ANNEX 4: AWARD QUESTIONS AND CRITERIA

The response to each question must be a stand-alone response. Unless specifically requested in the question, the response must not:

- cross refer to other questions;
- cross refer to other documents;
- include embedded documents;
- refer or link to additional documents;
- include URL links.

Bidders should note that, unless specifically requested, such information will not be considered when evaluating the response;

The Bidders entire response must not exceed the stated A4 page limit with a minimum font size of Arial 12 with single line spacing. The minimum margins in the response template must not be changed. Any element of a response beyond the stated page limit will be disregarded and not considered in the evaluation.

<table>
<tr><th>Question Number</th><th>Question</th><th>Methodology</th><th>Score</th><th>Scoring Criteria</th></tr>
<tr><td rowspan="2">AMR.1</td><td rowspan="2">Unmet Need
Please describe, with supporting evidence, the degree to which the antimicrobial proposed addresses an unmet need including any specific unmet need in the UK.

Your response should include each of the following Key Components:

<u>Key Component 1</u>

List the pathogens included on the WHO priority pathogen list and their relevant ranking, against which your antimicrobial is active and included within the antimicrobials Licensed Indications;

<u>Key Component 2</u>

For the Licensed Indications included in Key Component 1 above, please:
• describe the unmet need(s) the antimicrobial addresses; and
• specifically, how and why this is / these are relevant to the UK; and
• provide evidence, if available, to support your rationale

<u>Key Component 3</u>

There are a number of key resistance determinants in the UK relevant to the focus of this project, the 4 Ambler classes of beta-lactamases [including the top 5 carbapenem resistance genotypes (OXA-48, KPC, NDM, IMP, VIM) in addition to extended spectrum beta-lactamase (ESBL)] producers, and the non-mutational mechanisms of multidrug resistant (MDR) Pseudomonas (porin OprD, efflux pump).

To score highly, products will be active against pathogens producing beta-lactamases from all 4 Ambler classes and also active in presence of porin of efflux pump mechanisms of MDR Pseudomonas i.e. active against the 6 key resistance determinants described above.

Please list standard care for the disease area(s)/pathogen(s) covered by the Licensed Indication and for each provide an explanation, with supporting evidence if available, of why each proposed comparator is relevant and appropriate, how your antimicrobial performs against standard care i.e. equivalent efficacy, equivalent efficacy but less toxicity, superior efficacy to standard care, or a benefit over standard care other than efficacy or toxicity e.g. duration of treatment, time to microbiological or clinical cure, product stability, whether it does not require therapeutic dose monitoring.</td><td>Scored</td><td>Key Component 1</td><td>WHO Priority Pathogens

Points will be awarded as below for each category of pathogen listed (in response to Key Component 1) that are on the WHO priority pathogen list and included within the antimicrobials Licensed Indications:

• 6000 points for the first Priority 1 pathogen included within the Licensed Indications;
• 2500 points for the second Priority 1 pathogen included within the Licensed Indications;
• 1250 points for the third Priority 1 pathogen included within the Licensed Indications;
• 1000 points if the Licensed Indications include one or more Priority 2 pathogens;
• 500 points if the Licensed Indications include one or more Priority 3 pathogens.</td></tr>
<tr><td>Scored</td><td>Key Component 2</td><td>Unmet need by Licensed Indication

Points will be awarded as below for only the highest unmet need ascribed to any of the Licensed Indication (s) included in your response to Key Component 1 above.

<table><tr><th>Points</th><th>Criteria</th></tr><tr><td>6000</td><td><u>High unmet need</u> – the antimicrobial licensed indication addresses a disease area of key importance internationally and specifically is a key unmet need in the UK e.g. resistant gram-negative blood stream infections or ventilator associated pneumonia VAP</td></tr><tr><td>4000</td><td><u>Medium</u> – the antimicrobial licensed indication addresses an important disease area of significant concern but UK outcomes broadly acceptable e.g. gram-positive blood stream infections. A licensed indication that addresses a high international unmet need but not a particular issue in the UK would also be allocated a medium score</td></tr><tr><td>1000</td><td><u>Low unmet need</u> – the antimicrobial licensed indication addresses a disease area with adequate current treatment options/outcomes e.g. community acquired pneumonia</td></tr></table></td></tr>
</table>

<table>
<tr><th>Question Number</th><th>Question</th><th>Methodology</th><th>Score</th><th>Scoring Criteria</th></tr>
<tr><td></td><td>Please list the activity, or lack of activity, of your product against the 4 Ambler classes of Beta-lactamases and the non-mutational causes of multidrug resistant (MDR) Pseudomonas (Porin OprD, and efflux pump). In addition, list specific activity, or lack of activity of your product against the top 5 Carbapenemase producing genotypes in the UK (OXA-48, KPC, NDM, IMP, VIM).

<u>Key Component 4</u>

Describe the severity of the clinical setting for the disease area(s) covered by the Licensed Indication(s).

a) List the disease areas and their clinical severity, that are included within the antimicrobials Licensed Indications (e.g. community uncomplicated urinary tract infection (UTI); Hospital acquired pneumonia; Bacteraemia in ICU). If the licence is pathogen specific, then list the clinical disease area(s) relevant to the pathogen(s) listed in the licence.

b) The health setting (e.g. community, outpatient clinic, renal, transplant unit, oncology/haematology, secondary care ward, ICU) most relevant to the antimicrobial;

c) Demonstrate the benefit provided by the antimicrobial in the setting compared with standard care (e.g. reduced length of stay in ICU or other high-risk settings).

<u>To support your responses to Key Components 1 to 4, please also provide:</u>

(i) an objective summary of any available UK or EU data relevant to the effectiveness of your antimicrobial and/or its comparators against the pathogen(s) listed in Key Component 1 above, together with a copy of the relevant data, and

(ii) a literature review of the available evidence, together with the associated references.

The Page Limit for this question, excluding (i) & (ii), is: [20] pages
The Page Limit for (a) the objective summary, is: [20] pages;
The Page Limit for (b) the literature review, is: [20] pages;

A literature review is a comprehensive summary of previous research on a topic. The literature review surveys scholarly articles, books, and other sources relevant to a particular area of research. The review should enumerate, describe, summarize, objectively evaluate and clarify this previous research.</td><td>Scored</td><td>Key Component 3</td><td>Performance against key resistance determinants in the UK

Points will be awarded as set out below

<table><tr><th>Points</th><th>Criteria</th></tr><tr><td>6000</td><td>Active against pathogens producing beta lactamases from all 4 Ambler classes and active in the presence of the non-mutational mechanisms causing MDR Pseudomonas (porin OprD and efflux pump) i.e. address 6 or more key resistance determinants</td></tr><tr><td>4000</td><td>Addresses 3-5 out of the 6 key resistance determinants</td></tr><tr><td>1000</td><td>Addresses 1 or 2 out of the 6 key resistance determinants</td></tr><tr><td>0</td><td>No activity against Ambler class Beta-lactamases or the non-mutational mechanisms of MDR Pseudomonas</td></tr></table></td></tr>
<tr><td></td><td></td><td>Scored</td><td>Key Component 4</td><td>Points will be awarded as below for the highest risk clinical setting applicable to the antimicrobial

<table><tr><th>Criteria</th><th>Yes</th><th>No</th></tr><tr><td>High risk settings (ICU, cardiothoracic, renal, haematology/oncology, transplant unit, Neonatal, Cystic Fibrosis)</td><td>6000</td><td>0</td></tr><tr><td>Non-ICU / Low mortality hospital setting</td><td>4000</td><td>0</td></tr><tr><td>Primary care / community or long-term care facility</td><td>1000</td><td>0</td></tr></table></td></tr>
<tr><td>AMR.2</td><td>Degree of Novelty
Please describe any novel characteristics of the antimicrobial offered.

Your response should include each of the following key components:

1. Confirmation that the antimicrobial is either a new chemical class of antibiotic; or an adjustment to an existing class;

a) If it is a new chemical class of antibiotic, a description, together with any supporting evidence, of the additional benefits it offers / will offer;

b) If it is an adjustment to an existing class, a description, together with supporting evidence, of the additional benefit the adjustment confers compared with existing therapeutic options?

2. Confirmation of whether the antimicrobial acts on a different pathogen-specific target compared to existing agents in use for the relevant pathogen(s) and a description, together with supporting evidence, of any additional benefits this confers;

3. Confirmation of whether the antimicrobial has a different mechanism of action compared with relevant comparators and a description, together with supporting evidence, of any additional benefits this confers;

4. Confirmation of whether the antimicrobial bypasses current mechanisms of resistance, or has reduced susceptibility to development of resistance to antimicrobials (& by what mechanism), and a description, together with supporting evidence, of any additional benefits this confers;

5. Details of any reduced toxicity, or other benefits, associated with the antimicrobial compared with relevant comparators and a description, together with supporting evidence, of any additional benefits this confers; (e.g. Is the drug stable enough for it to be suitable for outpatient intravenous antibiotic regimens);</td><td>Scored</td><td></td><td>Points will be awarded for each novel characteristic as set out below.

<table><tr><th>Key Component</th><th>Criteria</th><th>Yes</th><th>No</th></tr><tr><td>1</td><td>The antimicrobial is a new chemical class of antibiotic</td><td>2000</td><td>0</td></tr><tr><td>2</td><td>The antimicrobial acts on a new pathogen specific target</td><td>1500</td><td>0</td></tr><tr><td>3</td><td>The antimicrobial has a new mode of action</td><td>1500</td><td>0</td></tr><tr><td>4</td><td>(i) The antimicrobial has reduced susceptibility to development of resistance compared to existing members of the same class and/or to other relevant antimicrobials
(ii) No cross resistance to other classes of antimicrobials</td><td>1500
1000</td><td>0</td></tr><tr><td>5</td><td>The antimicrobial is a modification of existing chemical class with additional benefits (e.g. dosing, less toxicity, easier route or lower frequency of administration, reduced duration of administration to achieve cure, or enhanced stability lending itself suitable for home intravenous antibiotic regimens; or enhanced entry into the bacterium)</td><td>500</td><td>0</td></tr></table></td></tr>
</table>

Question Number	Question	Methodology	Score	Scoring Criteria
	To support your responses to Key Components 1 to 5, please also provide a literature review of the available evidence, together with the associated references. The Page Limit for this question, excluding (a), is: [20] pages The Page Limit for the literature review, is: [20] pages			
AMR.3	**Surety of Supply** Please describe, with supporting evidence, your proposed arrangements to ensure the antimicrobial will be available to prescribe and dispense, when and where required in England. Your response should include each of the following Key Components: 1. Your commitment to good manufacturing practice; 2. Your commitment to environmental standards relevant to the manufacture of antimicrobials; 3. The proposed arrangements to ensure availability of raw ingredients including active pharmaceutical ingredient (APIs); 4. The proposed manufacturing, capacity, lead times, scheduling, quality control and continuity/contingency arrangements; 5. The proposed arrangements to transport the antimicrobial to England; 6. The proposed arrangements to avoid parallel exporting of the antimicrobial; 7. The proposed distribution model for England, including: the total minimum stock, holding points, distribution arrangements, guaranteed delivery times from receipt of order, proposed hospital stock, etc; 8. Any other arrangement you consider relevant to avoid issues or disruption to the availability of the antimicrobial to the NHS in England under usage consistent with appropriate antimicrobial stewardship; 9. The proposed arrangements to accommodate an unexpected increase in local demand (localised incident); 10. The proposed arrangements to accommodate an unexpected increase in national demand; 11. [Other Key Components may be included once the Surety of Supply Specification is further developed] Bidders should note that the components listed above are of equal importance. The Page Limit for this question is: [20] pages	Scored	Confidence 5000	Response / Evidence is sufficient in qualitative terms, convincing and credible such that the Authority has confidence that the antimicrobial will be available to prescribe and dispense, when and where required in England
			Minor Concerns 3500	Response / Evidence has only minor gaps, or to a small extent is unconvincing such that the Authority has only minor concerns that the antimicrobial will not be available to prescribe and dispense, when and where required in England
			Concerns 1000	Response / Evidence has gaps, or is unconvincing, or lacks credibility, or is irrelevant to the question such that the Authority has concerns that the antimicrobial will not be available to prescribe and dispense, when and where required in England
			Major Concerns 0	Response / Evidence has major gaps, is unconvincing in many respects, lacks credibility, or largely irrelevant to the question such that the Authority has major concerns that the antimicrobial will not be available to prescribe and dispense, when and where required in England
AMR.4	**Antimicrobial Manufacturing, Access and Stewardship** Please describe, with supporting evidence, your commitment to Antimicrobial Stewardship and proposed arrangements to comply with the Antimicrobial and Environmental Stewardship Specification. Your response should include each of the following Key Components: 1. Your commitment to comply with the Antimicrobial and Environmental Stewardship Specification; 2. Details, together with supporting evidence of your environmental strategy (e.g. setting manufacturing discharge limits at owned and/or supplier manufacturing sites and external wastewater treatment plants; auditing and publishing the results); 3. Your commitment to comply with any Antimicrobial and Environmental Stewardship recommendations resulting from the Health Technology Assessment and / or Public Health England; 4. Your suggested stewardship arrangements specific to your antimicrobial; 5. The proposed arrangements to promote and comply with Antimicrobial Stewardship within your organisation and with end users; e.g. do your sales representatives have their bonuses delinked from volume of sales? 6. The proposed arrangements to promote and comply with environmental standards at the site of manufacture and throughout the supply chain; 7. [Other Key Components may be included once the Stewardship Specification is further developed] Bidders should note that the components listed above are of equal importance. The Page Limit for this question is: [20] pages	Scored	Confidence 5000	Response / Evidence is sufficient in qualitative terms, convincing and credible such that the Authority has confidence that the Bidder will comply with the Antimicrobial Stewardship Specification
			Minor Concerns 3500	Response / Evidence has only minor gaps, or to a small extent is unconvincing such that the Authority has only minor concerns that the Bidder will not comply with the Antimicrobial Stewardship Specification
			Concerns 1000	Response / Evidence has gaps, or is unconvincing, or lacks credibility, or is irrelevant to the question such that the Authority has concerns that the Bidder will not comply with the Antimicrobial Stewardship Specification
			Major Concerns 0	Response / Evidence has major gaps, is unconvincing in many respects, lacks credibility, or largely irrelevant to the question such that the Authority has major concerns that the Bidder will not comply with the Antimicrobial Stewardship Specification

Question Number	Question	Methodology	Score	Scoring Criteria
AMR.5	**Antimicrobial Surveillance** Please describe, with supporting evidence, your proposed arrangements to support antimicrobial surveillance. Your response should include each of the following Key Components: 1. Your suggestions for antimicrobial surveillance arrangements in general; 2. Any suggested surveillance arrangements specific to your antimicrobial; 3. Your proposed arrangements to support antimicrobial surveillance of your antimicrobial and antimicrobials in general (e.g. patient level usage and emergence of resistance data); 4. If applicable, your proposed arrangements to comply with information governance standards / legislation; 5. Confirmation of your commitment to work with NICE and NHS England & NHS Improvement to implement antimicrobial surveillance requirements that may result from the antimicrobial evaluation (HTA) process; 6. [Other Key Components may be included once the antimicrobial surveillance requirements are further developed] Bidders should note that the components listed above are of equal importance. The Page Limit for this question is: [20] pages	Scored	Confidence 5000	Response / Evidence is sufficient in qualitative terms, convincing and credible such that the Authority has confidence that the Bidder will comply with the antimicrobial surveillance requirements.
			Minor Concerns 3500	Response / Evidence has only minor gaps, or to a small extent is unconvincing such that the Authority has only minor concerns that the Bidder will not comply with the antimicrobial surveillance requirements.
			Concerns 1000	Response / Evidence has gaps, or is unconvincing, or lacks credibility, or is irrelevant to the question such that the Authority has concerns that the Bidder will not comply with the antimicrobial surveillance requirements.
			Major Concerns 0	Response / Evidence has major gaps, is unconvincing in many respects, lacks credibility, or largely irrelevant to the question such that the Authority has major concerns that the Bidder will not comply with the antimicrobial surveillance requirements.