

CARB-X Long Form General Instructions

The applications will be managed through the CARB-X Digital Resources (CDR) web-portal in the system entitled 'Online Secure CARB-X Application and Review System' (OSCAR) for which you should already have access or should have received an email with instructions on how to obtain CDR access. The online application has many fields for direct online input. However, the majority of the information supporting the application will be uploaded as a PDF on the "Project details" tab and as an excel spreadsheet on the "Budget workbook and supportive document" tab.

Although the overall application will be handled in a confidential manner, the information marked 'non-confidential' below will be used internally as a project summary and to vet conflicts of interest. Information in these sections should be material you would discuss publicly and be acceptable for internal and external disclosure. In addition, such non-confidential material of successful applications may ultimately be shared as part of the description of CARB-X pipeline projects.

Please **strictly adhere** to the OVERALL page limit of 40 pages for the Long Form. Applications that exceed 40 pages will **NOT** be reviewed.

Application Section	Online Entry vs Document Upload	Comments, if required	Non-confidential or Confidential
Company Information	Online		Non-confidential (i.e., may be publicly disclosed)
Principal Investigator Information	Online		
Application Category	Online	See website	
Funding Information	Online	Note: CARB-X funding is expected to begin at or after January 1st, 2019 for this funding round . Funding is contingent on ability of Applicants to demonstrate significant matched funding (a minimum of 30% per development stage).	
Development Stage	Online	See definitions of the stages within CARB-X funding scope at CARB-X Description of Development Phases	
Non-confidential Project Summary	Online	Project summary of 2000 characters or less	
Additional Information: <ol style="list-style-type: none"> 1. History of prior application to CARB-X (if any). 2. Will CARB-X funding support: <ol style="list-style-type: none"> a. Trials in human and, if so, who will be the legal sponsor? b. Use of animals and will these studies include any of the following: Non-human primates, Dogs, Cats, Equines? 3. List of reviewers that applicant does not wish to evaluate application. 	Online		

<p>PART 1 - Project Details</p> <p>Long Form containing the following information: <i>Section A:</i> Detailed Description of Project and Plans which include:</p> <ul style="list-style-type: none"> • Quad Chart • Gantt Chart • Project Structuring Approach • Go/No-Go Project Milestones Table • Risk Register • Compound Selection Cascade (If in Hit to Lead or Lead Optimization) • Draft Target Product Profile (if in LO or later stages) <p><i>Section B:</i> Detailed Overview of People and Company Structure</p> <p>Optional Upload Additional Files:</p> <ul style="list-style-type: none"> • Original Gantt Chart (PDF) – recommended if version included in Section A is difficult to read 	<p>Upload</p>	<p>See detailed guidance below. All documents must include a 'CONFIDENTIAL' footer and page numbers on all uploaded documents.</p>	<p>Confidential</p>
<p>PART 2 - Detailed Budget Summary/Budget Workbook and Supportive Documents</p>	<p>Online/Upload</p>		

PART 1: Guidance for 'Project Details' Section

Formatting requirements - Applications that do not meet the following formatting requirements **WILL NOT** be reviewed.

1. The application should be formatted for Letter or A4 paper with a 12-point Times New Roman font and 1-inch margins. Pages may be landscape or portrait as best suits the content. When pasting in tables etc. from other documents, other fonts may be acceptable if text is in 12-point simple font and easily visualized on screen.
2. The total number of uploaded pages cannot exceed 40; however, the number of pages within each section are only indicative.
3. **Please add a 'CONFIDENTIAL' footer and page numbers to 'Project Details' document.** These can be within the 1-inch margin.

Content requirements - Applications will be screened prior to distribution to reviewers and if they do not meet the content requirements laid out below for Sections A & B of the 'Project Details' section, they **WILL NOT** progress into the review process.

Section A: Detailed Description of Project and Plans including (30 pages in total)

You should use this section to describe your project. This section should be **DATA-RICH** – it is your opportunity to make a compelling case for the 1) scientific hypothesis; 2) clinical relevance of the proposition; 3) your development plan and capabilities to deliver this. There is no specified layout for this section, however, some elements are **required** (see list below).

Applications will be screened prior to distribution to reviewers and if they do not meet the requirements laid out below, they **WILL NOT** progress in the process.

Do NOT include:

- References or citations
- Foundational information about the significance of antibiotic resistance – the reviewers will all be familiar with this

How to structure your plan and budget request for CARB-X:

CARB-X will make a milestone driven, risk-mitigated investment in the projects. Please consider this proactively as you put your proposal together. Consider what the Major Milestones are as decision points for CARB-X to consider whether to fund the subsequent stage of the project. Each Major Milestone should have a defined deliverable (e.g., preclinical candidate selected or IND approved, etc.).

There will likely be multiple go/go no milestones along the path of any stage ending in Major Milestone. Please see Project Structure Approach for an example.

Structure your budget in-line with these Major Milestone stages and avoid overlapping periods as much as is feasible. In the Project Details document, please refer to the Major Milestone stages as: Base Stage (the initial contracted stage of the project), Option Stage 1, Option Stage 2, etc.

Key Content of the Detailed Project and Plans Description:

All applications must:

- a. Sketch a plausible preclinical and clinical development pathway (OR the steps required to define the pathway).
- b. Quantify the magnitude of the unmet need addressed (e.g., # of patients benefiting).
- c. Explain how patients and any special populations would benefit from the product.
- d. Explain how those patients who could benefit from the product would be identified.
- e. Explain how this approach differs from (or improves on) existing related approaches; address how the opportunity fits within the competitive landscape of development, pre-registration and marketed products. Also, if previous companies have failed at the specific target or scientific/technology principle, please explain why your product/plan has a higher likelihood of success.
- f. Comment on tractability and project risks, how you plan to address these issues, and how these issues are linked to milestones.
- g. Comment on your IP position and Freedom to Operate and confirm that you fully own the IP or have executed the required licenses to be able to develop and commercialize the IP (CARB-X will only progress applications for which this is the case);
- h. Explain how the approach would support good antibiotic stewardship.
- i. Explain expected differences in use in more versus less developed countries.
- j. Consider any feedback or comments you received in your CARB-X invite letter to the Long Form process and be sure to cover those topics when completing the Long Form application. These comments are best addressed in the body of the Detailed Project and Plan Description and it is helpful to highlight that the information addresses a question raised in the Short Form Review.

Specific content must include:

- a. Explain mechanisms of action (or approach to elucidating the MOA).
- b. Provide exemplar chemical structures, data on physical properties and pharmacologic activities OR explain why this is not relevant.
- c. Provide data on PK-PD/safety if at Lead Optimization (or later stages). If not provided, explain why this is not relevant.
- d. Comment on whether or not the agent could be used as monotherapy for the target indication(s). If the agent will only be reliably used in combination with a partner product, the clinical development pathway outline must discuss the approach to showing the effect of the combination relative to the effect of the partner alone.
- e. Provide plans to evaluate in special populations.
- f. For programs in LO or later, provide a draft Target Product Profile with minimum acceptable and ideal attributes (see [NIH template](#)).

NIAID preclinical services:

Explain areas or challenges to your program where NIAID's partnership could be beneficial to the success of your program. Please refer to the following website providing a description of NIAID's standard preclinical services: <https://www.niaid.nih.gov/research/microbiology-and-infectious-diseases-resources>. NIAID is one of CARB-X's strategic partners and provide funding to CARB-X in the form of in-kind support. As such, **it is a requirement** that applicants consider what critical gaps NIAID services might fill in their programs.

For CARB-X purposes, NIAID's capabilities and expertise extend beyond the standard preclinical services described in the link above. Successful applicants in the CARB-X process will have streamlined access to NIAID's development resources. However, discussions with NIAID regarding such services will only occur after the CARB-X Advisory Board meeting in which your Long Form will be reviewed.

SAMPLE

The following documents **must** be included as part of the 30-page total Detailed Description of Project and Plans

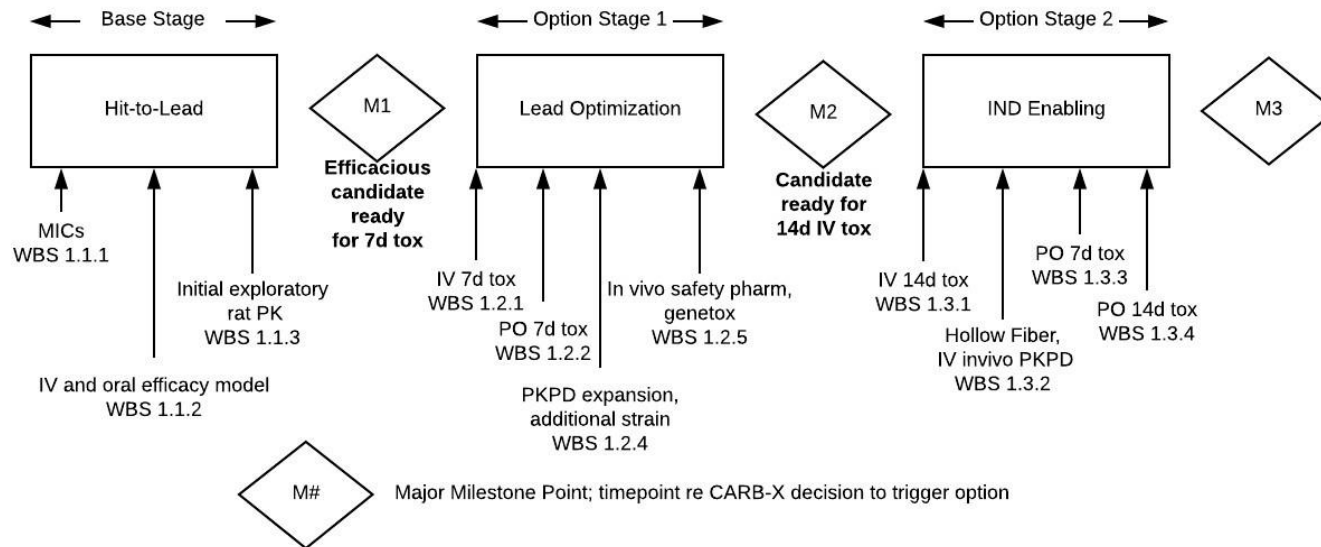
1. Quad Chart (landscape is preferred) – 1 page

<p><u>Vision</u>: <i>One sentence statement</i></p> <p><u>Objective</u>: <i>Clear, concise, 2-3 sentence description of the objectives and methodologies of the project</i></p> <p><u>Target Product Profile</u>: <i>Provide the following</i></p> <ul style="list-style-type: none"> • <i>Indication(s) and patient population(s)</i> • <i>Pathogen(s)</i> • <i>Route of administration and dose regimen</i> <p><u>Description of Effort</u>: <i>A bullet list (2-3 entries) of the scientific challenges being addressed using the proposed CARB-X funding</i></p>	<p>Picture or Graphic that illustrates the project or concept (e.g., data figures, molecule illustrations, or processes)</p>
<p><u>Benefits of Proposed Project</u>:</p> <p><u>Challenges</u>:</p> <p><u>Current Phase of Technology (choose from list below)</u>:</p> <p><u>Therapeutics</u>:</p> <ul style="list-style-type: none"> • Hit-to-Lead • Lead Optimization • Pre-Clinical • Phase 1 	<p>Base Stage: total \$XXX / CARB-X \$YYY. Company cost share Z% Bullet list of major goals/milestones by Major Milestones</p> <p>Option Stage 1: total \$XXX / CARB-X \$YYY. Company cost share Z% Bullet list of major goals/milestones by Major Milestones</p> <p>Option Stage 2: total \$XXX / CARB-X \$YYY. Company cost share Z% Bullet list of major goals/milestones by Major Milestones</p> <p>Option Stage 3: total \$XXX / CARB-X \$YYY. Company cost share Z% Bullet list of major goals/milestones by Major Milestones</p>

2. High-level Gantt Chart (or similar showing timeline) – 1 page

- Should show overall project flow structured into Major Milestone stages (Base, Option 1. etc.). Describe all activities critical to decision-making (including ones which will not be funded by CARB-X).
- Should indicate project elements that would be funded by CARB-X.
- To the extent possible, project elements should be categorized using Work Breakdown Schedule (WBS) codes (see Section 6; such categorization will be required if the project progresses to the final proposal/contracting stage).
- CARB-X will not fund projects beyond Phase 1, but including a high level downstream development plan is helpful to demonstrate that you understand the challenges and requirements of later stage clinical development and regulatory filings.

3. Project Structure Approach EXAMPLE – 1 page



The above example of project structuring is **indicative only**. In most cases, the stages follow the normal drug development phases i.e. BASE Stage = Hit to Lead, Option 1 = Lead Optimization, Option 2 = IND Enabling/Preclinical, Option 3 = Phase 1 but that is not a strict requirement. The proposed structure should be what makes most sense for the specific needs of the project. Projects are not required to start from Hit to Lead nor are they required to run through Phase 1. For example, it would be acceptable to have an applicant outline a project proposal in which the BASE Stage = Lead Optimization and there is only a single Option Stage (IND Enabling/Preclinical).

Examples of Go/No-Go Criteria

Hit to Lead	Lead Optimization	IND enabling	Phase I
<ul style="list-style-type: none"> a. Mechanism of action b. MIC90 target pathogen < 4 ug/ml c. Frequency of resistance not > than XX 	<ul style="list-style-type: none"> a. PK/PD index: median value vs target pathogens leads to achievable predicted human dose b. API: sufficient quantity with quality suitable for toxicity studies c. Oral bioavailability or PK profile consistent with intended dose regimen d. Therapeutic index: net stasis at #x below findings in pilot tox studies e. Regulatory path: pre-IND consultation 	<ul style="list-style-type: none"> a. GLP tox studies: toxicology issues identified that would prevent dosing humans. NOEL or NOAEL clearly defined (numeric) b. Acceptable safety margin (>X) in genotoxicity and safety pharmacology (cardiovascular, CNS, respiratory) 	<ul style="list-style-type: none"> a. Favorable benefit/risk for tolerability, safety, and pharmacokinetics of single and multiple ascending doses studies

*Go/No-Go criteria must specific, objective and quantifiable

4. GO/NO GO Project Milestones Table – 1-2 pages

- e. Identify measurable “Go Criteria” and “No Go Criteria” for each GO/NO GO Project Milestone including required reports to demonstrate completion of each GO/NO GO Project Milestone within the proposed stage. Define the key GO/NO GO milestones that will included in CARB-X’s decision to continue to support the project into the next project stage.
- f. Provide other milestones for other work (to be paid by other sources) that will be conducted concurrently during the CARB-X funding period.
- g. Only propose milestones through the phases of development you are requesting funding for. Do not include milestones that are already achieved or will be achieved after the CARB-X funded portion of the project has concluded.
- h. Definitive and rigorous milestones will be viewed positively as communicating your organization’s understanding of the importance of making early selection and down selection decisions.

GO/NO GO Project Milestones						
Milestone #	GO/NO GO Contract Milestones	Go Criteria*	No-Go Criteria*	SOW/Technical Report	WBS #	Stage of Plan (Base, Option 1, etc.)
1						
2						
3						

*Go/No-Go criteria must specific, objective and quantifiable

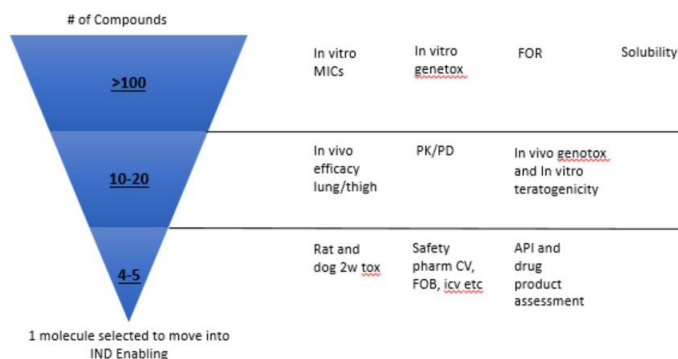
5. Risk Register – 1 page

- i. Please identify potential risks for your program, explaining the probability of occurrence and impact (level and nature) of the risk. Describe the potential mitigation strategy for each potential risk.

WBS	Risk	Probability of Occurrence (High, Medium, Low)	Impact to Project (High, Medium, Low)	Nature of Impact (Cost, schedule, product profile etc.)	Mitigation Strategy

6. Compound Selection Cascade (If in Hit to Lead or Lead Optimization) – 1 page

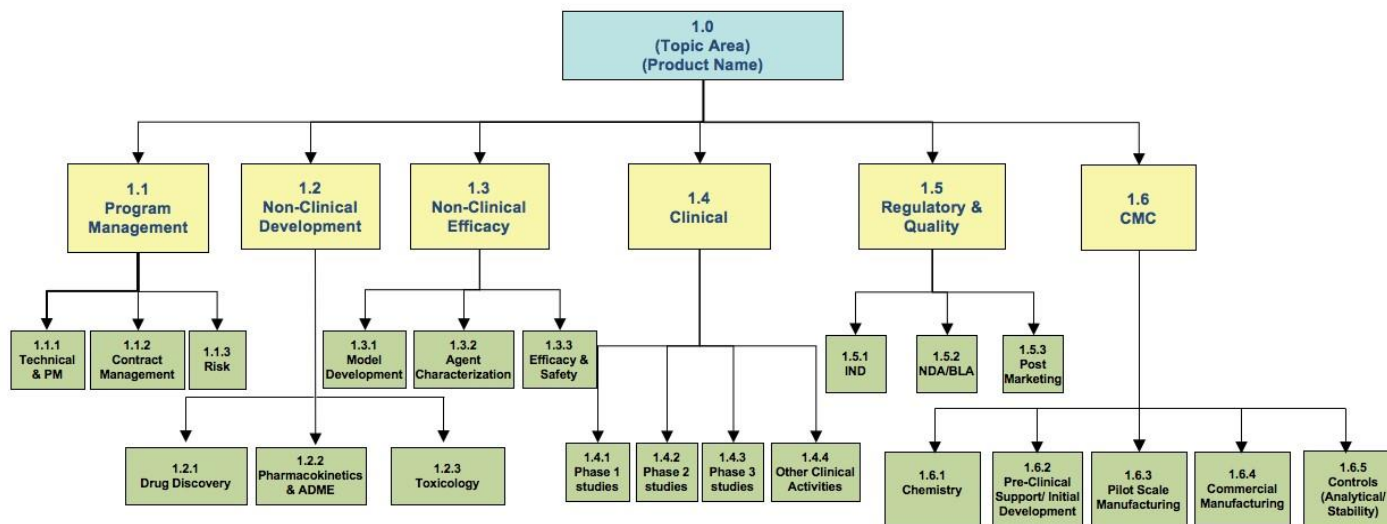
This is an Illustrative Guide for a Compound Selection Cascade



7. Work Breakdown Structure (WBS) – 1 page

- j. Elements within the Gantt Chart and the Budget Summary should, to the extent possible, categorize items using identifiers from the Work Breakdown Schedule (WBS) codes shown below. If your project does not fit this WBS, we encourage the applicant to make best effort to make minor modifications, while keeping the hierarchy of the levels intact.

THERAPEUTIC WORK BREAKDOWN STRUCTURE



Section B:

Detailed Overview of People and Company Structure (10 pages in total)

1. Provide abbreviated CVs on key personnel.
2. Describe (may be integrated with brief CVs as appropriate):
 - a. Your team's technical, clinical, regulatory, program management, and entrepreneurial expertise – it will be critical to explain how your project will be managed (including oversight of CROs/collaborators etc.) throughout the funding period;
 - b. Access to facilities, subcontractors, and infrastructure needed for the work.
 - c. Provide a list of collaborators and an explanation of the relationship with them.
 - d. Your use of an Advisory Board for both technical and business guidance.
 - e. Funding/financing:
 - Describe your company's access to and sources of cash and spend rates to support your cost share, and the sustainability of your company over the proposed project period.
 - Please clearly state where the funds will come from to meet the company cost share. Phase 1 SBIR or any other US federal or state government grants will not count towards the company's cost share.
 - Discuss how the CARB-X funding fits into the company's overall funding and the company's percent and sources of cost share; a minimum of 30% per project stage is required.
 - Discuss how existing available funding supports the company as a "going concern".
 - Your company's experience with raising capital, if this expertise is not in house please explain how you will access it.
 - f. Your company's experience commercializing technologies in the field.
 - g. Your business plan leading to either marketing or an exit plan with clear intent on continuity of the program at the end of the CARB-X funding.

PART 2: Detailed Budget Summary

A separate Excel workbook will be provided to enter detailed budget information. It will be sent with further instructions/guidelines. Please take note of the following important points when putting your budget together:

- A minimum cost share of 30% per stage is required, however, competitive applicants in prior funding cycles have provided 30% or more.
- Applicants cannot count phase 1 SBIR or any other federal or state government grants towards the cost share.

CARB-X can only fund indirect costs for US-based companies. For US-based companies, a 10% de minimis rate is applicable unless your organization has an existing Rate Agreement with the federal government. We will request copies of any such Rate Agreements. CARB-X cannot fund indirect costs of companies not based in the USA.

****CARB-X cannot sponsor any new requests for a federally negotiated rate agreement****

CARB-X cannot fund any costs related to work carried out prior to the start of the period of performance. CARB-X funding is expected to begin at or after January 1st, 2019 for this funding round. Do not include any costs prior to this date in your budget.

General Information:

Applicants who do not already have a DUNS number and are not already registered in the System for Award Management (SAM) should begin this process now to be able to move efficiently along the application process. Ultimately, successful applicants will be required to have a DUNS number and SAM registration.

To obtain a DUNS number, access the Dun and Bradstreet website at <http://www.dnb.com/duns-number.html>, or call 1-866-705-5711.

For SAM registration, access the SAM website at <http://www.sam.gov>, or by phone at 1-877-252-2700. User Guides and FAQ are available on the “Help” tab of the SAM website.