IARPA-BAA-16-08
Questions and Answers Round 3
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Fun GCAT BAA Questions 14 through 35 – Round 3

Q14. Does the entire software system need to be provided as source code (thus prohibiting use of existing commercial closed-source sequencing modules and libraries)?

A14. Source Code should be provided as a deliverable for all software system components developed through this Funding Opportunity. Offerors proposing to use existing data sets must provide written verification that all data were obtained according to U.S. laws, and identify any restrictions as outlined in 4.B.1.c Section 3.D - Data sources. If the performer combines newly developed software with commercial modules and libraries, IARPA requires the delivery of source code developed under this funding opportunity (even if the commercial source code cannot be provided).

Q15. Does the entire software system need to be able to run stand-alone on a single computer (thus prohibiting the system interacting with a public-Internet website to perform part of the functionality)?

A15. All systems should be able to run on a conventional high performance computing system for the purpose of Test and Evaluation, although databases and libraries may be accessed through networked computers. Systems that have additional architectures and functionalities may demonstrate benefits within the context of program reviews.

Q16. Is the deliverable purely source code or is IARPA wanting a user-friendly software executable with a GUI?

A16. The deliverable is comprised of both the source code, as well as any interface necessary for the operation of the source code to be evaluated by the independent Government T&E team. The GUI will allow the end user to be able to execute analyses of data to achieve the goals they are pursuing, such as, but not limited to prediction of functionality of novel sequences, or identification of motifs that are deemed novel and might possess biochemical functions of interest.

Q17. In 2014 our group annotated tens of thousands of antibiotic resistance sequences with ontology terms. Even starting with a gene ontology (GO)-type antibiotic resistance ontology, we found we had to create hundreds of ontology terms from scratch. We strongly suspect that this project will also require the invention of such terms. Is IARPA copacetic with this sort of innovation?

A17. Performers will be evaluated on their ability to match or improve upon assigned GO terms for a given sequence. As such, performers may propose additional GO terms as necessary to improve functional characterization.

Q18. Does IARPA desire that enzymatically inactive sequences that are otherwise "threatening" be recognized? Example: a catalytically dead botulinum toxin.

A18. Tools for the computational assessment of unknown DNA sequences should be able to assign a functional attribute to the product of any given sequence and assign a binary threat classification based upon those attributes. The decision as whether to classify a given sequence as a potential threat will be specific to each system, but should indicate that the sequence either in its current state or as part of a larger construct is capable of causing harm. In the example provided, a catalytically dead toxin is not capable of causing harm in its current state or as part of a larger construct, and as such would not be classified as a threat.

Q19. Section 4.B of the BAA seems to indicate that you want printed copies of the proposal, as well as electronic transmittal. Please clarify if this is the case and indicate the number of printed copies you would like to be submitted.

A19. Proposals must be submitted electronically through the IARPA Distribution and Evaluation Systems (IDEAS). Proposals submitted by any other means (i.e. delivered printed copies) will not be considered unless the offeror attempted electronic submission but was unsuccessful. See Section 4.C.2 for additional details.

Q20. Section 4.B.1.c.F, entitled Cost, Schedule, and Milestone, requests offeror to provide costs within the technical volume. Please clarify whether this is accurate, since normally costs are not provided in the technical volume.

A20. Yes, this is accurate. Please provide estimated costs by task, total cost, and company cost share. These should be provided along with the schedule and milestones to serve as a reference. Detailed cost information should be provided in Volume 2 (Cost Proposal).

Q21. The BAA has been provided as a pdf. Is it possible for the government to provide the appendices in Word, since many of them must be filled in?

A21. Fillable Appendices in a .docx format are available as a separate file and are posted in FedBizOpps along with the BAA.

Q22. Is IARPA interested in pathogenic sequences from organisms on the select agent lists alone? Would IARPA be willing to entertain threat sequences that originate from

other human diseases as well as toxins from poisonous snakes, jellyfish, sea anemones, etc.?

A22. Tools developed in Thrust 1 should be capable of correctly predicting the identity, function, and threat status of any given genetic sequences, including sequences that come from a variety of species and that convey a diversity of functions. The experimental methods and model systems developed in Thrust 2 may address sequences with diverse phenotypic effects derived from a diversity of model systems, including bacteria, viruses, and toxins beyond the select agent list. These model systems need not be based upon select agents and are not limited to addressing sequences from select agents. However, it is anticipated that in Thrust 2 the Test and Evaluation component of Phases 2 and 3 will incorporate sequences from the select agent list, and as such all offers should have the capability to work with such sequences by the end of Phase 1.

Q23. Since we understand that IARPA is interested in plant and animal diseases, can we limit these to the USDA select agents and the USDA plant protection and quarantine select agents? Background: While there has been voluminous work on the molecular mechanisms of microbial pathogenesis for animal diseases starting in the 1990s, until very recently (2007+) there has not been comparable work in plant diseases.

A23. Offerors may propose model systems capable of functionally characterizing the effect of plant pathogens. However, all systems should be extensible to a wide variety of model-appropriate sequences, and as such should not be limited to USDA select agents and/or the USDA plant protection and quarantine select agents.

Q24. Is IARPA interested in bacterial and fungal sequences that are responsible for antibiotic resistance? Is IARPA interested in sequences in pathogens (including mutated sequences) that convey resistance to antiviral and antibacterial agents?

A24. See answer to Question 22. The aim of Thrust 2 is to significantly advance the underlying experimental methods for the characterization of sequence function rather than to characterize a specific set of sequences. In Phase 1, proposers may select sequences appropriate for testing their experimental approaches, but all model systems should be able to functionally characterize a variety of sequences, including those derived from select agents, in later Phases.

Q25. Single nucleotide polymorphisms (SNPs), as well as broader mutations, in particular sequences (such as hemagglutinin and neuraminidase of the influenza virus) can alter host tropism and virulence. SNPs in bacterial gyrases can lead to antibiotic resistance. Does IARPA anticipate that these will need to be recognized and called-out in the reporting software?

A25. The tools developed in Thrust 1 should be capable of correctly predicting the identity, function, and threat status of a given genetic sequence. With the understanding

that variation in sequence can lead to altered function and/or threat status, it is desired that any tools developed will be capable of correctly predicting the encoded function with maximal specificity, and will assign an appropriate threat classification for the specific sequence provided.

Q26. Will any provision be made for keeping track of nucleotide blocks in terms of past/future orders from a particular ordering entity? Or will each nucleotide sequence presented for testing be an isolated example from which all inferences must be made?

A26. It is desired that tools developed under Thrust 1 should be able to computationally assess the identity, function, and threat status of any individual unknown genetic sequence with the ultimate goal of screening single 50 bp sequences, and individual sequences may be provided during Test and Evaluation. However, proposers are encouraged to be creative and tools that provide additional functionality or utilize a diversity of inputs to assess sequences will be considered, and any advantages gained can be demonstrated within the context of program reviews.

Q27. It is possible that individual short sequences (50 nt) may match to both threat and non-threat genomes making it impossible to determine a threat potential. However, there may be multiple sequences contained in a single synthesis order. By evaluating the matches of these together, contractors may be able to determine the threat potential with much greater confidence. Does this approach of joint evaluation fall within the scope of this BAA?

A27. See answer to Question 26.

Q28. Does the ability to identify sequences used for CRISPR/CAS9 modification of genes in threat organisms fall within the scope of the BAA?

A28. Computational tools developed in Thrust 1 should be able to assign a function and threat status to any given sequence. Proposers may incorporate the functional annotation of a genetic sequence as a reagent into their tools if desired, and as with all sequences a threat determination should be provided.

Q29. For the assertions on function for portions of the protein, does IARPA require a full-text document for each such assertion, or would it be amenable to the source being simply cited?

A29. Full-text descriptions for each functional annotation are not required, although supporting technical information may be requested as part of Government program management. The methods and approaches utilized to derive functional annotations for all sequences should be fully communicated.

Q30. Would the delivery of software in a format that consists of the source code of a front-end interface that relies on existing computational modules exposed as RESTful web services, and integrates and exposes the results of those computations to the user, either through a web browser or through an installable, executable desktop GUI, be an acceptable deliverable?

A30. Any deliverable system must be functional within a non-networked conventional high performance computer system for the purposes of Test and Evaluation. Any advantages gained through unique system architectures can be demonstrated within the context of program reviews. See Q&A 14 and 15.

Q31. This section states "The following are examples of topics that are considered to be out of scope for this program: Commercial off-the-shelf technology or other off-the-shelf tools that require a proprietary system architecture; Commercialization and/or commercialization plan development technology; Dual Use Research of Concern". Would the Government consider a total system that is not a COTS product but that contains a COTS software module component, to be out of scope?

A31. The Government seeks to develop new approaches and tools under this Funding Opportunity, but recognizes that in certain instances existing components may provide the best solution and are acceptable as part of a larger novel effort. COTS or software systems developed for another application should not be repurposed for this effort in its original entirety and should be considered out of scope for funding under this BAA. As noted in Q&A 14, offerors proposing to use existing data sets must provide written verification that all data were obtained according to U.S. laws, and identify any restrictions as outlined in 4.B.1.c Section 3.D - Data sources. Offerors should also identify all relevant technical data and commercial computer software as outlined in Section 6.B.2. Intellectual Property.

Q32. In Thrust 1, Ease of Implementation discusses restrictions on working space for computing infrastructure. Is it the intention of the Government to allow offerors to have 1 TB of space for delivered databases and code, but take up to 10 TB of space with intermediate/temporary files during the actual run time?

A32. Performers in Thrust 1 will be restricted to no more than 10 TB of total space during all Phases of the program, with the intention that access to increased space during the initial development and testing process will allow for optimal flexibility and reliable Test and Evaluation. The ultimate goal is to develop a final implementation at program completion that consumes <1 TB of space including all intermediate and temporary files during the actual run time, with further reductions viewed favorable.

Q33. Would the Government consider not counting the Gantt chart in the page count?

A33. The Gantt chart should be included along with the Statement of Work and will count toward the total allowed pages in Volume 1.

Q34. The requirement to present the Statement of Work (SOW) and a Gantt chart for all activities proposed in a multi-phase program may require a significant number of pages. Would the Government consider allowing offerors to present only the first phase of the program in detail in the SOW/Gantt chart?

A34. A Statement of Work and Gantt chart should be provided for all program Phases, and for each task and sub-task should contain the criteria outlined in 4.B.1.c. Section 3 – Detailed Proposal Information.

Q35. This paragraph states: "If subcontractors have concerns about proprietary cost information, subcontractors can submit their detailed cost proposals directly to the Contracting Officer." What e-mail address should subcontractors use to submit proprietary cost details?

A35. The offeror is responsible for providing all subcontractor proposals with the Cost Volume, including cost element sheets for the base period, each option period, and a total cost summary. If the proposal is selected for negotiation, the Contracting Officer may request additional information from the subcontractor, including all direct and indirect costs. At that time, subcontractors can submit proprietary cost information directly to the Contracting Officer if desired.