CARB-X

CARB-X Application 2018 Funding Round 1
Frequently Asked Questions

Scope Questions:

1. Are lytic phage therapeutics considered direct-acting large molecule therapeutics and thus in scope for Round 1?
    a. Yes, if they directly act on the Gram-negative pathogens specified in focus for Round 1 (I.e., have a MIC).
2. Are all DHFR inhibitors out of scope for Round 1 or just "trimethoprim"?
    a. Round 2 would be the appropriate round for submission of an EOI for DHFR inhibitors.
3. Is tuberculosis in scope for CARB-X?
    a. TB is not in scope for CARB-X as there are other important groups with particular expertise addressing this challenge including the Gates Foundation and TB Alliance.
4. Are virulence blockers in scope?
    a. Virulence blockers are NOT in scope for Round 1 but ARE in scope for Round 2 if they address the in-scope pathogens as outlined.
5. Would Candida be in scope?
    a. Candida (Fungi generally) are not in scope for CARB-X. We focus on bacteria only.
6. How is 'new class' defined? Would repurposing an older antibiotic that has not been previously studied for Gram-negative organisms constitute a "new class" and/or meet the requirements for the March submission deadline?
    a. The definition we are applying for Round 1 for 'new class' is as follows: NEW class small molecule is defined as a core chemical structure (scaffold) that does not have an antibiotic for human use approved by the FDA or EMA as of March 1, 2018.
    b. New molecular entities in known classes and also repurposed older antibiotics would be welcome in Round 2 (EOI in June) assuming they address the in-scope pathogens.
7. Regarding the statement that 2018 Funding Round 1 is restricted to 1) *NEW classes of direct acting small molecule therapeutics and 2) direct-acting large molecule therapeutics for the specified Gram-negative pathogens,* does the Gram-negative condition only refer to point 1) or to both 1) and 2)?
    a. For Round 1 we are only accepting applications for projects that target the 6 Gram-negative pathogens on the table provided on the website and the projects must be either a new class direct-acting small molecule or a direct acting large molecule (<u>so the Gram-negative condition applies to both 1) and 2)</u>).

8. Are direct-acting therapies for *H. pylori* in scope?
    a. We are welcoming EOIs in Round 2 for indirect-acting agents, preventatives or diagnostics for clarithromycin resistant *H. pylori*. Direct-acting agents against this pathogen are not in scope for CARB-X 2018 funding rounds. For this pathogen, it would be important in any EOI to include a discussion of intended/potential routes for sourcing of funding for later stages of clinical development.
9. I thought CARB-X is focused on G-negative pathogens only but Round 2 seems to include MRSA as long as it has activity against G-negative. Please confirm?
    a. CARB-X has a strong focus on Gram-negative pathogens but not to the exclusion of important Gram-positive challenges. However, we have quite well-defined interests (some may only be in scope if they target an important Gram-negative pathogen as well, some may only be in scope for indirect-acting approaches, etc.) so we encourage you to review the scope slides on our website carefully. http://carb-x.org/files/1a_CARB-X_portfolio_strategy_2018.pdf
10. Do you only fund projects in clinical development (like BARDA)?
    a. No, CARB-X's funding scope is from 'hit-to-lead' to Ph1 SAD/MAD.
11. Does our drug need to be active against all 6 pathogens (March cycle)?
    a. No, as long as it is active against one of the Gram-negative pathogens listed and is either a NEW CLASS direct-acting small molecule or a direct-acting large molecule and is between 'hit-to-lead' and Phase 1 development, it would be in scope for Round 1.
12. Does round 2 include host-based dx that differentiate bacterial and viral infections?
    a. Yes, as long as it covers the pathogens of interest.
13. We have non-antibiotic compounds which are effective against pathogens on your list. Would you support academic project to advance it?
    a. Academic partners are possible as long as they are associated with drug development centers and meet other criteria as outlined on our website. http://carb-x.org/application. We assume these are indirect-acting compounds and therefore may be eligible for Round 2 EOI submission in June.
14. Does CARB-X also support universities to develop novel pipelines/software that facilitates novel drug discovery against bacterial drug resistance?
    a. Academic partners are possible as long as they are associated with drug development centers and meet other criteria as outlined on our website. http://carb-x.org/application. Development of discovery platform tools are important, but outside of CARB-X scope.
15. We have compounds that modulates the body's innate immunity and also kills Gram negative bacteria. Would CARB-X support this class that is not direct acting?
    a. Applications for indirect-acting projects are welcome in Round 2 presuming it meets the other scope elements (pathogens, stage of development, etc.)
16. The current focus seems to be on therapeutics. I assume that the next round will include diagnostic approaches?

a. Yes

17. Is there an interest/support needed in collecting multidrug resistant bacteria, listed in the CDC/WHO priority list, recovered from animal sources?
    a. No.

Organization and Funding Questions:

1. For a European entity to apply is SME (Small and medium-sized enterprise) status required?
    a. No, SME status is not required to qualify as an application for CARB-X. As long as the criteria outlined in our application section of carb-x.org are met, the applicant may apply.
2. Do you know what the funding is for each application and scope?
    a. It is variable and dependent on the individual project. You can read some of our press releases on the website or the company profiles on the pipeline/snapshot page to get a sense of prior investments.
3. Is the funding 100% or is co-financing required by the company?
    a. The company needs to provide at least 30% of the cost of the project. More is welcome and makes the project more competitive for a positive funding decision.
4. For the 30% of cost share required from the applicant organization is this actual cash or in-kind contribution such as FTE, materials and equipment etc.
    a. The 30% cost share can be met through those in-kind costs you have outlined as well as travel, contractor (CRO) and consultant payments, so long as all of the cost share meets the US "uniform guidance" requirements that are typical for NIH grants.
5. What does the subsidy cover in terms of materials, personnel, and consumables?
    a. It covers personnel/fringe, travel, supplies, contracts, consultants, etc., but there are clear guidelines that we need to follow as to what are reasonable, allowable costs, etc., as are typical for NIH grants.
6. Are co-applicants required from the USA for international applicants?
    a. No.
7. Does the applicant legal entity need to have a SAM requisition in order to (1) apply and (2) receive CARB-X funding?
    a. You do not need a SAM registration to apply but you do need it at the contracting stage – we cannot sign an agreement with you without one.

8. Applicants must own or have rights to the intellectual property and have reasonable expectation of freedom to operate required to carry out the project. Does that mean that a program that is not yet patented would not qualify (let's say the priority filing is scheduled mid-2018)?
    a. That would qualify as long as whomever submit the application will own/control those patent filings.
9. Does having an option to the IP qualify as 'owning or having the rights to the IP'?
    a. No.
10. I will be submitting an EOI with the support of 3 other groups. Do we all need to provide 30% funding towards the project?
    a. There must only be one applicant for a project with a Principle Investigator clearly identified from the applying organization. The applicant must commit at least 30% of the cost of the project but the source of the funding behind that 30% can come from, in part, the other groups which would be subcontractors to or partners with the applying organization.
11. In the case of collaborations between academic and industry/CROs, does it matter which entity applies? E.g., it may be that neither the academic nor the CRO intends to conduct PH2 and beyond, but they wish to collaborate to see the asset to value inflection point and then out-license to biopharma/pharma. As long as the capabilities and expertise are there, between the collaborating parties, does it matter which entity applies?
    a. The entity that has rights to the IP should be the applicant. CARB-X does not see a rationale for a CRO to be the applicant.
12. How would CARB-X view join ventures between companies?
    a. Joint ventures are welcome; however, we would need one lead organization to be the applicant, not two.
13. Please explain more on cost sharing. Does an early stage start up need to have matching money in order to be qualified for funding from CARB-X?
    a. Yes, applicants must be able to cost-share at least 30% of the project budget. Applicants with more financial resources will make their applications more competitive by proposing a higher applicant cost share.
14. The CARB-X website states: "Commercial drug developers must have an appropriate operations or capabilities in place to support product development, particularly through the development stages in scope for CARB-X". If the applicant applies to CARB-X for a project that goes from hit to lead to candidate selection, does that applicant only need the capabilities and expertise only for those activities? Or does the applicant need to demonstrate that it has the "appropriate operations or capabilities in place to support" clinical development – i.e., all stages of development within scope for CARB-X even if their project for which they apply for funding does not go that far?
    a. They would have to have the basic capabilities for the stages they are requesting support for (whether in house or existing/planned collaborations) but CARB-X would reasonably want to understand the applicant's intent for supporting the project beyond (building out own organization or out-licensing etc) so that project has some certainty of progression beyond the CARB-X funded period.

15. Are there any future revenue sharing and royalty commitment for CARB-X funded project?
    a. No.
16. Is there a project review with CARB-X at the end of each phase, i.e., like a phase gate review to determine next steps for the project?
    a. Yes, toward the end of each phase (CARB-X uses the term 'stage'), there is a review of project progress against the milestones / expectations for that phase at a CARB-X Milestone Review Board (MRB). During this meeting the company presents it's perspectives on progress/outcomes to the MRB followed by a Q&A. Subsequent to that interaction, the MRB advises the CARB-X Joint Oversite Committee (our Board) on their recommendations regarding the next stage (Option stage).
17. Are entities such as the Broad Institute, etc. accelerators? How do companies in the CARB-X portfolio access the drug development and business support from accelerators?
    a. The Broad Institute and RTI are not an accelerator. MassBio, CLSI and the Wellcome Trust are currently the accelerators within CARB-X. A support team will be developed for each company based on their specific needs.
18. How frequently the required activity reports are (daily, weekly or monthly)? Time card reporting frequency?
    a. Progress reports and invoices are expected on a monthly basis. There is no time-card frequency requirement, but for most of our PDs, CARB-X requires payroll documentation as part of the invoice backup.
19. Any rules or mandatory requirements for selecting subcontractors by awardees?
    a. No mandatory requirements for selection of subcontractors or vendors. However, the PD must maintain records sufficient to detail the history of procurement of vendors. These records will include, but are not necessarily limited to the following: rationale for the method of procurement, selection of contract type, contractor selection or rejection, and the basis for the contract price (see: HHS Uniform Guidance - General Procurement Standards: https://www.ecfr.gov/cgi-bin/text-idx?node=pt45.1.75#se45.1.75_1327)
20. Does CARB-X require financial or audit reports for compliance on chosen subcontractors/ collaborators? If so when in the development process?
    a. PDs expending $750k or more in federal awards during their fiscal year must have a single or program-specific audit conducted for that year, per the Uniform Guidance for HHS awards: https://www.ecfr.gov/cgi-bin/text-idx?node=pt45.1.75#se45.1.75_1501
21. Can the 30% match that comes from the company be supplied by existing NIH and/or DOD grants that are already approved and funded?
    a. No. Funding from federal sources (eg federal grants) cannot be used to meet cost-share obligations.

Process Questions:

1. I could not locate how to access EOI application forms on the CARB-X website. Are applications only emailed to interested parties who request them?
    a. The actual fillable EOI form is not available on the website as yet. We will make it available only during the open periods. A sample EOI form is on the website currently carb-x.org.
2. Can we include tables and figures (charts etc) in our EOI form?
    a. No. Only text is supported in the EOI.
3. It takes eight months from the EOI phase to final funding decision. How long might it take for CARB-X to respond to the initial EOI's?
    a. Round 1 applicants should expect to be informed whether they are accepted to progress to the next stage (Short Form) by the end of April.
4. In the ~ eight months of waiting time, how much can the proposal be updated to reflect discovery for the project over that time span? How do we handle updates or revisions to the proposal with the understanding the overall project cost is set? Is it necessary to update CARB-X?
    a. We understand (and hope!) that the project will progress in this timeframe and adjustments can be made to the plan supporting the application at each step of the process (Short Form, Long Form, final contracting).
5. Can companies have more than one Carb-X funded projects?
    a. Yes. If you are applying for more than one project, please ensure you submit a separate EOI for each distinct project.
6. Is the EOI form the same for both 2018 rounds?
    a. The basic EOI form is the same for both rounds however as we have a more narrowly defined scope for Round 1, we will be programming the EOI form to only ask the relevant questions as specific to that scope.
7. Where can I find the application package that is due at the end of the month?
    a. The sample EOI form is available here: http://carb-x.org/files/2018_Funding_Round_1-EOI_Sample.pdf
    b. The version that will allow entry of information and submission will only become available on the website at the start of the open session on March 22nd.
8. What should be the focus of the 1000-word product description in the EOI? We're in lead optimization stage. Should the product description more about the data we have now, or more about the plan for optimize the lead? Do we have to describe a roadmap all the way to Phase I?
    a. We would encourage you to provide a description of the data you have now in as much detail as you can (respecting the non-confidential nature of this step) demonstrating how it fits within the scope of interest of CARB-X along with a description of the subsequent critical steps to progress your current stage (to candidate selection) and, should there be any specific challenges to your technology, how you would propose to address these at a high level in the subsequent development stages.
9. The request for a budget estimate in the EOI states "estimation purposes only (you

may update this subsequently),". When in the process budget numbers need to be final?

a. At the third and final step in the applications process, the Long Form step, there is a requirement to submit a detailed budget workbook. This budget should be seen as fixed for CARB-X decision making.

10. What is the detail that CARB-X program is looking for in the project schedule and expenses for each at the time of the proposal in the application phase before the negotiation phase?
    a. The amount of detail required in the application processes with each step of the process. However, by Short Form, you will need to share a detailed Gantt chart and description of the program including go/no go milestones and key deliverables at each stage of development. Regarding the budget, at EOI this is at a very high level summary. Should you progress through to Short Form and Long Form, the amount of detail regarding how the budget has been built up increases. In Long Form there is a detailed budget workbook that CARB-X shares with applicants to complete at that stage.
11. Can estimated technology license cost to be built into the budget?
    a. Yes; refer to FAR 31.205-37 for Royalties and other costs for use of patents: https://www.ecfr.gov/cgi-bin/text-idx?SID=24317b71f06191dd8cc0a41e826185bd&mc=true&node=sp48.1.31.31_12&rgn=div6#se48.1.31_1204
12. What are the accounting rules? Do FAR cost principles apply"?
    a. The award is a cooperative agreement from BARDA (not a contract), so is governed by DHHS Uniform Guidance for general post-award requirements. https://www.ecfr.gov/cgi-bin/text-idx?node=pt45.1.75#sp45.1.75.d

       Cost Principles (allowability of charges) for PDs though, are governed by the FAR 48 CFR 31.2 https://www.ecfr.gov/cgi-bin/text-idx?SID=24317b71f06191dd8cc0a41e826185bd&mc=true&node=sp48.1.31.31_12&rgn=div6#se48.1.31_1204
13. To be considered for funding, CARB-X requires Applicants to "own or have rights to the intellectual property and have reasonable expectation of freedom to operate required to carry out the project." At the proof of concept stage, many times it is difficult to conduct a freedom to operate inquiry. Is a preliminary assessment sufficient? Also, at this stage of a project IP rights may not yet have been filed (waiting for data, etc.). Would an applicant still qualify if no patents have yet been filed?
    a. Yes, a preliminary assessment of FTO is acceptable. If patents are not yet filed, the application would qualify as long as whomever submit the application will own/control those patent filings.
14. Can an external co-applicant, e.g., technology partner, join the application at different phases of the application? Does the co-applicant need a SAM too?
    a. We require there to be a single legal entity as signatory to the subaward and responsible for the management of the subaward but they can have subcontractors/collaborators, fee-for-service organizations support the project as it makes sense; only the applicant/signatory to the subaward requires a

SAM.

15. Do I need to register on the website/obtain a log-in to submit an EOI?
    a. No. On March 22nd, the fillable PDF EOI form will go live and you access it directly from the carb-x.org website and submit it through the website. You do not need to email it to CARB-X.