include clinical experts from the evaluation panel (see below);

- In addition to making a recommendation to the authorities as to an applicant's eligibility, the eligibility panel may also recommend the population(s) within the marketing authorisation indications to be included within the scope of the award stage and assessed against the award criteria. Applicants will be advised of the proposed scope, which must be accepted as a condition of progressing to the award stage;

- To establish, on behalf of the authorities, a standing panel of clinical experts from across the UK to evaluate each product against clear award criteria; the 'evaluation panel'. The panel will be recruited, hosted and operationalised by NICE, with input from the authorities as appropriate. For example, recruitment of panel members will adhere to typical NICE processes for committee recruitment, with representatives from the authorities also involved in assessing applications and agreeing appointments.

The evaluation panel will be an integral part of the NHS procurement process. The authorities may need to charge an application fee to companies as an entry requirement at each stage of the process to cover the respective administrative costs incurred by NICE. Any charge will be calculated on a cost recovery basis.

Section 3: Public Contract Regulation Compliance

Compliance with the Public Contract Regulations is a legal requirement for all UK authorities seeking to award a contract with a value above threshold. To deliver the Antimicrobial Products Subscription Model, in compliance with Public Contract Regulations, interested organisations will be able to express interest in the advertised selection process.

The selection process proposed will be open to all interested organisations and consist of two stages:

Stage 1) an eligibility stage where potential suppliers will be required to demonstrate that they satisfy minimum eligibility criteria to be awarded a subscription style contract; and subject to passing Stage 1, eligible suppliers will be invited to

Stage 2) an award stage where potential suppliers will be required to provide evidence for assessment by the evaluation panel to demonstrate the extent to which their product satisfies the award criteria.

Stage 2 will determine if a supplier is awarded a subscription style contract and the quantum of the associated annual fee. The eligibility and award criteria, together with the subscription style contract terms and process instructions for suppliers, will be published when the opportunity is advertised. The precise eligibility criteria will be considered and set each year as part of the invitation to tender documentation. Whilst there will be no opportunity for potential suppliers to vary the criteria or contract terms, there will be an opportunity to seek clarification about the process and associated documents.

Use of a PCR compliant approach also provides a mechanism to select a limited number of products from those available, should there be a limited number of subscription style contracts available. NHS England have considered the potential procurement routes available within the Regulations and currently propose to use the Restricted Procedure to award subscription type payment contracts. The principal reasons for proposing the restricted procedure are:

a) it facilitates the proposed two stage approach (eligibility and award)

b) it is a relatively simple, well understood and quick (6-8 month) process from advertising the opportunity, completing the eligibility and award stages and having signed contracts in place.
c) Based upon the learning from the pilot procurement process and management of the two initial contracts:
    i. NHSE currently do not see the need for detailed dialogue with suppliers during the procurement process;
    ii. NHSE have already developed a tried and tested form of subscription style contract ; and
d) The existing contract and proposed award process, will enable suppliers to respond to the NHS requirements.

NHS England anticipate updating the procurement approach for subsequent procurements once the new public contract regulations are published, however, NHS England anticipate the process will largely reflect the Restricted Procedure described above.

Under the public contract regulations, the authority will publish documentation that includes all the information needed for companies to apply for a tender opportunity. The documentation will include the eligibility and the award criteria. These will be reviewed each year before notice of the tender is given. Where the material in the documentation is changed, the authority will look to hold a pre-market engagement to inform companies of the details in the tender.

Section 4. Eligibility Criteria

Compliance with the Public Contract Regulations is a legal requirement for all UK

Only products that meet certain eligibility criteria will be considered for full evaluation for a contract. These criteria will be clinically lead and focus on areas recognised by the WHO as areas in need for new antimicrobial treatment options.

Clinical criteria

- *WHO priority pathogen* - products that are active against pathogens on the WHO Priority List will be eligible. The key target will be products that treat infections caused by pathogens designated as 'critical' on the WHO priority list.

WHO priority pathogens list for R&D of new antibiotics

Priority 1: CRITICAL

- Acinetobacter baumannii, carbapenem-resistant
- Pseudomonas aeruginosa, carbapenem-resistant
- Enterobacteriaceae, carbapenem-resistant, ESBL-producing

Priority 2: HIGH

- Enterococcus faecium, vancomycin-resistant
- Staphylococcus aureus, methicillin-resistant, vancomycin-intermediate and resistant
- Helicobacter pylori, clarithromycin-resistant
- Campylobacter spp., fluoroquinolone-resistant
- Salmonellae, fluoroquinolone-resistant
- Neisseria gonorrhoeae, cephalosporin-resistant, fluoroquinolone-resistant

Priority 3: MEDIUM

- Streptococcus pneumoniae, penicillin-non-susceptible
- Haemophilus influenzae, ampicillin-resistant
- Shigella spp., fluoroquinolone-resistant

Other criteria

- *Confirm agreement to the model contract terms, including:*
  - *surety of supply* – contractual requirements for companies to provide assurance that they will always have supply, ensuring antimicrobial product availability at the right time and right place to meet need and demand

    - *antimicrobial stewardship*
        - *sales force stewardship* – reinforce appropriate organisational behaviours, delinking remuneration incentives for company sales representatives from antimicrobial sales
        - *promotional activities* – activity on use of products should be informative and educational. For products with a subscription style contract, companies must keep the NHS informed of the activities they intend to undertake through the year.
    - *Performance*
        - *Key performance measures and reporting requirements*
    - *Payment terms*
- *Environmental Standards* - companies must demonstrate, via independent assessment, compliance with specified antibiotic manufacturing standards which aim to reduce the development of resistance and ecotoxicity in the environment as a result of manufacturing operations.
- *Economic and Financial Standing* – it is a standard requirement of all public sector contracts that companies demonstrate they have a sufficient economic and financial standing to justify award of the proposed contract.
- *Probity - companies must demonstrate they don't 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 carbon emissions.*

The assessment of eligibility is largely administrative. The scoring for this criteria is normally "pass" or "fail" depending on whether than company submits the specified information and demonstrates a minimum financial standing. The inclusion of a section on the willingness to agree to the terms of the model contract on supply, stewardship and promotion is intended to draw the attention of applicants to those terms at an early stage.

In addition, to the clinical criteria above, eligibility to apply for a contract will be limited to products that either:

- have received marketing authorisation in the UK since the previous invitation to tender for antimicrobial subscription contracts; or
- where companies can demonstrate that they expect the product to receive marketing authorisation in the UK within 12 months following the issue date of the invitation to tender

For the first invitation to tender under these arrangements, the NHS will consider applications for products that have achieved their UK marketing authorisation and were launched in the UK prior to the pilot project of July 2020, subject to those products satisfying all other eligibility criteria. The opportunity documentation will give more details.

Section 5: Route to Commissioning

The route to commissioning antimicrobial products differs from other medicines. New branded pharmaceuticals in England are expected to undergo an appropriate NICE health technology assessment (HTA) unless there is a clear rationale not to do so. The HTA typically leads to a recommendation for routine use if deemed clinically- and cost- effective, which is accompanied by a funding mandate. The lead commissioner will be either locally integrated care boards or nationally NHS England specialised commissioning depending on the services in which the medicine is prescribed.

In the standard route to market for antimicrobial products, a NICE HTA is not normally undertaken. For all antimicrobial products in the standard route, companies would be required to apply for market authorisation from the Medicines and Healthcare products Regulatory Agency (MHRA) and seek a list price from the Department for Health and Social Care (DHSC) in the same way as other medicines.

In this new model, in addition to products already launched, companies with products that are expected to receive marketing authorisation within 12 months of the tender invitation launch date can apply for a subscription style contract. Companies will need to demonstrate that the timeline for marketing authorisation is realistic. NHS England and NICE will be liaising with the Medicines and Healthcare Products Regulation Agency (MHRA) to verify the timeline. Antimicrobials that offer significant value to patients and the NHS, may apply for a subscription style contract, and will then be assessed against eligibility and award criteria published by the authority.

Subject to any limit on the number of contract available, products that meet the eligibility criteria and demonstrate sufficient value against the award criteria will be offered a contract reflecting the products assessed value. The contract length will be for an initial period of three years, with the authorities having the option to extend the contract for a period or periods up to a maximum total period of up to 15 years to cover the patent exclusivity period of the product. The intention is that the contracts will be extended up to the patent expiry date but not beyond. It is possible that the product could change between value bands (in either direction) during the contract term, depending on how the value of the product to the NHS evolves over time. The authorities reserves the right to terminate a contract should

it determine that the value of the product to the NHS no longer warrants a subscription contract.

Products that do not meet the eligibility criteria for a subscription style contract will still be able to access the NHS market via the standard route mentioned above. The steps of the commissioning process for subscription style contracts are set out in Figure 1 below.

The window for considering new products will be open periodically (e.g. once a year).

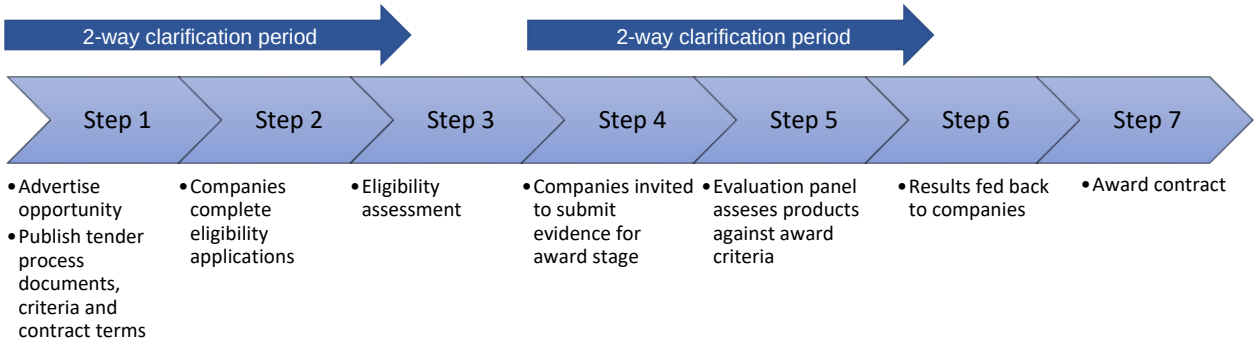

Figure 1. Schematic representation of the procurement process

Ongoing Clarification

Companies will have the opportunity throughout the process to seek clarification from the lead authority to help companies fully understand the requirements. Any clarification information provided to a company in response to a question received during the eligibility or award stage may be shared with all companies applying for a contract to make sure the process is as transparent as possible.

Step 1: Advertise Opportunity & Publish Tender Documents

Each opportunity will be advertised via a Prior Information Notice and/or Contract Notice. These will provide information on where to access the relevant tender documents and how to submit an expression of interest.

The Contract Notice will also confirm the participating contracting authorities and the lead contracting authority responsible for the procurement process.

As set out above, companies that have products launched since the previous opportunity, or expect to receive marketing authorisation for their product within 12 months of the Contract Notice being published, may apply for a subscription style contract.

The tender documents will include instructions for potential suppliers, the eligibility criteria, the award criteria and the evidence that companies will need to provide, together with the contract terms.

Step 2: Completion of application

Companies wishing to apply for a subscription contract will need to complete an application responding to the Contract Notice. The application will require submission of documentation and evidence to demonstrate that the company and product meet the eligibility criteria, which will include both clinical and non-clinical requirements.

Step 3: Eligibility assessment

An eligibility assessment panel will assess the documentation provided by the company against the eligibility criteria. Companies that meet the criteria will be informed of the assessment decision by the authority and invited to progress to the next step of the process.

During the eligibility stage, the assessment panel may request companies to clarify details included within their application. No additional evidence or data may by requested or provided at this stage; clarification requests will be restricted to questions to help with the panel's interpretation and understanding of the evidence submitted.

During the eligibility stage, in addition to determining an applicant's eligibility, the eligibility panel will also recommend the population(s) and/or marketing authorisation indications to be included within the scope of the award stage and assessed against the award criteria. Applicants will be advised of the proposed scope, which must be accepted as a condition of progressing to the award stage.

Companies may also be invited to submit information about the scope of the use of the product within the marketing authorisation as part of the initial application. The

eligibility panel can take account of any such information when considering their recommendation on scope for the award stage.

Steps 4-5: Evaluation panel assesses products against award criteria

Companies will be required to submit evidence showing how the product performs against pre-specified award criteria, which will be published with the opportunity.

A UK panel of clinical experts, convened by NICE to provide recommendations to the authorities, will meet in private to assess the documentation provided by the company against the award criteria which include a points-based scoring systems. The product's points score will determine the value band of the contract offered by the authority to the company. The score given will depend on the evaluation panel's view of the strength and quality of the evidence provided by the company. During the award process, the evaluation panel may request clarification or additional information or evidence from companies as part of its quality assurance of the evidence.

The evaluation panel can recommend one of four possible contract 'value bands' (see Figure 2). The lowest category is for products with relatively low clinical value but value nonetheless from controlling their use, and the top band is for innovative breakthrough products which offer exceptional value. The value of the bands shown in the table are for England only. Each nation will determine the values that will apply for their health system. The table also shows the proportion of the points needed from the evaluation process for a product to be placed in each contract band. These are subject to the consultation and legal review. The values and points will be reviewed each year and published in the documentation that accompanies the tender opportunity.

Figure 2. Value bands, linked to the award criteria scoring system

Band 1: £20m per year Breakthrough antimicrobials	**Band 2: £15m per year Critical new antimicrobial**	**Band 3: £10m per year Priority new antimicrobial**	**Band 4: £5m per year Important new antimicrobial**
achieves ≥80% of max score against evaluation criteria	achieves between 70%-79% of max score against evaluation criteria	achieves between 60%-69% of max score against evaluation criteria	achieves between 50%-59% of max score against evaluation criteria

Steps 6-7: Results and Contract awarding

Once the evaluation process has been completed and the authority has approved implementation of the recommendations from the evaluation panel, companies will be informed of the proposed value of the contract based on the assessment against the award criteria. The evaluation panel recommendations to the authorities will not be subject to consultation.

Following the decision to award, the authorities intend to publish information on the organisations awarded a contract. This will include the value band agreed for the product, the scores awarded for each criteria, and an account of the evaluation panel's rationale for awarding each score. At its discretion, NICE may also publish stewardship statement for the NHS on the optimal use of the product. Publications of these documents will happen only after the contract has been awarded. This is in line with best practice under public contract regulations.

Subject to the agreement of the companies, NHS England and the devolved governments, at their discretion, will offer a contract in the relevant value band. The Antimicrobial Products Subscription Model will use a model contract based on the standard NHS contract. This contract includes key performance indicators to support surety of supply. An example of the model contract used during the pilot project is provided in a separate document *Antimicrobial Products Subscription Model: Model Contract from Pilot Project*. The model contract that will be used will be subject to amendment in light of the consultation and any pre-market engagement exercise.

Once companies have been informed of the contract award outcome, the authority will observe the public contract regulations mandatory minimum standstill period of 10 days before entering into a contract with the successful applicant(s). Any applicant may seek clarification or raise any concerns about the award outcome with the authority during this period. Applicants will have up to 30 days to accept the award, if offered, by the authority.

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