DARPA-BAA-16-59

Frequently Asked Questions

Last Updated: 11/8/2016

GENERAL INFORMATION

Q: If my research is not geared specifically to meet the Biological Control Program goals. Is there a solicitation that I can respond to?

A: Yes. DARPA/BTO has an open solicitation (DARPA-BAA-16-33) for this purpose. Responses are being collected through April 28, 2017.

Q: Is Dr. Wegrzyn available for a call to discuss our proposed approach?

A: The best way to receive feedback on an approach is through the submission of a proposal abstract prior to the deadline specified in the BAA. The BAA describes the program, including metrics, in detail. If you have specific questions, please submit them by email to SafeGenes@darpa.mil. Please be aware that your question and its answer may be published on this FAQ page, after the question has been revised to remove proprietary information.

Q: Will the Proposers Day slides be posted online?

A: Yes, information relayed during the Proposers Day will be made available on the BTO section of the DARPA Opportunities page: http://www.darpa.mil/work-with-us/opportunities.

Q: Do I need to submit an abstract? What is the advantage of submitting an abstract? Does my abstract need to match the full proposal submitted?

A: Abstracts are strongly encouraged, but not required, to submit a full proposal. DARPA will provide written and/or verbal feedback for each abstract submitted. DARPA will provide feedback regarding technical approach, and will highlight components for proposers where additional information or clarification should be provided to meet the requirements of the BAA and vision of the program. Feedback will also be provided to encourage or discourage submission of a full proposal to the Safe Genes solicitation based on alignment with Safe Genes program vision and technical innovation. Finally, DARPA understands that final proposals and team make-up may vary somewhat from initial Abstracts as content of teams and concepts proposed matures during preparation of the proposals.

Q: I have received information about the Safe Genes Broad Agency Announcement (BAA) from multiple places, including the DARPA news update, press articles that cite the news update, the BAA, slides from Proposers Day, FAQ, and during my sidebar at Proposers Day. Which information should I use to write my proposal?

A: The Broad Agency Announcement takes precedence and provides authoritative information on the Safe Genes solicitation. Subsequent clarifications will be provided publicly on the FAQ.

PROGRAM STRUCTURE

Q: What is the anticipated start date (or date range) of funded proposals?

A: Proposers may anticipate starting Phase I in May, June or July of 2017. Actual start dates will vary based on source selection and award negotiations.

Q: What defines DARPA relevance and is it limited to use in the United States?

A: DARPA relevance includes applications that advance our national security capabilities both at home and abroad. These applications may range from improving security to reducing disease burden. Proposers should choose an application and provide justification for its DARPA relevance as well as advancement over the state of the art. Use is not limited to the United States.

Q: For *in vivo* and *in situ* proof-of-concept in plants, how does DARPA work with the proposer to manage regulatory hurdles, such as review and approval times?

A: DARPA focuses on the development of technology and does not manage the regulatory process. As stated on pg 20, "Performers are also expected to present a plan for early and continued engagement with regulators (e.g., EPA, FDA, etc.) throughout the program to discuss developing technologies and challenges to facilitate the eventual translation of the tools generated for practical use." Proposers may consider including milestones and metrics that include engagement with regulatory bodies as part of their project strategy, to ensure successful technologies stemming from the Safe Genes program are well-positioned for regulatory approval at the completion of the program.

Q: Is there a preference for prokaryotic or eukaryotic demonstrations in the program?

A: Proposers may choose any DARPA-relevant organism to meet the Safe Genes requirements (both prokaryotes and eukaryotes are welcome). However, the Safe Genes program seeks proposals that represent "a significant improvement over the state of the art" in addition to selection of a DARPA-relevant application and demonstration of generalization to other systems, which must be clearly articulated by the proposers.

Q: How will the communication of dual use research of concern (DURC) be managed and who will make determinations of what constitutes DURC?

A: As defined in the United States Government Policy for Institutional Oversight of Life Sciences Dual Use Research of Concern (DURC) (http://www.phe.gov/s3/dualuse/Documents/durc-policy.pdf), proposers should indicate if their research may constitute DURC based on the Listed Agents and Experiments of Concern. Institutional definitions of DURC outside of the Listed Agents and Experiments of Concern do not meet the requirement for notification of a United States Government funding agency. Proposing institutions should follow the procedures of their Institutional Review Entities and notify DARPA if the IRE finds that the proposal falls within the iDURC policy definition. For further information on the DURC guidance, visit http://osp.od.nih.gov/office-biotechnology-activities/biosecurity/dual-use-research-concern.

Q: Can testing plans include release of the engineered organism?

A: No, proposals that include open release of engineered organisms will not be considered this program.

Q: Does detection and surveillance methods fall within the scope of the program?

A: Detection and surveillance methods alone do not satisfy the requirements of the Safe Genes program. However, they may support the development of technologies directly addressing the program's aims.

Q: What role does innovation play in the overall evaluation?

A: Innovation is one of the central goals of any DARPA program. Safe Genes is no exception.

Q: Since this is a four year program, will there be more opportunities to apply for funding throughout the program's lifecycle?

A: No, this will be the only open call for proposals for the Safe Genes program.

Q: BAA pg 24 section 4 Application and Submission Info – "This notice with the classified addendum consists the total solicitation." Where can we find the Classified Addendum?

A: Safe Genes will be an open and unclassified research program. This language was included in error from a previous BAA template version. There is no classified addendum to the Safe Genes BAA. No classified information will be received in applications. Classified applications will not be accepted.

Q: For the Safe Genes program, is it more appropriate to engage communities where the eventual release of a gene drive might be considered; or broader, more generic public audiences?

A: Community engagement plans are welcome to be included in submissions to the Safe Genes program, but they must be directly related to the technology that is under development. Proposers can include engagement at multiple levels and/or at multiple stages of technology development as long as they are well justified (such justification may include, for example, milestones related to the regulatory process, etc). Such plans should be described and proposed as separate tasks with separate funding listed for each level and/or stage of community engagement.

PROPOSALS

Q: Per 4.3.2.A Volume I, Technical and Management Proposal, is the cover letter included in the page count for full proposal?

A: No. Per the BAA, "A submission letter is optional and is not included in the page count."

Q: Per 4.3.2.C Volume I, Technical and Management Proposal, are the executive summary slides included in page count for full proposal?

A: No.

Q: The BAA states the proposer must address the following: Data Sharing, Biocontainment and Biosafety and Ethical, Legal, and Societal Implications (ELSI). Please confirm this is not included in the 20 page count limit outlined at the top of page 32.

A: These items are not listed as separate sections of the proposal and should be addressed as part of the Technical and Management plans defined in Volume 1.

Q: Under the requirements for Section II – Detailed Proposal Information, A. Executive Summary, please confirm the Executive Summary is not included in the 20 page count limit outlined at the top of page 32.

A: The slides do not count towards the page limit, the summary itself does.

Q: Under the requirements for Section II – Detailed Proposal Information, F. Statement of Work, please confirm that Attachment 3 is not included in the 20 page count limit outlined at the top of page 32.

A: None of the attachments count towards the page limit.

Q: Do we have to have 1-inch margins or is 0.5-inch okay?

A: Standard 1-inch margins should be used in all proposals.

Q: Will the Safe Genes program accept grant proposals?

A: DARPA does not intend to award grants under the Safe Genes program. Safe Genes awards may include cooperative agreements, contracts, or other transactions.

Q: Is a declaration table sufficient to satisfy the Intellectual Property requirement? Where in the proposal should this information be stated and does this count against page count?

A: Yes, a declaration table will suffice. Per the BAA, "Proposers shall follow the format under DFARS 252.227-7017 for this stated purpose. The table should be placed either Volume I - Section III, or Volume II. No the table does not count against the page count.
http://farsite.hill.af.mil/reghtml/regs/far2afmcfars/fardfars/dfars/dfars252_227.htm#P1175_92448

Q: What is the role of a performer project manager?

A: Proposers may include a project manager to manage the coordination between teams and with DARPA. Project managers may be particularly useful for large teams addressing multiple TAs. Project managers can be PIs, senior post-docs, staff, or external consultants.

Q: How does one address access to technologies outside of a proposer's reach? Does DARPA facilitate such dialogues?

A: Teaming and collaboration are the responsibility of the proposers.

Q: Where should proposal abstracts be submitted? And will late submissions be accepted?

A: Proposal abstracts should be submitted by October 6, 2016 at https://baa.darpa.mil. Late abstract submissions will not be accepted. Abstracts are strongly encouraged and will receive feedback, but are not required for consideration for funding under the program. Therefore, proposers may still apply with full proposals without submitting an abstract.

Q: Please clarify if submittal of the Abstract and Proposal by the DARPA BAA Submission Portal is allowed. Please clarify if the Abstract and Proposal may be hand carried for delivery to the 675 North Randolph Street, Arlington, Virginia address.

A: Per the BAA, "Abstracts and Full Proposals sent in response to DARPA-BAA-16-59 may be submitted via DARPA's BAA Website (https://baa.darpa.mil)." The lone exception is that proposals requesting cooperative agreements must be submitted via Grants.gov or in hardcopy (not via http://baa.darpa.mil). Abstracts and Proposals may be hand carried for delivery to DARPA, though we recommend using the DARPA BAA Portal.

Q: How many proposals can an institution submit?

A: On pg. 24 the BAA states that "Proposers may join any number of teams as a subcontractor and still submit a separate proposal as the PI (with or without subcontractors)." Proposers are reminded that each proposal will be independently evaluated, not weighed against each other during review. Multiple proposals should not be submitted in an effort to increase the likelihood of selection. Proposers should only propose a level of effort that can be met in each proposal individually and overall if the PI is prime or a subcontractor on multiple teams. DARPA will expect that all selected proposals will be able to achieve the milestones and deliverables as awarded.

COST/FUNDING/SPREADSHEET

Q: Can we modify the "Expenditures by Month" budget template tab Phase I and Phase II lengths?

A: Yes, "Expenditures by Month" can be edited and should align with the dates and phases in the technical and cost proposal.

Q: For our subcontractors who are also universities, will they need to complete both the Phase I and Phase II sheets along with the "Sub - University XYZ Budget" sheet?

A: Per the BAA, "All subcontractor cost proposal documentation must be prepared at the same level of detail as that required of the prime." The "Sub - University XY Budget" tab is for subcontractors with total costs less than $500,000 per phase. DARPA encourages subcontractors with a cost per phase greater than $500,000 to complete the more detailed "phase" style tab as the prime does in order to meet the same level of detail. Alternatively, subcontractors may complete their own workbooks, as long as these costs are incorporated in the total budget collated and provided by the prime in the Cost Proposal.

Q: What is a cooperative agreement?

A: A cooperative agreement is a financial assistance award that enables the United States Government funding agency, such as DARPA, to engage in active program management, direct milestones, and guide deliverables. See DARPA's Contracts Management Offices page for additional information: http://www.darpa.mil/work-with-us/contract-management#GrantsCooperativeAgreements

Q: How should a proposer determine an appropriate budget?

A: Cost realism is an important evaluation criteria for proposers to include. Proposers must provide a realistic estimate of the costs (e.g. staff, resources, equipment) to successfully complete milestones and deliverables.

Q: How is cost share considered in cost proposal evaluations?

A: As stated in the BAA, 3.2. COST SHARING/MATCHING, "Cost sharing is not required; however, it will be carefully considered where there is an applicable statutory condition relating to the selected funding instrument (e.g., for any Other Transactions under the authority of 10 U.S.C. § 2371). Cost sharing is encouraged where there is a reasonable probability of a potential commercial application related to the proposed research and development effort." If the proposer includes cost sharing, it should be incorporated in the cost proposal as indicated on pg. 37 of the BAA, so that it can be evaluated under the criteria of Cost Realism (5.1.4. Cost Realism). "For efforts with a likelihood of commercial application, appropriate direct cost sharing may be a positive factor in the evaluation." Proposals including cost sharing must determine and communicate how it would impact data rights. As stated on pg. 49, "Proposals will not be evaluated against each other since they are not submitted in accordance with a common work statement." Therefore, cost sharing would not give advantage to one team over another.

TECHNICAL

Q: What genome editors should be considered?

A: Safe Genes is open to proposals involving any genome editor(s) and is not limited to a specific type (e.g. CRISPR-Cas) or activity (e.g. nuclease, epigenome editor, etc).

Q: Will this funding opportunity (DARPA-BAA-16-59) consider all life organisms or just for animal or insect species at this time?

A: Yes, all life organisms will be considered.

Q: Can genetic remediation (TA3) be engineered into the organism that is released? Or should it be applied to previously engineered and released organisms (e.g. in a bioterror event)?

A: Built-in or intrinsic systems to control or reverse engineered genes are categorized under TA1 (control of genome editing activity). In TA3 (genetic remediation), proposers should focus on extrinsic solutions to remove or replace engineered genes that are pre-existing or introduced in an environment that are present due to intentional or accidental release. Genetic remediation should result in a return to a proposer-defined baseline state including a phenotypic (required) and genotypic (aspirational) wild type state.

Q: How specific does the DARPA relevant application have to be? For example, is DARPA more interested in novel cell therapies or solutions that can cover many different engineered cell types?

A: A specific model system and approach should be identified and justified within the context of the proposal. Solutions that are broadly applicable or generalizable are desired. DARPA relevant applications may include, but are not limited to, vector control strategies to mitigate infectious disease, strategies to maintain and protect ecosystem biodiversity, or novel cellular therapeutics to promote host defenses or combat disease. If proposals address multiple TAs, a single DARPA-relevant application should remain consistent throughout the proposal.

Q: Does prophylaxis only mean agents that are administered to the animal before introduction of gene editing agents or engineered cells? Or, could prophylaxis apply to methods that could be administered to engineered cells ex vivo to increase their safety when administered to patients?

A: Prophylaxis refers to the administration of a countermeasure before the introduction of gene editing agents to prevent the editing activity entirely, therefore applying methods to engineered cells ex vivo and then administering them to increase safety would not be a prophylactic application. However, engineering cells ex vivo to increase their safety through new temporal and spatial controls when administered to patients could be an appropriate application to TA1 if all of the other TA1 requirements are met.

Q: Is DARPA most interested in technology that can have broad applications to many types of engineered cell therapies or is there a particular cell therapy area in which DARPA is most interested?

A: The proposer should determine the DARPA relevant application and provide the rationale for their choice in the proposal. Solutions that are broadly applicable or generalizable are desired. For example, a solution that covers genome editing system can be broadly applicable or generalizable through a demonstration of activity in at least one additional cell type, tissue, organ, or species, and/or control of at least one additional genome editing system.

Q: What type of application is TA2 looking for? For example, should it be used in animals or across a field of crops?

A: The type of application (e.g., population or environmental level genome editing activity inhibition in animals or across a crop field) should be decided by the proposer. However, in choosing an application, proposers should provide the relevant rationale for their choice and include it in the proposal, which must include consideration of the likelihood for successful prophylactic and therapeutic in vivo use.

Q: Does Safe Genes envision the use of advanced analytic techniques to better extract insights from the data collected?

A: Yes, successful teams may include analytical approaches as well as other supporting technology to meet the Safe Genes requirements and milestones. These include, but are not limited to mathematical modeling, assay development, and optimization of existing assays.

Q: What is the depth of modeling necessary and how should it be incorporated?

A: Modeling is dependent on the application. For example, if the proposal plans to utilize a simulated natural environment, proposers may consider modeling gene flow, population dynamics, environmental variables, etc. Models should integrate empirical data and help predict function of a given application in more complex contexts.

Q: How is spatial and temporal control defined?

A: Spatial and temporal control is dependent on the proposed application and should be defined and justified by the proposer. For example, temporal and spatial control for a cellular therapeutic application may be defined on the timescale of seconds to minutes and in the spatial context of cell or tissue type, whereas temporal and spatial control for a gene drive vector control application may be defined as number of generations and geographic isolation. Proposers must clearly articulate the target temporal and spatial control parameters and quantitative performance metrics they aim to achieve that is

consistent with the DARPA-relevant application of their choosing and represents a significant improvement over the state of the art.

Q: How is generalizability defined?

A: Broadly. Generalizability is dependent on the TA and the application. TA1 states that “the genome editing system can be broadly applicable or generalizable through a demonstration of activity in at least one additional cell type, tissue, organ, or species, and/or control of at least one additional genome editing system.” Countermeasures and prophylaxes in TA2 should “inhibit more than one class of genome editor in more than one species.” Proposers must specify how generalizability will be demonstrated for their selected DARPA relevant application.

Q: May reversal drives be considered as part of a TA3 approach?

A: DARPA is aware of multiple approaches that may be considered a "reversal drive", some of which may be appropriate for TA1 or TA3. It is anticipated that control mechanisms that are intrinsic to a given system will align to TA1. Extrinsic control mechanisms, like a secondary overwrite drive, are more obviously aligned with TA3. Proposers to TA3 should focus on extrinsic solutions to remove or replace engineered genes that are pre-existing or introduced in an environment that are present due to intentional or accidental release. Genetic remediation should result in a return to a proposer-defined baseline state including a phenotypic (required) and genotypic (aspirational) wild type state. Proposers that choose to pursue gene drive technologies must address TA1 and at least one additional TA.

Q: Is riboswitch technology of interest to the Safe Genes program?

A: While we cannot comment on DARPA level of interest in a given technology, a riboswitch targeting Cas9 and/or sgRNAs is within the scope of Safe Genes.