CARB-X

Combating Antibiotic-Resistant Bacteria

Applying to CARB-X

Frequently Asked Questions

If you have questions that are not addressed below, please input your questions in the form on our Applicant Questions webpage: https://carb-x.org/apply/applicant-questions/ We will continue to augment these FAQs on an ongoing basis.

If you need technical assistance submitting your application through the CARB-X Portal, please reach out to carbxit@bu.edu.

General application and technical questions

1. **Q: What is the link to the application portal?**
   A: https://carb-x.force.com/fundingportal/

2. **Q: Can I save the EOI as a draft?**
   A: Yes. Select **Save as Draft**. You will see the message below. Be sure to click **OK.** If you do not click OK, your entire application will be lost.

   Your application will be saved as a Draft. You can return to the My Applications page to resume at any time. Click OK to Save as Draft.

   To resume your application, navigate to **My Applications** on the Portal homepage and click **Resume.**

3. **Q: Do the character limits include spaces or only actual characters?**
   A: All character limits include spaces, with one space equivalent to one character.

4. **Q: Can I have a list of the questions and possible responses?**
   A: The questions are outlined on our website: https://carb-x.org/apply/apply-here/ Responses are not exportable from the EOI at this time. You can use the Save as Draft feature to draft an EOI for review prior to submission.

5. **Q: Are templates available for the EOI or the Project Narrative?**
   A: EOI templates are downloadable from within the Portal and via the links below. The Project Narrative template will be provided to all applicants that are invited to progress to the Project Narrative stage, when that invitation is issued.

   EOI template for therapeutics
   EOI template for vaccines
   EOI template for diagnostics

6. **Q: Will feedback be provided on EOIs?**
   A: No. We recommend that you consider a CARB-X Connect submission, as this is also non-confidential but offers the possibility of feedback.

7. **Q: Will CARB-X offer accelerator support to applicants for the EOI stage?**
   A: No.

8. **Q: When can we expect a decision on whether we are selected for the next application stage?**
   A: Please see https://carb-x.org/apply/omnibus-solicitation/ for the application timelines.

9. **If my application is rejected during cycle 1 or 2, can I submit to cycle 3 for this omnibus funding call?**
   A: Yes, please see https://carb-x.org/apply/omnibus-solicitation/ for the cycle 3 application timeline. Please note that you will need to submit a new EOI (even if it is for the same topic) as earlier applications cannot be updated.

10. **Q: if I submit an EOI to funding cycle 1, and it advances to the Project Narrative stage, is my Project Narrative due on 23-Dec-2022 (the cycle 1 deadline) or can I submit it in accordance with the deadline for cycle 2 or even cycle 3 (27-Mar-2023 or 26-Jun-2023)?**
    A: Your Project Narrative is due on 23-Dec-2022. Once in a cycle, you should follow the deadlines for that funding cycle.

11. **Q: If I apply during cycle 1 for a H2L program, can I withdraw my application and submit a new application for LO in cycle 2 if I have obtained fresh data that would fulfil the LO criteria?**
    A: By the time you withdraw the application, you could have received an EOI Disposition Notice (28-Nov-22), submitted your Project Narrative Submission data (23-Dec-22) or undergone the Advisory Review Period (09-January-2023 to 27-January-2023). You can certainly withdraw your application during this process and submit a new EOI before the EOI submission date on 30-January-2023, but the risk is that the new EOI might not be competitive in this next round.

12. **Q: Can Product Developers apply for funding for multiple stages of development (i.e., Feasibility and Development, or Preclinical and Phase 1)?**
    A: Yes, please indicate all of the stages of development for which you intend to request CARB-X funding. However, please focus your application on the initial development stage and include a more general description of later stages. Using a milestone-driven approach, CARB-X only commits funding for a single development stage (or portion thereof) at a time, but it is important that we understand the scope of your intended program, as well as the total amount of support that may potentially be requested.

13. **Q: Regarding the susceptibility/resistance pattern question in the EOI, a list of antibiotics is given for every pathogen. Please can you clarify what ticking a box means, so that we are able to provide the appropriate information?**
    A: If you tick a box, it indicates that your product can cover strains of that pathogen that are resistant to that antibiotic class. E.g., if you tick “beta-lactams” for *A. baumannii*, it means that your product works against *A. baumannii* strains that are resistant to beta-lactams. If you tick no boxes, it means that your product does not (or is not yet known to) work against any antibiotic-resistant isolates of that pathogen.

14. **Q: When checking the boxes for pathogen coverage, should this be based on what is theoretically possible or based on data already obtained?**
A: Please complete the checkboxes (and responses to any other EOI questions) based on data that you have already obtained. You can present arguments in the written section regarding your product's theoretical performance characteristics.

15. **Q: Some EOI applications have been rejected because they provided "insufficient information." Can guidance please be provided on what information should be presented in the EOI application to satisfy the requirement?**
A: Rejection due to insufficient information typically means that the EOI did not include data or other important information regarding the proposed product. We acknowledge that the EOI should only contain non-confidential information, but descriptive claims without supporting data are not sufficient. Some examples are provided below:

Pillar	**Type of omission**	**Example of insufficient information**	**Example of improved claim**
Therapeutics	Quantitative data	"Our molecule is active against key TPP pathogens and demonstrates initial oral bioavailability."	"Our molecule is active against key TPP pathogens (MICs of 0.25 - 2 µg/mL against MSSA/MRSA and *S. pneumoniae*) and demonstrates initial oral bioavailability (F = 15%)."
Preventatives	Antigens not specified	"x antigens have been identified/tested..."	"The vaccine contains antigen A and antigen B…"
	Predicted coverage not specified	"Antigen A is an important virulence factor."	"Antigen A is present in x% of relevant clinical isolates; 90% of alleles are at least y% identical in aa sequence. This includes the extracellularly exposed epitopes."
	Envisioned mechanism of protection (in particular relevant for maternal vaccines to protect against neonatal sepsis)	"Antigen A is immunogenic in mice."	"Immunization of adult mice resulted in a strong IgG response that in pregnant mice are expected to transfer via the placenta to, and thus protect, the fetus."

Diagnostics	*Neisseria gonorrhoeae* data is lacking	"We plan to demonstrate detection of *N. gonorrhoeae* in contrived samples during technical feasibility."	"Our assay detected 100 cfu/mL *N. gonorrhoeae* using contrived urine and vaginal swab matrix samples."
	Lack of detail regarding sample types to be addressed in the proposed work (e.g., vaginal swab samples)	"The LOD in urine samples is 100 cfu/mL for *N. gonorrhoeae*."	"The LOD in urine samples is 100 cfu/mL for *N. gonorrhoeae*. We will demonstrate performance using vaginal swab matrix with contrived and clinical vaginal swab samples in technical feasibility."

Funding questions

1. **Q: What is the nature of CARB-X funding? Is it 100% non-dilutive?**
   A: CARB-X funding is 100% non-dilutive.

2. **Q: Does CARB-X have maximum allowable budgets for each stage of development?**
   A: Yes, the budget caps for different stages of development are described below.

   A: For therapeutics: the PD contribution is 30% for H2L, LO and PC, and 40% for Phase 1. The CARB-X funding caps (i.e., maximum contribution from CARB-X) for H2L, LO, PC and Phase 1 are US$3.27M, $3.27M, $4.08M, and $3.94M, respectively.

   B: For vaccines: the PD contribution is 30% PD for H2L, LO and PC, and 40% for Phase 1. The CARB-X funding caps (i.e., maximum contribution from CARB-X) for H2L, LO, PC and Phase 1 are US$3.27M, $3.27M, $7.35M and $3.94M, respectively.

   C: For Dx: the PD contribution is 30% for Feasibility and Product Development. The CARB-X funding caps (i.e., maximum contribution from CARB-X) for Feasibility and Product Development are US$5.71M and $8.17M, respectively.

CARB-X Funding "Up To" Caps, by Stage ($M, USD)											
		Therapeutics				Preventatives				Diagnostics	
	Phase of Development	Hit-to-Lead	Lead Op	Pre-clin	Phase 1	Hit-to-Lead	Lead Op	Pre-clin	Phase 1	Feasibility	Prod Dev't
	Full stage cost basis	**4.66**	**4.66**	**5.84**	**6.56**	**4.66**	**4.66**	**10.5**	**6.56**	**8.17**	**11.67**
For Profit	CARB-X funding cap	3.27	3.27	4.08	3.94	3.27	3.27	7.35	3.94	5.71	8.17
	PD Cost Share	1.39	1.39	1.76	2.62	1.39	1.39	3.15	2.62	2.46	3.5
	Cost Share %	30%	30%	30%	40%	30%	30%	30%	40%	30%	30%
Non-Profit	CARB-X funding cap	3.96	3.96	4.96	5.58	3.96	3.96	8.92	5.58	6.94	9.92
	PD Cost Share	0.7	0.7	0.88	0.98	0.7	0.7	1.58	0.98	1.23	1.75
	Cost Share %	15%	15%	15%	15%	15%	15%	15%	15%	15%	15%

3. **Q: Is there a cap on personnel salaries funded by CARB-X?**
   A: Applicants may budget for salary up to the US NIH salary cap, which is posted here: https://grants.nih.gov/grants/policy/salcap_summary.htm. Salary costs beyond this cap cannot be claimed either as reimbursable cost or as cost share.

4. **Q: Can the PD cost share come from other grant funding for an overlapping scope of activities?**
   A: Yes, if the other granting agency's terms are compatible with CARB-X's terms. Scopes of work cannot be duplicative but can be complementary. US federal funding usually cannot be used to meet cost share.

5. **Q: Can the PD cost share include in-kind matching (e.g., labor/time) versus only cash?**
   A: The PD needs to provide monetary cost share equal to the relevant percentage of the total US$ cost of the program. In-kind matching is not permitted as cost share.

6. **Q: When and how are CARB-X funds transferred to a company after entry into the portfolio?**
   A: After a contract has been signed between the PD and CARB-X, funds will be transferred monthly as reimbursement for expenses incurred by the Product Developers (PDs).

7. **Q: In the EOI Project Costs tab, is the amount requested the cost of the current/initial stage of development (e.g., H2L) or the total cost of the program (e.g., H2L + LO + Preclinical + Ph1)?**
   A: For this question in the EOI application, please indicate the total cost of all project stages for which you intend to request CARB-X funding. In this particular example, it would be H2L + LO + Preclinical + Ph1.

8. **Q: Does CARB-X provide only funding, or can it also provide access to specimens or other resources?**
   A: CARB-X provides various support services in addition to direct funding. We will do our best to support access to specimens for funded companies.

Eligibility and program scope questions

1. **Q: Can a company that is already in the CARB-X portfolio apply to the current funding round?**
   A: Yes.

2. **Q: Can an existing Product Developer (PD) re-position their program for a new TPP submission? Would this be considered a new program for new funding?**
   A: Yes, but we strongly encourage you to focus efforts on the strongest TPP.

3. **Q: Are academic institutions and research hospitals eligible to apply for CARB-X funding?**
   A: Yes, academic institutions and research hospitals from anywhere in the world are welcome to apply. CARB-X funding is not exclusively directed to companies.

4. **Q: Can a consortium of 2 or more entities apply?**
   A: Yes, but contributions from the different partners should be specified, and a Principal Investigator should be named.

5. **Q: Can investigators/applicants be on multiple applications (e.g., an applicant listed as CI on one application and AI on another application)?**
   A: Yes, applicants can have roles on multiple applications. Conflicts of interest must be appropriately managed.

6. **Q: Is there a requirement for a novel mechanism of action, or are 'known MOAs' within scope?**
   A: Known MOAs are in scope but require strong differentiation versus what is currently available in the clinical setting.

7. **Q: Can a proposed therapeutic be a novel entity belonging to an existing antibiotic chemical class?**
   A: Yes.

8. **Q: Is an oral adjunctive therapy, such as a BLI or potentiator, responsive?**
   A: Yes.

9. **Q: Are non-traditional modalities responsive to the current funding call TPPs?**
   A: Yes, as long as orally active.

10. **Q: Are host-modulating therapeutic approaches responsive to the current funding call TPPs?**
    A: No, if the product targets the host exclusively. Yes, if the product has a dual mechanism, one targeting the pathogen directly and the other targeting the host.

11. **Q: We have identified an unexplored target present in all bacteria and are at the earliest stages of identifying inhibitors of this target. Does CARB-X fund this very basic research at this early stage, or only after positive hits have been identified?**
    A: CARB-X only funds work from Hit-to-Lead through Phase 1. Please refer to the minimum entry criteria posted on the CARB-X website for details regarding what is considered a hit.

12. **Q: If a single novel technology, or compound class, could be targeted to any of several narrow spectrum pathogens individually, can a separate proposal be submitted for each targeted pathogen (i.e., one product for oral UTI, and one product for oral Gram+ respiratory)?**
    A: Yes, but we strongly encourage you to focus efforts on the strongest TPP.

13. **Q: For a clinical stage compound, are formulation development, manufacturing of API and DP, and microbiological assay development to support Phase 2 clinical study, within scope for funding under "additional CMC, formulation, and analytical activities required to support further clinical development"?**
    A: Yes, formulation development, manufacturing of API and DP, and microbiological assay development to support further clinical development are within scope for Phase 1 funding from CARB-X, but please be aware that of the CARB-X funding cap for this stage (see above).

14. **Q: Our product is not within scope for the current call. Do you have guidance on funding possibilities in the near future? Can we get feedback on our current data package, even if it is currently out-of-scope?**
    A: We have no guidance at this time regarding the scope of future funding calls. If you are interested in obtaining feedback on your program, you can submit it to CARB-X Connect at any time.

15. **Q: Would a (probably) non-oral antibody recruiting molecule developed to prevent neonatal sepsis be considered under the "vaccines for neonatal sepsis" theme?**
    A: No.

16. **Q: My company's product is an intravaginal ring to prevent gonorrhea infection in women. This does not fit any of the examples listed the gonorrhea products theme and thus none of the TPPs. Is our product responsive to the solicitation?**
    A: No.

17. **Q: Would a therapeutic agent delivered via inhalation for respiratory infections (Gram-negative or -positive pathogens) be eligible for the 2022-2023 funding call?**
    A: No, the inhalational route of administration is out-of-scope for the current funding call.

18. **Q: We have developed an oral administered agent with limited bioavailability to target Gram-positive pathogens in intestines, specifically C. difficile. Is this within the funding scope?**
    A: No, *C. difficile* is out-of-scope for the current funding call.

19. **Q: This question concerns a program developing a novel Gram-positive specific antibiotic for IV and oral delivery, with a focus on ABSSSI and possible future development for Gram-positive bacteremia/endocarditis, diabetic foot infections and/or bone/joint infections. Your TPP for Gram-positives lists CABP first, with fastidious Gram-negatives listed as pathogens to be covered. If our program lacks activity vs. fastidious Gram-negatives, this project would not be ideal for CABP. Is our program eligible to apply for CARB-X funding under the current omnibus solicitation?**
    A: Community-acquired pneumonia is only one of the indications we are interested to target, and you are correct, for CABP it would be ideal to have activity against the fastidious Gram-negatives. However, we are also interested in skin infections, which do not require activity against the Gram-negatives, and your program is eligible to apply.

20. **Q: In the Development Stages in Scope Therapeutics pdf, it is stated that a candidate molecule should "demonstrate in vitro activity against wild-type representatives of all TPP-targeted pathogen(s)." Is it necessary to demonstrate activity against all the TPP-targeted Gram-positive pathogen(s): "S. aureus, S. pneumoniae, S. agalactiae, S. pyogenes, with additional coverage of fastidious Gram-negatives including H. influenzae and M. catarrhalis"?**
A: There is no requirement to demonstrate activity against each of the pathogens listed here, as the specific indication should guide the ideal spectrum. For example, it would be important to show activity against *S. aureus* and *S. pneumoniae* if the applicant is focusing on CAP (additional activity against the fastidious Gram-negatives would enhance the application) or HAP; and *S. aureus* and *S. pyogenes* if the applicant is focusing on SSTI.

21. **Q: If the application will be for infections caused primarily by Gram-positive organisms in the Hit to Lead stage, the compounds must show activity against all these strains "S. aureus (MR/MS), S. pneumoniae, S. agalactiae, S. pyogenes, with additional coverage of fastidious Gram-negatives including H. influenzae and M. catarrhalis" if it indication is CABP? Also, if the main indication is S. aureus wound and skin infections, should the compounds show also activity against these strains?**
A: Activity against *S. aureus, S. pneumoniae, H. influenzae* and *M. catarrhalis* is required for CABP. Activity against only *S. aureus* is sufficient for a narrow spectrum product which targets wound and skin infections caused by this organism; however additional activity against *S. pyogenes* and *S. agalactiae* would enable broad-spectrum activity against these wound and skin infections.

22. **Q: Enterotoxigenic E. coli (ETEC) is listed under the call for neonatal sepsis vaccines. Since ETEC is almost always an intraluminal non-invasive diarrheal pathogen that seldom causes bacteremia, please can you clarify whether ETEC is really intended as a target pathogen for this round? Maternal vaccination could certainly benefit very young children who otherwise succumb to severe infections from ETEC and are at risk for death from diarrhea and other infections, but I would not anticipate that it would prevent sepsis per se.**
A: We are seeking proposals for maternal vaccines against neonatal sepsis caused by *E. coli*. Your choice of antigens should be promising of high coverage among clinically relevant strains, and we also want to know what the prevalence of these antigens is among ETEC strains.

Diagnostics-related questions

1. **Q: Is a molecular diagnostic test/platform considered within scope for the current solicitation?**
A: Yes.

2. **Q: Are non-lateral flow cartridge & reader solutions in scope?**
A: Yes.

3. **Q: Are readers for LFA within scope and what stage of development is required for the reader to be considered for funding?**
   A: Yes, TRLs 3-5 are in scope. Please provide as much information as possible with regard to potential compatibility with LFA platforms.

4. **Q: Do you have any caps on the cost of the instrument, and cost of the consumable kits?**
   A: Proposed products should be affordable and accessible in their target markets. If you are targeting LMICs, FIND has published very detailed TPPs that you may find useful.

5. **What are the metrics requirements associated with your AST test result? Generally, CLSI serial microdilution results are accurate/precise to within +/- 1 serial dilution. Do you have any comparable guidance, or can this be defined in the context of the clinical utility?**
   A: You should propose to adhere to guidelines that are relevant in the markets that your product is targeting. For the U.S. markets, CLSI guidelines would make sense.

6. **Q: When clarifying clinical specificity and sensitivity for possible NG diagnostics, can such values be calculated from essential and categorical agreement with tests like Etest as opposed to agar dilution despite the latter being the gold standard?**
   A: Yes, please state the reference test.

7. **Q: I understand CARB-X's focus is in the translational phase, from feasibility up to development of alpha prototype. The current funding call has one TPP component for Dx, which is for Ng. This TPP states preference for commercially available technologies, and current research use instruments are out of scope. This seems contradictory to the general funding phase for CARB-X, which is before commercial launch. Can you clarify? Do you expect the same TPP to be used for all three rounds of funding?**
   A: As the TPP states, there is a preference for existing platforms, but novel platforms will also be considered and are eligible for funding. The TPP is not expected to change across the three cycles of the current omnibus call.

8. **Q: For diagnostic platforms, should we speak to other relevant targets that we can test for, in addition to gonorrhea? Is there an advantage or goal to fund projects that have enhanced multiplexing capability?**
   A: Yes, please note any additional targets, as these would offer additional value.

9. **Q: Regarding what is "in scope" for diagnostics, the development description includes work toward a "fully integrated prototype using clinical samples, preferably in the hands of external users." However, it also states that clinical validation is considered "out of scope". Can you clarify if clinical studies can be funded by the CARB-X grant?**
   A: Clinical studies are not funded by the CARB-X grant for diagnostics. We encourage companies to use clinical samples in Development, and resources may be available to support the procurement of these samples.

10. **Q: In the diagnostics development stages document, the feasibility stage covers "benchtop feasibility demonstrated with clinical specimens". What type of data is required in the EOI?**
    A: If clinical specimens are not available, then data using contrived samples with spiked isolates or isolates alone will be considered.

11. **Q: We understand that ID-phenotypic AST platforms are preferred but challenging due to bacterial doubling times. Are all results (ID+AST) expected within the TPP TTR of >30 or >60 minutes, or can they be staggered so that pathogen ID results would be available within this time and AST after? If so, what is an acceptable amount of time for AST results?**
    A: The preference is for a solution that provides an actionable result within the timeframe of a patient visit. Consideration of the clinical path and competitor products should inform the time to aim for an AST result.

12. **Q: Many of the questions regarding time to result for the gonorrhea area of interest are in the context of phenotypic AST, which requires well over an hour for result. Is a rapid phenotypic gonorrhea AST platform/technology responsive if it requires over an hour time-to-result and cannot ID NG?**
    A: Consideration of the clinical pathway and competitor solutions should inform the time to result acceptability. If ID solution is not part of the technology, then describing how existing technology can be used to provide the ID in concert with the AST solution is required.

13. **Q: There is a 30- to 60-minute target for time to results for diagnostics. When does the clock start - is it from the time when the sample is collected from the patient?**
    A: Please speak to how your product fits within the clinical care pathway. If sample transport is required (not a point-of-care technology), please speak to how the pathogen will be maintained during transport. The time officially starts once the hands-on process for the diagnostic test begins (please include any sample prep).

14. **Q: If time-to-result for a diagnostic requires more than 60 minutes, could that diagnostic still be eligible for funding?**
    A: Yes, but please speak to how your product fits within the clinical care pathway.

15. **Q: The TTR requirements are relatively long, especially for pathogen ID only. How important is speed, ease-of-use, eventual cost of use in terms of eventual accessibility to LMICs?**
    A: Speed, ease-of-use, eventual cost of use in terms of eventual accessibility to LMICs are very important. Please speak to how your product would fit into the clinical care pathway in the target setting of use and put forth a competitive proposal.

16. **Q: Analytical specificity data using other non-commensals (ideally other Neisseria species) is preferred." Can you please clarify if any analytical specificity data is required at a minimum and the data with non-commensals would be a bonus?**
    A: Analytical specificity data using other non-commensals is preferred, but it is not a minimum entry criterion. However, applications with this information will be prioritized.