CARB-X 2019 Funding Rounds
Supporting innovation to fight drug-resistant bacteria

Kevin Outterson, CARB-X Executive Director
Karen Gallant, CARB-X Global R&D Project Director
2019 Funding Rounds
May 16, 2019 webinar
Today’s agenda

• CARB-X in brief
• How CARB-X funding works
• CARB-X 2019 Funding Rounds in detail
  • Non-traditional approaches
  • Vaccines and Biotherapeutics
  • Diagnostics
  • Direct-acting small molecule
• Questions and discussion
CARB-X
Combating Antibiotic Resistant Bacteria

A global public-private partnership supporting great science to fight drug-resistant bacteria

FUNDERS

ASPR
Assistant Secretary for Preparedness and Response

BARDA
Biomedical Advanced Research and Development Authority

Wellcome

NIH
National Institute of Allergy and Infectious Diseases

UK aid
from the British people

Federal Ministry of Education and Research

ALLIANCE PARTNER

Bill & Melinda Gates Foundation

ACCELERATORS

BASEL AREA. SWISS

BII BioInnovation Institute

CLSI California Life Sciences Institute

C-CAMP Center for Cellular and Molecular Platforms

DZIF German Center for Infection Research

CARB-X

MassBio

RTI International

Wellcome

Boston University
CARB-X is investing > $550 million in 2016-2021

• Non-profit partnership supporting R&D from around the world to address the most serious drug-resistant bacteria
  
  • Non-dilutive funding and accelerator support for the early development of antibiotics, diagnostics, vaccines and other life-saving products

  • Since it was established in 2016, CARB-X has announced $118 million in awards, plus an additional $113+ million if project milestones are met

  • Since it was established, CARB-X has supported 43 projects in 7 countries
CARB-X Portfolio currently has 30 Projects in 5 Countries

**North America**

- Forge Therapeutics**
  San Diego, CA
- Inhibrx
  La Jolla CA
- Amicrobe Inc.
  Calsbad, CA
- Recida Therapeutics
  Menlo Park, CA
- Talis Biomedical
  Menlo Park, CA
- MicuRx Pharmaceuticals
  Hayward, CA
- SciBac
  San Francisco, CA
- Specific Diagnostics
  Mountain View, CA
- Curza
  Salt Lake City, UT
- VenatoRx Pharmaceuticals
  Malvern, PA
- Integrated Biotherapeutics
  Rockville, MD
- Contrafect Corporation**
  Yonkers, NY
- Seres Therapeutics
  Cambridge, MA
- T2 Biotics
  Lexington, MA
- Helixbind Inc.
  Marlborough, MA
- Tetraphase Pharmaceuticals
  Watertown, MA
- Macrolide Pharmaceuticals
  Watertown, MA
- Entasis Therapeutics **
  Waltham, MA
- Microbiotix Inc.
  Worcester, MA

**Europe and Asia**

- Proteus IRC
  Edinburgh, Scotland
- Summit Therapeutics
  Oxford, UK
- Antabio
  Labège, France
- Idorsia
  Allschwil, Switzerland
- Polyphor
  Allschwil, Switzerland
- Debiopharm International S.A.**
  Lausanne, Switzerland
- Bugworks Research India Pvt Ltd.
  Bangalore, India

* As of May 14, 2019
** More than 1 project funded
Diversified portfolio, continually growing and evolving

- **3** projects in Ph 1 clinical trials; plus 3 graduates in the clinic
- **13** projects focused on new classes of antibiotics
- **8** non-traditional projects including 2 microbiome
- **12** projects focused on new molecular targets
- **5** rapid diagnostics
- **1** vaccine

More awards to be announced soon
Global Accelerator Network

Business and Scientific Expertise and Support

• Non-dilutive funding
• CARB-X Support Team established for each company
• CARB-X Support Team Lead
• Accelerator support aligned to company profile and needs – business mentoring and scientific expertise
• Streamlined access to NIAID preclinical services
• Benefits of CARB-X ecosystem

10 world class accelerators in 6 countries supporting the development of antibiotics and other life-saving products to fight drug-resistant superbugs
The CARB-X Advantage

• A global approach, with the world’s largest early development antibacterial portfolio

• Entrepreneurial culture, accelerating the most urgently needed innovative products with both funding and expert business, technical and regulatory support

• Focused on the most dangerous bacterial pathogens. Making a difference in the fight against drug resistance

• Investment community and policy makers gain valuable insight into potential new products, science and technology

• Bias towards more innovative, ground-breaking projects
What CARB-X Funds

- Early development projects that address serious bacterial threats
  - antibiotics and therapeutics
  - prevention such as vaccines, microbiome, antibodies
  - rapid diagnostics (pathogen ID/AST)

- Projects must target specific bacteria on the Antibiotic Resistance Threats List issued by the Centers for Disease Control and Prevention (CDC) in 2013 or on the Priority Bacterial Pathogens list published by the World Health Organization (WHO) in 2017
CARB-X supports projects in Early Development

**Therapeutics & Preventatives**
- Hit to lead
- Lead optimization
- Pre-clinical
- Phase 1

**Diagnostics**
- Feasibility demonstration
- Optimization & prep for development
- Product development
- System integration & testing

NB - scope definitions will be refined prior to the opening of that specific funding round
How Funding Decisions are Made

- Projects are selected through a global competitive process
- Science Advisory Board reviews applications and makes recommendations
- Joint Oversight Committee makes funding decisions
Who Can Apply for CARB-X Funding? (1)

CARB-X welcomes applications from around the world

- Projects must be in scope – CARB-X and specific round
- Applicants must have a legal entity
- Applicants must be able to contribute to the cost of the project (“cost share”) during all contractual stages - base (initial) period and each option period.
  - For Therapeutic and Preventative projects, the minimal cost-share requirement is as follows
    - 10% for the Hit-to-Lead, Lead Optimization and Pre-clinical (IND-Enabling) stages
    - 20% for the Phase 1 stage
  - For Diagnostic projects, the minimal cost-share requirement is as follows
    - 10% for the Feasibility Demonstration, Optimization & Prep for Development and Product Development stages
    - 20% for the System Integration and Testing stage
- Prior to completion of the CARB-X subaward negotiations with Boston University, applicants must
  - Have secured cost-share funds for the base (initial) stage of the project
  - Be a going concern or have a viable strategy to achieve/maintain financial sustainability
Who Can Apply for CARB-X Funding? (2)

CARB-X welcomes applications from around the world

- At the time of submission of a Long Form application, if the applicant does not yet fully own the intellectual property supporting the project submitted to CARB-X, the PD must have, as a minimum, an executed option agreement or letter of intent with any third parties from which they are seeking to access rights to the core intellectual property.

- At the time of execution of a sub-award (contract) with CARB-X/BU however, applicants must own or have rights to the intellectual property through an executed license or asset purchase agreement and reasonable expectation of freedom to operate required to carry out the project.

- Applicants must have operations or capabilities in place to support product development, particularly through development stages in scope for CARB-X.

- Applicants must be able to comply with UK NC3R requirements and US regulatory requirements for animal and human subjects research.

- Applicants from noncommercial centers or academic institutions must meet additional requirements (next slide).
CARB-X Welcomes Applications from Academic and Non-commercial Developers

Organization must be able to demonstrate R&D/business capabilities

- Capabilities similar to those expected of a drug development industry partner, particularly through the development stages in scope for CARB-X.
- Access to and use of relevant experts (internal and/or external) to advance projects toward clinical investigation within the framework of a major regulatory agency, e.g. FDA, EMA, PMDA
- Active management of IP supporting the project
- Well-developed strategy for advancement to early clinical development
- Capabilities in commercial (business) development and technology transfer with options for ‘exit strategy’ (e.g. spin out, licensure to biotech)
- Financial commitment and stability to cover cost share of at least 20% of the base stage (and any subsequent option stages as these are contracted)

Please note: CARB-X does not fund basic research/drug discovery including screening for novel targets
Research Compliance Requirements

• CARB-X is committed to the highest ethical standards in all research and business operations.

• CARB-X funded companies must comply with US Government regulatory requirements for animal research and human subjects research, even if the research is conducted outside the United States
  • **Office of Laboratory Animal Welfare (OLAW)** requirements for studies involving any vertebrate species
  • **USDA Registration** requirements for US-based research facilities performing studies involving warm-blooded animals not specifically excluded from the definition of “animal” in the US Animal Welfare Act and Animal Welfare Regulations
  • **Office of Human Research Protections (OHRP)** requirements for human subjects research

• CARB-X funded companies must make every reasonable effort to comply with NC3R guidance for studies involving large animals (primates, cats, dogs, equines)

• These requirements may impact both time and budget; they are critical to consider when building your project plan
UK Government Funding to CARB-X

• The UK Government's contribution to CARB-X is designated as 'official development assistance' or ODA

• The CARB-X application process uses the term ‘ODA’ to categorize this specific funding stream

• These funds are for R&D which can demonstrate specific benefits to people living in low- and middle-income countries (LMICs)

• Companies with projects that are applicable or can be adapted to suit the needs of people in LMICs are welcome to apply for these funds

• Applicability 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
  • As well as other solutions
UK Government Funding to CARB-X cont’d

• Scope includes programs which can be designated as ‘alternatives to traditional antibiotics’, e.g.
  • Bacteriophage
  • Microbiome
  • Vaccines
  • Antibodies
  • potentiatiors (including beta-lactamase inhibitors)
  • anti-biofilm approaches
  • anti-virulence approaches
  • and other approaches exemplified in the Lancet publication by Czaplewski et al entitled ‘Alternatives to antibiotics—a pipeline portfolio review’ (if within the general CARB-X funding scope)

• Direct-acting small molecule and diagnostic programs are not included in the GAMRIF funding scope

• ODA-eligible research and development
  • Must target problems directly and primarily relevant to LMICs
  • Should investigate a specific problem or seek a specific outcome which will impact LMICs in the immediate or longer-term
  • Demonstrate appropriate pathways to ensure LMIC benefits from the research
  • While LMICs should be the primary beneficiaries, the research can also be relevant and have secondary benefits for higher-income countries

Details https://carb-x.org/apply
## What to Expect When You Apply

### About 8 months from EOI to decision

<table>
<thead>
<tr>
<th>Cycle begins</th>
<th>Expression of Interest</th>
<th>Review by CARB-X</th>
<th>Short Form</th>
<th>Review by CARB-X</th>
<th>Long form</th>
<th>Final Review</th>
<th>Funding</th>
</tr>
</thead>
<tbody>
<tr>
<td>CARB-X sets the scope and timing of funding cycle, and opens the application period.</td>
<td>Product developers submit a non-confidential Expression of Interest (EOI) summarizing the product proposed as a candidate for support.</td>
<td>CARB-X evaluates the application and selects qualifying projects. CARB-X invites selected applicants via email to provide more detail in a confidential Short Form.</td>
<td>Selected companies submit a confidential Short Form.</td>
<td>CARB-X evaluates the Short Form and invites selected applicants via email to provide more detail in a confidential Long Form.</td>
<td>Selected applicants submit a Long Form and detailed budget.</td>
<td>Long Form applicants are invited to present their project proposals in person to an Advisory Board panel. Applicants undergo due diligence.</td>
<td>Final funding decisions made by CARB-X’s JOC. Sub-award negotiations begin on project plan, milestones and budgets. Applicants must agree contractually to certain standards and conditions. Project support begins.</td>
</tr>
</tbody>
</table>
2019: Four Funding Rounds

- Funding Round 1 – Non-traditional approaches
  - Open for applications: June 3 – June 10, 2019, 5 PM ET
- Funding Round 2 – Vaccines and biotherapeutics
  - Open for applications: July 8 – July 15, 2019, 5 PM ET
- Funding Round 3 – Diagnostics
  - Open for applications: August 12 – August 19, 2019, 5 PM ET
- Funding Round 4 – Direct-acting small molecule
  - Open for applications: November 12 – November 19, 2019, 5 PM ET

The only way to apply
Applicants must complete and submit the online Expression of interest form at https://carb-x.org/apply during the periods specified for each round. The online application tool will be functional only during these periods.
CARB-X 2019 Funding Round 1

• **Scope:** Non-traditional approaches
  - Indirect acting small molecules (virulence, potentiators, BLI combinations etc.)
  - Direct- and indirect-acting large molecules (peptides, etc.)
  - Phage
  - Microbiome
  - Nucleic acid/anti-sense
  - Drug conjugates (ADC, other dual acting drug conjugates)
  - See next slide for scope in detail

• Expressions of Interest (EOI) accepted online only [https://carb-x.org/apply](https://carb-x.org/apply)

• EOI must be submitted June 3 - June 10, 2019, 5 PM ET
# CARB-X 2019 Funding Round 1 – Non-traditional approaches

Examples: indirect-acting small molecules (anti-virulence approaches, potentiators, BLI combinations etc.), direct acting or indirect-acting large molecules (peptides etc.), microbiome, phage, nucleic acid/antisense, drug conjugates (ADC, other dual acting drug conjugates) etc. as per the pathogens below. Host-directed therapies are not in scope. Biocides/antiseptics/disinfectants are not in scope. EOI must be submitted online June 3 - June 10, 2019, 5 PM ET. [https://carb-x.org/apply](https://carb-x.org/apply)

<table>
<thead>
<tr>
<th>Pathogen Scope</th>
<th>Prevention</th>
<th>Indirect Tx</th>
<th>Direct Tx*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acinetobacter baumannii, carbapenem-R</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa, carbapenem-R</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Enterobacteriaceae, carbapenem-R, 3rd-gen ceph-R (ESBL+)</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Enterococcus faecium, vancomycin-R</td>
<td>YES</td>
<td>YES</td>
<td>NO</td>
</tr>
<tr>
<td>Staphylococcus aureus, methicillin-R, vancomycin-I/R</td>
<td>YES</td>
<td>YES</td>
<td>NO</td>
</tr>
<tr>
<td>Campylobacter spp., fluoroquinolone-R</td>
<td>YES</td>
<td>YES</td>
<td>NO</td>
</tr>
<tr>
<td>Salmonellae spp., fluoroquinolone-R</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Neisseria gonorrhoeae, 3rd-gen ceph-R, fluoroquinolone-R</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Streptococcus pneumoniae, penicillin-NS</td>
<td>YES</td>
<td>YES</td>
<td>NO</td>
</tr>
<tr>
<td>Shigella spp., fluoroquinolone-R</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Group A Streptococcus</td>
<td>YES</td>
<td>YES</td>
<td>NO</td>
</tr>
<tr>
<td>Group B Streptococcus</td>
<td>YES</td>
<td>YES</td>
<td>NO</td>
</tr>
</tbody>
</table>

Tx = therapeutic

NB: For BLI products – scope is restricted to products that are both 1) broad spectrum (product needs to address both serine and metallo-betalactamases) and 2) have oral delivery

*the spectrum of direct acting products can include Gram-positive pathogens however the program must prioritize the Gram-negative pathogens included in the product’s spectrum, as evidenced by the data developed at time of application and the workplan/TPP presented to CARB-X

**Mode of administration preference guidance:**
For Enterobacteriaceae offerings: If Tx is only for ESBL (e.g. lacks CRE), PO options are higher priority than IV only
For *Salmonellae spp.*, *Shigella spp.* and *Neisseria gonorrhoeae* offerings – if Tx (direct or indirect), oral delivery is strongly preferred
The only topical delivery in scope is inhalation (e.g. dermal, nasal, intra-wound/surgical site, ocular etc. are not in scope)
CARB-X 2019 Funding Round 2

• Scope: Vaccines & Biotherapeutics
  – Vaccines
  – Therapeutic and preventative antibodies and fragments
  – Other large molecule biotherapeutics (not direct- or indirect-acting peptides)
  – See next slide for scope in detail

• Expressions of Interest (EOI) accepted online only [https://carb-x.org/apply](https://carb-x.org/apply)
• EOI must be submitted July 8 – July 15, 2019, 5 PM ET
CARB-X 2019 Funding Round 2 – Vaccines & Biotherapeutics

Vaccines, therapeutic and preventative antibodies and fragments, other large molecule biotherapeutic approaches (not including direct- or indirect-acting peptides) as per the pathogens below. Host-directed approaches are not in scope.

EOI must be submitted online July 8 – July 15, 2019, 5 PM ET. https://carb-x.org/apply

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<td>YES</td>
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<td>YES</td>
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<td>YES</td>
<td>YES</td>
<td>NO</td>
</tr>
<tr>
<td>Campylobacter spp., fluoroquinolone-R³</td>
<td>YES</td>
<td>YES</td>
<td>NO</td>
</tr>
<tr>
<td>Salmonellae spp., fluoroquinolone-R¹</td>
<td>YES</td>
<td>YES</td>
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<td>Neisseria gonorrhoeae, 3rd-gen ceph-R, fluoroquinolone-R</td>
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<td>Group A Streptococcus</td>
<td>YES</td>
<td>YES</td>
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Tx = therapeutic

*the spectrum of direct acting products can include Gram-positive pathogens however the program must prioritize the Gram-negative pathogens included in the product’s spectrum, as evidenced by the data developed at time of application and the workplan/TPP presented to CARB-X
CARB-X 2019 Funding Round 3

• Scope: Diagnostics
  – Pathogen ID/AST
  – See next slide for detailed pathogen list
• Expressions of Interest (EOI) accepted online only [https://carb-x.org/apply](https://carb-x.org/apply)
• EOI must be submitted August 12 – August 19, 2019, 5 PM ET
CARB-X 2019 Funding Round 3 – Diagnostics

Only pathogen ID/AST approaches are in scope, as per the pathogens below. Host-biomarker approaches are not in scope.

EOI must be submitted online August 12 – August 19, 2019, 5 PM ET. [https://carb-x.org/apply](https://carb-x.org/apply)

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<td>Clostridium difficile</td>
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</tbody>
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CARB-X 2019 Funding Round 4

• Scope: Direct-acting small molecule
  – Restricted to new class and/or new target
  – See next slide for scope in detail

• Expressions of Interest (EOI) accepted online only https://carb-x.org/apply
• EOI must be submitted November 12 – November 19, 2019, 5 PM ET
CARB-X 2019 Funding Round 4 – Direct-acting small molecule

Restricted to new classes and/or new targets only

EOI must be submitted online November 12 – November 19, 2019, 5 PM ET. [https://carb-x.org/apply](https://carb-x.org/apply)

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*the spectrum of direct acting products can include Gram-positive pathogens however the program must prioritize the Gram-negative pathogens included in the product’s spectrum, as evidenced by the data developed at time of application and the workplan/TPP presented to CARB-X

New class is defined as: a core chemical structure (or scaffold) that does not have an antibiotic approved for human use by the FDA, EMA as of May 1, 2019

If program is an LpxC inhibitor program, applicants should access information available on the PEW Spark database, particularly, if the program is hydroxymate based to ensure proposals have considered the learnings appropriately and have these addressed upfront in these applications submitted to CARB-X

**Mode of administration preference guidance:**

For Enterobacteriaceae offerings: If only for ESBL (e.g. lacks CRE), PO options are higher priority than IV only

For Salmonellae spp., Shigella spp. and Neisseria gonorrhoeae offerings – oral delivery is strongly preferred

The only topical delivery in scope is inhalation (e.g. dermal, nasal, intra-wound/surgical site, ocular etc. are all not in scope)

Biocides /antiseptics/disinfectants are not in scope
Applying for CARB-X funding, in brief

- Funding Round 1 – Non-traditional approaches
  - June 3 – June 10, 2019, 5 PM ET
- Funding Round 2 – Vaccines and biotherapeutics
  - July 8 – July 15, 2019, 5 PM ET
- Funding Round 3 – Diagnostics
  - August 12 – August 19, 2019, 5 PM ET
- Funding Round 4 – Direct-acting small molecule
  - November 12 – November 19, 2019, 5 PM ET

- CARB-X welcomes applications from around the world
- Expressions of Interest applications must be submitted online, only during the periods indicated [https://carb-x.org/apply/](https://carb-x.org/apply/)
- To qualify for funding and support, projects must be in scope and organizations must meet certain criteria
  
  For full details, please visit [https://carb-x.org/apply/](https://carb-x.org/apply/)
  For specific questions, please contact carbxapp@bu.edu

NB: Watch for webinars on Research Compliance and ODA in the coming weeks
Thank you!

Questions and discussion
Research Compliance Requirements

- CARB-X is committed to the highest ethical standards in all research and business operations. CARB-X funded companies **must comply** with United States Government regulatory requirements for animal research and human subjects research, even if this research is conducted outside the United States. Requirements include
  - **Office of Laboratory Animal Welfare (OLAW)** requirements for studies involving any vertebrate species
    - Every performance site for CARB-X funded studies must have either domestic or foreign OLAW Assurance.
    - An Inter-Institutional Assurance (IIA) is required for product developers that do not/cannot have their own Assurance and must rely on a CRO or other third party performance site that has an Assurance
    - Boston University must prompt OLAW on behalf of the CARB-X subawardees. OLAW does not accept or process unsolicited applications
  - **USDA Registration** requirements for US-based research facilities performing studies involving warm-blooded animals not specifically excluded from the definition of “animal” in the US Animal Welfare Act and Animal Welfare Regulations
  - **Office of Human Research Protections (OHRP)** requirements for human subjects research
    - Study start prerequisites including, but not limited to, the approved study protocol, investigator brochure, IRB or IEC approved informed consent document, OHRP FWA number, and IRB or IEC approval letter. Note that BARDA and BU must review and approve all documents before a study may begin
    - Monitoring including bi-weekly clinical teleconferences and independent monitoring.
    - Monthly, annual, and ad hoc reporting, including certain reports that must be filed within either 24 hours or 3 days of occurrence.

- CARB-X funded companies must make every reasonable effort to comply with NC3R guidance for studies involving large animals (primates, cats, dogs, equines)

- These requirements will impact both time and budget; they are critical to consider when building your project plan
Research Compliance Requirements

• Consider requirements and the approximate timelines when building your project plan
• Submit the Attachment A and A-1 form detailing all planned animal studies and human subjects research when your application reaches the Long Form stage
• CARB-X will review and determine whether further action is required. This may be in advance of a positive funding decision
• Here is what you can be doing now in case you receiving a positive funding decision and successfully negotiate a sub-award with CARB-X
  – For animal studies
    • Select a CRO that has OLAW assurance if possible. If this is not possible, confirm the CRO meets OLAW requirements for assurance and begin compiling the required documentation (VAS describing studies per OLAW guidelines and IACUC approval letters for the protocols under which the studies will be conducted)
    • If your studies involve large animals, confirm the CRO is familiar with NC3R guidelines. Reach out to CARB-X for further guidance
    • Prepare the required documentation: the VAS describing studies per OLAW guidelines and IACUC (or IACUC equivalent) approval letters for the protocols under which the studies will be conducted
  – For human subjects research
    • Review Human Subjects Research Checklist; begin compiling the required documentation
Human Subjects Research Checklist: Prerequisites to Study Start

- Study Protocol
- Investigator Brochure
- Institutional Review Board (IRB) or Institutional Ethics Committee (IEC) approved informed consent document
- Office for Human Research Protection (OHRP) federal wide assurance (FWA) number, or the IRB or IEC name and registration number, for each of the following:
  - Each Study Site (e.g. university, hospital, etc.)
  - IRB or IEC that will review the study
  - Any other body directly involved in the research
- Name and contact information for the primary physician at the center and/or CRO that will be primarily accountable for managing a subject/AE/SAE/etc.
- Approval letter from an IRB or IEC
- Documentation that the sub-recipient and all study staff responsible for the design or conduct of the research have received training in the protection of human subjects.
- Approval letter (or equivalent) from the relevant regulatory agency in the US or any other country involved, e.g. FDA approval letter for an IND application for a US trial. Written documentation from FDA regarding comments, etc.
- Statement acknowledging satisfaction of all regulatory requirements of any country involved in the clinical trial, and responsibility for ongoing regulatory compliance.
- Description of the process used for scientific review of the Clinical Trial Protocol, e.g. who reviewed it, when it was reviewed, sign-off, etc.
- Written summary of PD’s plans and procedures for: (1) Management of side effects; (2) Assessing and reporting adverse events; and (3) Data and safety monitoring, and monitoring of the clinical study site, pharmacy, and laboratory.
- Existing FDA or other regulatory agency submission documentation and correspondence
- Documentation of registration on ClinicalTrials.gov

NB: BARDA and BU must review and approve all documents before a study may begin
## Human Subjects Research: Monitoring Requirements

<table>
<thead>
<tr>
<th>Form</th>
<th>Expectations</th>
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</table>
| **Bi-Weekly Clinical Teleconferences** | • PDs will be expected to participate in calls every two weeks (in addition to CST calls) at least one month prior to study start and through final study report.  
• PDs will be expected to provide status updates about the trial and report findings.  
• PDs will be expected to circulate an agenda in advance and email minutes in follow up to the call.  
• At least one PD expert associated with the trial will be expected to provide this update; BARDA clinical experts and a CARB-X representative will participate. |
| **Non-HSR Specific Monitoring**   | • Monthly Company Support Team Meetings, to provide support and guidance with respect to the position of HSR work in the overall PD program.  
• Establishment or demonstration of an SAB with adequate oversight over HSR work.                                                                                                                                 |
| **Independent Monitoring**        | • *This is strongly recommended* for any clinical research involving more than minimal risk to volunteers.  
• The type of monitoring appropriate for the research should be determined jointly by the PD and BU prior to enrollment, and may take the form of an Independent Safety Monitor, Committee, or DSMB.  
• If independent monitoring is used,  
  1) PD should inform BU of any upcoming site visits or audits;  
  2) BU and BARDA may attend such site visits or audits; and  
  3) The PD should provide a written summary to BARDA of all monitoring reviews within 3 days of the review. |
# Human Subjects Research: Reporting Requirements

<table>
<thead>
<tr>
<th>Timing</th>
<th>Reporting Requirement</th>
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<tbody>
<tr>
<td><strong>Reports Required Immediately or Within 24 Hours</strong></td>
<td>• All FDA submissions, reports, or correspondence</td>
</tr>
<tr>
<td></td>
<td>• <strong>Required Time Sensitive Notifications</strong> are FDA safety reports of serious adverse events under IND or IDE</td>
</tr>
<tr>
<td></td>
<td>• Notification to BU of an FDA or EMA audits is required within 5 days of a scheduled audit or site visit OR within 12 hours of an ad hoc audit or site visit</td>
</tr>
<tr>
<td><strong>Reports Required Within 3 Business Days of Occurrence</strong></td>
<td>• Major changes to the status of IRB approvals and ongoing protocols</td>
</tr>
<tr>
<td></td>
<td>• Any reviews by an institutional biosafety committee or the NIH Recombinant DNA Advisory Committee</td>
</tr>
<tr>
<td><strong>Monthly Reporting</strong></td>
<td>• Monthly technical/progress reporting as outlined in Attachment 4 &amp; 6, including a comprehensive status update of clinical studies actively enrolling patients for each study site</td>
</tr>
<tr>
<td><strong>Annual Reporting</strong></td>
<td>• Continuing IRB review by each institution involved in the research or the central IRB, if review is ceded to a single IRB</td>
</tr>
<tr>
<td></td>
<td>• Adverse events documented during the trial and which are reportable in the annual IND or IDE report</td>
</tr>
<tr>
<td><strong>Other Ad Hoc Reporting</strong></td>
<td>• Ongoing safety reporting for research not performed under an IND/IDE</td>
</tr>
<tr>
<td></td>
<td>• Ad hoc reporting as requested under Attachment 4a regarding clinical study information</td>
</tr>
<tr>
<td></td>
<td>• A written report when the PD completes a Milestone</td>
</tr>
<tr>
<td></td>
<td>• A final technical/progress report is required to be submitted within 30 days after the end of the period of performance</td>
</tr>
</tbody>
</table>
# Animal Research: Key Terms & Resources

<table>
<thead>
<tr>
<th>Term</th>
<th>Acronym</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Office for Laboratory Animal Welfare</td>
<td>OLAW</td>
<td>OLAW is a United States Government agency responsible for ensuring the humane care and use of animals in Public Health Service-supported research, testing, and training. OLAW is responsible for granting assurance and Interinstitutional Assurance. More detail is available on the OLAW website <a href="https://olaw.nih.gov/">https://olaw.nih.gov/</a>.</td>
</tr>
</tbody>
</table>
| Domestic Assurance                                                   |         | Domestic Assurance is required for any US-based performance site performing animal studies as part of a CARB-X subaward. OLAW negotiates domestic assurance with US-based performance sites that  \  - control their own animal facilities  \  - conduct animal research on-site  \  - have an animal care and use program with:  \  - an Institutional Official (IO)  \  - an Institutional Animal Care and Use Committee (IACUC)  \  - a veterinarian with program authority  
The OLAW website includes a list of performance sites with domestic assurance [https://grants.nih.gov/grants/olaw/assurance/300index.htm](https://grants.nih.gov/grants/olaw/assurance/300index.htm). |
| Foreign Assurance                                                    |         | Foreign Assurance is required for any performance site outside the United States performing animal studies as part of a CARB-X subaward. OLAW negotiates foreign assurance with non-US based performance sites that  \  - control their own animal facilities  \  - conduct animal research on-site  \  - have an animal care and use program with an authorized institutional signing official  
The OLAW website includes a list of performance sites with foreign assurance [https://grants.nih.gov/grants/olaw/assurance/500index.htm](https://grants.nih.gov/grants/olaw/assurance/500index.htm). |
<p>| Interinstitutional Assurance                                         | IIA     | OLAW negotiates IIAs with PDs who do not have their own domestic or foreign assurance and are contracting with an external performance site that does.                                                                 |
| National Centre for the Replacement, Refinement and Reduction of Animals in Research | NC3R    | NC3R is a UK-based scientific organization dedicated to replacing, refining and reducing the use of animals in research and testing. CARB-X funded companies must make every reasonable effort to comply with NC3R guidance on treatment of large animals (primates, cats, dogs, equines). More detail is available on the NC3R website <a href="https://www.nc3rs.org.uk/">https://www.nc3rs.org.uk/</a>. |</p>
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<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Contract Research Organization</td>
<td>CRO</td>
<td>An organization that provides research services to a PD on a contract basis.</td>
</tr>
<tr>
<td>Institutional Animal Care and Use Committee</td>
<td>IACUC</td>
<td>An IACUC is a federally mandated committee that oversees its institution’s (PD, CRO, academic site) animal care and use program, facilities, and procedures</td>
</tr>
<tr>
<td>Joint Oversight Committee</td>
<td>JOC</td>
<td>CARB-X’s governing board</td>
</tr>
<tr>
<td>Memorandum of Understanding</td>
<td>MOU</td>
<td>An agreement required between Boston University, the PD, and, if applicable, the performance site. The MOU must be fully executed before a PD can invoice CARB-X for its studies</td>
</tr>
<tr>
<td>Office of Sponsored Programs</td>
<td>SP</td>
<td>SP is the group within Boston University Research Administration which requests assurance on behalf of PDs</td>
</tr>
<tr>
<td>Performance Site</td>
<td></td>
<td>The physical location where animal research is conducted. OLAW assurance is specific to a performance site. If a PD or CRO has more than one site, each site must have the proper assurance</td>
</tr>
<tr>
<td>Product Developer</td>
<td>PD</td>
<td>A CARB-X funded entity</td>
</tr>
<tr>
<td>Vertebrate Animal Section</td>
<td>VAS</td>
<td>A document describing the planned animal studies required by OLAW prior to issuing an assurance or IIA. PDs working with their CROs (if applicable) must include a sufficient level of detail on 1. Description of Procedures 2. Justifications of Animal Use 3. Minimization of Pain and Distress 4. Method of Euthanasia For a full description of the VAS, visit the OLAW website <a href="https://olaw.nih.gov/guidance/vertebrate-animal-section.htm">https://olaw.nih.gov/guidance/vertebrate-animal-section.htm</a></td>
</tr>
</tbody>
</table>
ODA Eligibility - Checklist

- Applying for ODA support is optional but encouraged
- The target country/countries is featured on the OECD DAC list*
- The primary objective of the project, or portion of the project, is the promotion of economic development and welfare of an LMIC
- The project, or portion of project, seeks a specific outcome which will have an impact on a developing country or countries
- The applicant can articulate with credible evidence what the specific need is and why this is a problem for the LMIC(s)
- The applicant has identified and articulated appropriate pathways to impact to ensure that the LMIC(s) benefits from the research
- The project team has the appropriate knowledge and expertise to deliver


UK GAMRIF investment funds will be focused on those projects which 1) comply with ODA eligibility requirements and 2) meet the GAMRIF scope which includes programs which can be designated as ‘alternatives to traditional antibiotics’, for example: bacteriophage, microbiome, vaccines, antibodies, potentiators (including beta-lactamase inhibitors), anti-biofilm approaches, anti-virulence approaches and other approaches exemplified in the Lancet publication by Czaplewski et al entitled ‘Alternatives to antibiotics—a pipeline portfolio review’ (if within the general CARB-X funding scope). Direct-acting small molecule and diagnostic programs are not included in the GAMRIF funding scope.
<table>
<thead>
<tr>
<th>Key Criteria</th>
<th>Applicability to CARB-X Applicants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Promote the welfare and economic development of LMICs</td>
<td>This might be accomplished through ▪ New development- e.g., a new vaccine or therapeutic ▪ Meeting unmet challenges of LMICs ▪ Building research capacity - e.g., a program that increases the skills and knowledge base and supports the development of the research capability within LMIC(s)</td>
</tr>
<tr>
<td>Directly and primarily relevant to the problems of LMICs</td>
<td>▪ Research does not need to be solely relevant to LMICs, but LMICs must be the primary beneficiaries ▪ Commercialization of research cannot solely take place in developed countries ▪ Issues which are global in nature (e.g. global good) are not necessarily ODA compliant unless the research (or a particular work package of the research) can articulate the primary intention of benefitting people in LMIC (i.e. LMICs as the primary beneficiaries)</td>
</tr>
<tr>
<td>Investigate a specific problem or seek a specific outcome which will impact LMICs in the immediate or longer-term</td>
<td>▪ The problem or need must be clearly articulated, credible and backed up (where possible) with evidence/statistics; applications should articulate a development impact even if outside the timeframe of CARB-X funding ▪ The pathways to impact must be realistic and appropriate to the particular LMIC’s context ▪ Applications should describe the nature and scale of the problem or challenge they are seeking to address through this research (e.g., how many people would be affected by progress in this area?) ▪ The LMIC must be able to access or make use of the data, technology or model beyond the grant period ▪ Where the research could lead to commercialization, the LMIC(s) must have an existing or potential ability to grow the industry</td>
</tr>
<tr>
<td>Demonstrate appropriate pathways to impact that ensure the LMIC benefits from the research.</td>
<td>The likelihood and scale of beneficial impact are increased by the following factors ▪ If the research is orientated towards a problem or challenge where there is potential to benefit a large number of people to a significant degree ▪ If the research team can demonstrate experience or understanding of successful impacts within the specific context ▪ If stakeholders that are close to the problem private sector and/or public sector and government, are actively involved in the research ▪ If there are specific commitments from institutions/enterprises from LMICs to adopt/apply outcomes of the research ▪ If stakeholder collaboration and knowledge exchange activities enhance local innovation and research capacity at an individual, institutional or whole system level</td>
</tr>
</tbody>
</table>
ODA Eligibility - FAQs

1. Which countries are considered low and middle income countries (LMICs)?
   Countries on the Development Assistance Committee (DAC) list are considered LMICs. The DAC list designation is based on gross national income (GNI) per capita as published by the World Bank. The link to the list can be found here at http://www.oecd.org/dac/financing-sustainable-development/development-finance-standards/DAC_List_ODA_Recipients2018to2020_flows_En.pdf

2. Can ODA eligible research also be relevant to developed countries?
   Yes. Research does not need to be solely relevant to LMICs, but LMICs should be the primary beneficiaries. Any benefit to developed countries has to be a secondary consideration. Also, commercialization of research cannot solely take place in developed countries.

3. AMR is a global issue. Does this mean that every AMR project is ODA eligible?
   It depends on how the primary intention of the project is articulated. The primary objective of the research must have a specific impact in the developing country. The applicant must identify the challenge in the context of the impact upon the welfare of developing country populations and back it up with figures if available.

4. My project is in an early stage of development; do I need to articulate a development impact?
   Applications must articulate a development impact even if outside the timeframe of the CARB-X funding. The focus should be on the impact upon LMIC populations, and how their lives will be improved.

5. Can research carried out in a developed (non LMIC) country be ODA eligible?
   Yes, as long as the intention of the research directly and primarily benefits LMICs.

6. How does an applicant balance the uncertainty of research in assessing impact?
   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.

7. Is it possible to have just a part of a project be considered as ODA eligible?
   Yes, it is possible that a discrete package of work within a project complies with ODA.
Thank you!