Official Development Assistance (ODA)
Funding Opportunity for CARB-X Applicants

July 2019
1. About ODA Funding (Kevin Outterson)
   - What is ODA Funding?
   - Why consider ODA funding?

2. Eligibility and justification for ODA funding (Emma Back)
   - How to apply for ODA funding
   - Completing the ODA Justification Form

3. Next Steps and Resources (Karen Gallant)
Bacteria ignore borders
UK Government Funding to CARB-X

- Through the Global AMR Innovation Fund (GAMRIF), the UK Department of Health and Social Care has provided up to £20m to CARB-X
- The UK Government's contribution to CARB-X is designated as 'official development assistance' or ODA; CARB-X uses the term 'ODA' to categorize this specific funding stream
- ODA funds are for R&D which can demonstrate direct benefit to people living in low- and middle-income countries (LMICs)
- Companies with projects that are in the UK funding scope and can be adapted to suit the needs of people in LMICs are welcome to apply for these funds
- Eligibility can be demonstrated in a number of ways including, but not limited to:
  - The method of intervention designed for use in resource-poor healthcare settings
  - The choice of target pathogen which has a demonstrably high burden in LMICs
  - The ability to reduce costs of the product to increase affordability for LMICs
The UK funding scope includes programs which can be designated as ‘alternatives to traditional antibiotics.’ Examples include:

- Bacteriophage
- Microbiome
- Vaccines
- Antibodies
- Potentiators (including beta-lactamase inhibitors)
- Anti-biofilm approaches
- Anti-virulence approaches
- Other approaches exemplified in the Lancet publication by Czaplewski et al* entitled Alternatives to antibiotics—a pipeline portfolio review (if they fall within the general CARB-X funding scope)

Direct-acting small molecule and diagnostic programs are not included in the UK funding scope.

Why Consider ODA Funding?

Applying for ODA support is optional but encouraged. Benefits to applicants include:

1. Exposure of your project to, other funding agencies and resources beyond CARB-X
   - GAMRIF
   - The Department for International Development (DFID) in the UK
   - The Bill and Melinda Gates Foundation
   - The German Federal Ministry of Education and Research (BMBF)
   - Wellcome Trust

2. Potential for expanded work package support
   - Exploring other clinical uses
   - Profiling activity against global isolates
   - CMC formulation work for LMIC environments

3. Broader reach for products generally
   - More comprehensive, globally applicable data packages
   - Access to clinical trial sites in LMICs with emerging pathogens

4. Access to LMIC experts and resources through CARB-X funding
   - Isolates from LMICs
   - CARB-X Global Accelerator Network (GAN)

5. Opportunity to demonstrate Corporate Social Responsibility
How to Apply for ODA Funding

As part of the CARB-X application process, a six question **ODA Justification Form** must be completed. The ODA Justification Form should describe how the research will have a positive impact on the economic development and welfare of people in LMICs. Strong ODA justifications include the following:

- Credible data with references that demonstrates why a particular pathogen is a problem for one or more LMIC(s) on the OECD DAC list*
- Collaboration with partners including research organizations or experts in LMICs
- A focus on specific LMIC countries from which isolates will be sourced
- Clear objectives and plans for capacity building in an LMIC
- Evidence that the project team has the knowledge and expertise to deliver

Completing the ODA Justification Form

Question:

1. Please explain how your research is DIRECTLY relevant to the burden of disease, and specifically the burden of anti-microbial resistance, in countries on the OECD-DAC list. (You should cite evidence such as data and reports from the World Health Organization and/or US Centers for Disease Control, surveillance data from sources such as the Global Antimicrobial Resistance Surveillance System (GLASS), in policy documents, monographs and situational analyses used to inform National Action Plans, conference presentations available as references and research results documented in published journals.)

Key Considerations:

➢ Provide credible, referenced data that demonstrates why a particular pathogen is a problem for one or more LMIC(s) on the OECD DAC list

Sample Responses:

Salmonella spp is considered “High” on the WHO priority list. Evidence of drug resistant (especially ciprofloxacin resistant) Salmonella in countries on the OECD-DAC list includes:

• In Nepal over 90% of S. Typhi clinical isolates show reduced susceptibility to ciprofloxacin.¹

• In Bangladesh, 69% of S. Typhi clinical isolates show resistance to ciprofloxacin.²

• In Cambodia, S. Typhi displayed high rates (90%) of decreased ciprofloxacin susceptibility.³

The problem of MRSA prevalence in the developing world:

• A prospective nationwide study in South Africa determined the prevalence of MRSA at 36%.¹

• A retrospective pediatric study in a setting with high prevalence of HIV determined the prevalence of MRSA to be 39%.² Another large study (13,746 isolates) between 2007 and 2011 showed a prevalence of 24% for tertiary and secondary health care centers in South Africa.³

• Similarly, the prevalence of MRSA has been reported as high as 35% in Algeria, 44% in Botswana, between 82% and 52% in Egypt, 32% in Nigeria, 55% in Ethiopia, and 39% in Ivory Coast.⁴
Completing the ODA Justification Form

Question:

2. Please explain how your project will be of PRIMARY benefit to low- and middle-income countries (LMICs) on the OECD-DAC list. (Refer to section B2 of ODA Considerations for CARB-X Funded Projects. You may want to consider accessibility (e.g., ease of administration and use) and affordability (e.g., cost of goods). Please note: while LMICs should be the primary beneficiaries, the research can also be relevant and have secondary benefits for other countries).

Key Considerations:

- The project, or portion of the project, must seek a specific outcome which will have an impact on a LMIC. The impact should be backed up with figures if available.
- How you conduct your research is key; the process for developing the product is as important as the product itself. For example:
  - Run through in vivo/in vitro models with LMIC isolates to demonstrate that your product is applicable
  - A vaccine adopted for LMICs would consider heat stability and ease of administration
- Partnerships, even potential ones, are important to describe (and can be expanded on in Question 3)
- It is recognized that regulatory approval must often need to be secured in US or EU for a product to be used in LMICs however, commercialization of research cannot solely take place in developed countries.

Sample Responses:

“Given the high economic burden that AMR has created in the developing world, availability of a cost-effective vaccine will save badly needed resources for the public health system of these countries.”

“The proposed research plan is focused on clinical isolates from several LMICs. We have established collaborations with partner organizations active in these countries.”

“We intend to obtain isolates from Ghana, Vietnam, Nepal, Kenya, Jordan, and extend additional requests for collaboration with research groups active in other LMIC countries.”

“We intend to seek WHO prequalification for our product through the WHO Prequalification of Medicines Program (PQP)”
Completing the ODA Justification Form

Question:

3. Will you be engaging any research institutions in countries on the OECD-DAC list in your project? (For example, by partnering with them to collect isolates, gather data or conduct trials.) If so, will your project include any support to those institutions to build their research capacity?

Key Considerations:

- Even if the specific details are unclear at the moment, applicants should demonstrate a solid framework to achieve the aims and be willing to work with CARB-X to refine the activities.
- Provided you have the funds and skills, describe how capacity building would take place.

Sample Responses:

“We have already reached out to three groups which have banks of clinical isolates from a number of LMICs as well as in vivo models that are validated for these. These groups have expressed strong enthusiasm for supporting our program. We will continue to reach out to such groups to expand the network.”

“We will join [research institution X] staff trainings during site visits to support their learning and for our team to understand better the requirements to ensure how our efforts can be better shaped for optimal impact. Our scientific, clinical and trial leadership will benefit through discussion with [research institution X] what needs to be considered to design the trial for local needs and train our partners on the requisite study components to ensure that all trial pieces are conducted per study protocol and SOPs.”

“Funded clinical activities in this award will go to [LMIC research institution]. Funded clinical activities include the identification, recruitment, administration and clinical follow up.”
Completing the ODA Justification Form

Question:
4. Does your project intend to create wider socio-economic benefits for countries on the OECD-DAC list, for example through the transfer of technology, sharing of knowledge, or out-licensing of intellectual property for further product development or manufacture?

Key Considerations:
- Wider benefits do not need to be health related
- Open access journals are a good means of sharing knowledge
- Out licensing can occur further downstream than the CARB-X award

Sample Responses:

- "A direct outcome of this trial will be the increase of local knowledge and expertise in [approach]. We will provide exposure to researchers from [research institution] to clinical trials and microbiome sequencing analysis, and open further avenues for collaboration between the two institutions."
- "We will be exploring manufacturing and commercial partnerships in LMICs."
- "Anticipated novel and innovative work will be published in high impact, open access journals and presented at relevant conferences to ensure access to worldwide researchers"
**Completing the ODA Justification Form**

**Question:**

5. Please describe your pathway to impact in LMICs on the OECD-DAC list. What are the key steps to achieving the objectives outlined above, and over what timescale? When and how would funding from CARB-X support this pathway to impact?

**Key Considerations:**

It is recognized that the impact of research is uncertain, often unexpected and cannot be guaranteed; however, it is important that the pathways to impact are realistic and appropriate to the particular LMIC’s context.

**Sample Responses:**

“Any proposed deal to progress our program would require consideration of access and sustainability, in line with WHO principles, to ensure access to new medicines in all markets.

“This project application is to fund lead optimisation through to completion of phase 1 clinical trials by 2022. Post CARB-X funding, we will seek external investment/licensing deals and further grant funding to support development through phase 2 trials towards approval, estimated to be 2027. Phase 2 trials are likely to include clinical trial centres in Sri Lanka, Vietnam and the Philippines.”
6. Please identify the specific activities in your CARB-X project plan that will enable you to achieve your ODA-eligible objectives outlined within this justification form. Activities must be articulated in the project plan and include timescales and costs.

Sample Responses:

<table>
<thead>
<tr>
<th>Milestone</th>
<th>Timescale</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Milestone 1: work with CARB-X to establish plan for obtaining isolates from LMIC countries</td>
<td>Q3 2019</td>
<td>$0</td>
</tr>
<tr>
<td>Milestone 2: Formulation development completed.</td>
<td>Q2 2020</td>
<td>$425,000</td>
</tr>
<tr>
<td>Milestone 3: Demonstrate functional equivalence to liquid formulation in vitro and in vivo.</td>
<td>Q4 2020</td>
<td>$600,000</td>
</tr>
<tr>
<td>Milestone 4: Demonstrate &gt; 3-month stability at 30° C.</td>
<td>Q2 2021</td>
<td>$125,000</td>
</tr>
<tr>
<td>Milestone 5: Demonstrate efficacy of heat-stable formulation in animal models of skin infection, muscle infection, and bacteremia against selected S. aureus strains from the developing world.</td>
<td>Q1 2022</td>
<td>$975,000</td>
</tr>
</tbody>
</table>
Next Steps & Resources

- Determine whether your project is within scope for UK funding – CARB-X will inform in review process, questions can be sent to carbxapp@bu.edu

- Visit the CARB-X website for additional resources including:
  - ODA Eligibility Requirements – includes a checklist and FAQs
  - ODA Considerations Guidance – this memo provides a framework for thinking about how an AMR project promotes the welfare and economic development of LMICs and benefits people in LMICs directly and primarily
  - DAC List of ODA Recipients – this list is updated tri-annually
  - Alternatives to Antibiotics – Lancet Article

- Complete the ODA Justification Form and submit it with your Short Form application. Ensure alignment between your ODA Justification and your project plan and budget.

- If your application is selected to progress to Long Form based on its scientific and technical merits, you will receive individualized feedback on your initial ODA Justification to enable an updated Justification to be submitted with the Long Form application. See process flow.

- Consult other Antibiotic resistance data sources including:
  - Global Antibiotic Resistance Partnership (GARP) data and reports particularly their resistance map
  - Global Antimicrobial Resistance Surveillance System (GLASS) Report: Early implementation 2016-17 which includes some LMIC country profiles with 2016 resistance data for key bacteria and supplementary country data
  - National Action Plans on antimicrobial resistance
  - Federation of Infectious Diseases Societies of Southern Africa publications list
  - Gates Foundation Project: Antibiotic Resistance Situation Analysis and Needs Assessment (ARSANA) in Uganda and Zambia
CARB-X ODA Process

**ODA Eligibility**
- Applicants submit Short Form and ODA Justification Form
- ODA Consultant advises successful Short Form applicants on how to strengthen the ODA justification
- ODA Consultant reviews and scores ODA Justification; submits ODA Assessment
- UK reviews ODA Assessment; confirms the application is in/out of ODA scope
- Subaward issued with ODA funding

**Applicant**
- Applicants submit Short Form and ODA Justification Form
- Short Form Application
- Long Form Application
- Applicants submit Long Form and updated ODA Justification Form
- Applicants present at AdBoard
- AdBoard reviews Long Form submissions
- AdBoard Review Recommendations to JOC
- CARB-X submits documentation to JOC for decision, identifying ODA-eligible projects

**Scientific Merit**
- EOI applicants are selected to advance to Short Form
- Reviewers select SF applicants to advance to Long Form
- CARB-X approves project?

**Outcomes**
- Yes
- No
- End
- JOC vote
This concludes the ODA Recorded Webinar