GENERAL TECHNICAL QUESTIONS

1. Can you please provide some general guidelines on key technical information to be included in the proposal?

A: At a minimum, all required elements and milestones described in the BAA should be discussed. Where multiple potential approaches are described, outline plans, selection criteria, and a timeline for down selection, or preferably, select a starting candidate and outline plans for risk mitigation. To aid proposal reviewers, please ensure that the following information is clearly stated and easy to identify:

- Please describe how your approach will control and deliver an appropriate therapeutic dose.
- State your best estimate of the approximate time from communication to initiate therapy and the start of therapeutic delivery, as well as the time period and frequency over which the therapy will be delivered (e.g., single bolus dose, once daily dose for 5 days, etc.). If a course of therapy will be used, how often must therapy initiation/communication be triggered by the warfighter (e.g., one time, daily, etc.)?
- Please clearly state mechanisms for both therapy initiation and cessation (e.g., therapy runs out after a fixed time, warfighter communicates to end therapy, etc.).
- The full life cycle of the system from in vivo installation to the kill switch mechanism and/or device removal (if applicable) should be described.
- Please be clear about the specific intended anatomic location of the device, means of localization, and potential health and safety implications of its presence or installation.
- For ingested devices, describe how the carrier form factor will change over time (if applicable) from initial ingestion to ultimate disassembly and how this will be controlled.
- All small and large animal models, along with the proposed sample sizes, experimental approaches, and justification of your choice of model(s), should be identified.
- Identify the institution where the human trial will be performed and clinician(s) who will lead the human trial.

2. Is the system intended to provide treatment for one episode of traveler’s diarrhea or sleep disturbance or to provide several doses for multiple distinct episodes? If multiple doses are required, how many doses should be available to the warfighter?

A: Because the needs of individual warfighters may differ, the system should provide multiple therapeutic interventions during the 60+ day implantation/ingestion duration. An ideal system would provide as much therapy as needed at any point in time. Proposers should clearly indicate the maximum number of interventions that the system can provide if there are such limitations.
3. **Does the kill switch require removal, expulsion, or dissolution of the carrier or simply the ability to make the system no longer functional?**

   A: There is no specific requirement for removal, only conversion to a non-functional state. The need for removal will depend on potential safety risks associated with leaving the system in the body long term. If the system will remain in the body, proposers must demonstrate that the therapy has been fully deactivated. There is no expectation that system functionality can be restored once the kill switch is triggered. For this reason, the kill switch is distinct from the therapy on/off mechanism employed during the 60+ day usage period and is intended to represent a more permanent termination of the system. A natural time that the kill switch may be triggered is at the end of the 60+ day period. However, the kill switch should allow for earlier termination in the case of an adverse reaction or when the warfighter decides to discontinue therapy.

4. **Section 1.2 specifies the development of “at least one *in vivo* generation and delivery mechanism per *in vivo* therapy.” Does this mean that therapies are not allowed to use the same delivery mechanism?**

   A: Multiple therapies are allowed to use the same delivery mechanism.

5. **Does performing experimental screens for bioactive molecules/microbes constitute exploratory studies and thus considered non-responsive to the BAA?**

   A: Highly exploratory or mechanistic studies are not allowed and proposals should not begin with an exploratory screen. However, knowledge generation is expected and some initial screens/development of established technologies for this specific application may be allowed. All development work needs to be achievable within the BAA time frame and all milestones must still be met within the appropriate timelines.

6. **Is there a required time frame in which the treatment must be delivered?**

   A: There are no specific timing requirements other than the ability to “demonstrate on demand complete termination of production within 6 hours.” The time between an external communication triggering the initiation of therapy and the start of administration should occur within a reasonable time frame and proposals should include discussion related to this topic.

7. **What types of *in vitro* and *in vivo* models are appropriate for demonstrating the efficacy of the therapeutic and the integrated device?**

   A: *In vitro* and *in vivo* models should be chosen based on current literature and the chosen intervention track. It is up to the proposers to justify their selections and approaches.
8. **How will inflammatory responses caused by physical activity be taken into consideration?**

A: Proposers should address biocompatibility of proposed systems, including potential inflammatory responses and impacts of physical activity, and inflammatory responses will be accounted for via biocompatibility testing through the performer contracted CRO. While we acknowledge that physical activity can activate the inflammatory response, particularly rigorous activity typical of the warfighter, standard conditions for CRO biocompatibility testing will be sufficient. However, if the size or localization of proposed implants or ingestibles would have a significant risk of increased inflammation in response to physical activity, proposals should include risk mitigation strategies and outline experimental plans to demonstrate the risks has been mitigated.

9. **Beyond the initial two goals of ADAPTER, is there any future potential for nutrient delivery?**

A: ADAPTER is focused on developing bioelectronic devices with synthetic biology, enabling interventions to be deployed on demand. Successful completion of the program would open a broad range of applications, including nutrient delivery, but those are not the goals of ADAPTER.

10. **What are the current methods used by the military for treating jet lag and traveler's diarrhea? Imagined use case (user needs) for the deployed warfighter?**

A: Many policies and instruction documents for the Department of Defense are publically available, a few of which are listed below. Note that these references are not exhaustive and may be irrelevant to your specific proposal, and so should serve only as a starting point. Proposers are responsible for conducting a thorough literature review.

- Sleep in the Military: Promoting Healthy Sleep Among U.S. Servicemembers. [https://www.rand.org/pubs/research_reports/RR739.html](https://www.rand.org/pubs/research_reports/RR739.html)
- [https://goflightmedicine.com/stimulants-sleep-aids/](https://goflightmedicine.com/stimulants-sleep-aids/)
11. Can you please be more specific about the environmental storage conditions and volume constraints?

A: Biological components stored within the device must remain viable throughout the duration of use, as described in the BAA. The volume of the overall device should be consistent with internal use in humans.

12. How will onset of symptoms and/or need for intervention be determined in the warfighter?

A: Initiation of therapy will be controlled by the warfighter at his/her discretion. It is acceptable to provide feedback to the warfighter to inform this decision.

13. How will encryption/security be tested?

A: Security of communications and the system is not the focus of program and will not be specifically evaluated; however, proposers should describe how their system meets the fundamental security requirements outlined in the BAA.

14. Are there any requirements for or expectations of system deployment in austere environments?

A: No, the travel adapter system can be implanted/ingested/installed within the warfighter at a medical facility. The system must be introduced into the body without significant medical intervention (i.e., no more than a minor surgery) and full system “installation” should be completed a reasonable time frame (e.g., 1-2 days).

15. Can the system be adapted for different geographical regions based on the most common pathogenic bacterial strains in that region or should the system be geographically agnostic?

A: For this BAA, the system should be more general. In the future, it may be desirable to have region-specific options. Similarly, this BAA does not target a specific branch or group of the military.

QUESTIONS SPECIFIC TO TECHNICAL AREA 1 (ACCURATE THERAPIES), BOTH TRACKS

16. "Any proposed therapy should have a published basis: new mechanistic or exploratory therapeutic studies are not of interest. Can you elaborate on the "published basis" requirement?

A: Implementation and delivery of established therapies, rather than therapy discovery or development, is the intent of the program. Therefore, proposed therapies must have an established basis. Proposers are not required to base proposals on their own publications but
cannot base their proposal solely on unpublished data. Proposed therapies are not required to have FDA approval.

17. "The intervention or therapy produced *in vivo* must be amplified by at least 1:1:(load volume):(released dose) by the end of Phase I and by at least 1:4 by the end of Phase II." It is unclear what the load volume means. Also, the units of measurement for volume and dose sometimes differ, so how is this ratio meant to be calculated?

A: Load volume would be defined by the space occupied by therapies (preloaded chemicals and living components) in the system. Released dose volume would be defined by the volume of equivalent therapy capable of being delivered over the functional life of the system if taken conventionally, including inactive ingredients. The system should produce more of the therapy than is originally supplied at the time the carrier is administered or than would be included in a single-use pill dose. The intention is not to preload a capsule with a fixed volume of drug that is stored and dispensed over time.

18. Regarding the "biological therapy," are fungi or viruses acceptable for delivering therapy? Can phages or phage-derived particles be used? Finally, are proven natural molecules acceptable?

A: All of these are within scope provided that intervention therapeutics are produced or amplified *in vivo*. ADAPTER envisions the use of biological interventions/therapies, combining relevant portions of synthetic biology and bioelectronic devices. There is no requirement that the therapy is a drug and there are no restrictions on the mode of action. Similarly, it is acceptable for therapies to activate or inhibit physiologic responses.

19. Prophylactic antibiotics are sometimes prescribed to deal with traveler's diarrhea, what precludes this line of treatment for warfighters?

A: One objective of this program is to eliminate the need for warfighters to carry antibiotics and other medications. The use of antibiotics is within scope of the program, as long as they are generated *in vivo* and the microbiome is returned to relatively similar beta-diversity within 5 days for Phase I and 3 days for Phase II as outlined in the BAA.

20. Are GMO-based therapies acceptable?

A: Yes. GMOs and genetically engineered cells are within scope, but proposers should discuss and justify safety and other related issues, such as release into the environment through human waste. The role of the kill switch in deactivation of the GMOs should be also adequately clarified. Additionally, we encourage proposers to engage in early conversations with the FDA about their specific therapy as it relates to the human trial in Phase III.
21. Can therapies be administered prophylactically to reduce or eliminate symptoms, or should therapy only be administered after symptoms arise?

A: It may be acceptable to have a therapy that is prophylactic provided that delivery is fully under control of the warfighter and that the therapy is administered as needed rather than continuously. In other words, the therapy could be turned on before symptoms develop but at the time sleep disturbance or traveler’s diarrhea is expected (e.g., following consumption of food/water presumed contaminated or just prior to a long flight).

22. What is meant by Therapy 1 and Therapy 2? Can these be the same biological output (e.g., the same hormone) but produced with different time dynamics or control mechanisms? Or does it refer to two distinct biological outputs (e.g., different hormones)?

A: The two therapies must be two different outputs, though the therapies can be similar (e.g., two, different hormones). All dosage and timing dynamics should be physiologically relevant for the specific therapy. Similar control mechanisms may be utilized for both therapies.

23. Is there any required relationship (i.e., synergistic, additive, same type of drug, etc.) between the ≥ 2 therapies?

A: There is no required relationship between therapies. The purpose of requiring multiple therapies is to maximize the versatility of the technology to meet warfighter needs.

24. What is the process if we want to use a deliverable that is patented (e.g., a patented drug)? Do we need approval of the company who owns the patent? Do we need to have the drug company that owns the patent as part of the team submitting?

A: This depends on the therapy and it is up to the proposer to determine the appropriate relationship with the organization which owns the rights. The Proposer is expected to notify DARPA if it anticipates infringing on any patent or if the Proposer intends to indemnify the Government against such infringement.

QUESTIONS SPECIFIC TO TECHNICAL AREA 2 (CARRIER AND COMMUNICATION), BOTH TRACKS

25. Is there a requirement related to size of the external device?

A: While there are no specific size requirements, the system is intended for travel and should be designed accordingly. Although portability is not required at this point, proposers must at least have a plan for addressing portability in the future. Our intent is to reduce both the physical and mental burden on the warfighter through this program. Of note, it may be acceptable for the initial administration of the system to involve a larger device, but the external controller used by the warfighter should be portable.
26. Can the *in vivo* carrier be physically replaced or upgraded during the 60+ day usage period? Can additional components be introduced/ingested during the 60+ days?

A: No, we expect there to be one initial administration to introduce the carrier into the body, which can then deliver the therapy to the warfighter on demand, as needed. Self-regeneration or renewal of carrier components is acceptable provided there is no external intervention, including ingestion, to replace components or reload the therapy into the carrier. The goal of a single carrier administration is to reduce burden on the warfighter.

27. Do we have to use a device that delivers a drug if another approach works?

A: Any biological therapy, produced *in vivo*, that meets the requirements of TA1 is acceptable. Technologies not produced internally, such as light boxes, or that are not produced *in vivo*, such as electric stimulation of a nerve, are not in scope.

28. Are external and/or wearable devices allowed (i.e., transdermal patches, watches, belts, etc.)?

A: It is a requirement of the ADAPTER BAA that therapies must be produced and delivered internally and that the therapy carrier must also be inside of the body. The communication device and physiologic or environmental sensors may be wearables. For any external device, both portability and comfort should be considered as these will be key factors towards adoption. While portability is not required in the context of the ADAPTER program, proposers must at least have a reasonable plan for addressing portability in the future.

29. Is a device-based carrier required to contain the living chassis?

A: The intent of the TA2 carrier component is to maintain, localize and deliver the biological component in TA1 in a manner that allows for controlled deployment and cessation of the therapy. The biological component does not necessarily have to be contained within a secondary carrier for the entirety of the 60 days to carry out its therapeutic function provided that appropriate safeguards and kill switches are in place. Given the requirements to secure, maintain, and localize, it is unlikely that a solution without physical containment would be convincing as a proposal for this program.

30. Does the carrier need to be ingested? Will you accept implantable devices?

A: Subcutaneous implants are allowed. Other internal carriers will also be considered provided that they can be introduced into the body without significant medical intervention and could be relatively easily removed if needed. Carriers should be appropriately sized to fit within the body. External carriers, such as transdermal patches, are outside the scope of the BAA.
31. Are multiple ingestions of the carrier allowed?

   A: Multiple ingestions may be acceptable if they all occur at the time of initial system deployment. Ingestions that occur across multiple time points during the 60+ day usage period are not acceptable.

32. Is light an appropriate technical strategy to modulate cellular activity? Is RF or ultrasound stimulation allowed?

   A: All methods listed are within scope. While light communication between the external controller and carrier is allowed, light-based therapy is not.

33. Phase 1 milestones for TA2 specify demonstration in vitro (9 months) followed by demonstration in a realistic physiological model/phantom (12 months). Could researchers skip in vitro demonstration and begin in phantoms?

   A: Yes, provided that investigators can still demonstrate that the carrier maintains viability of the living chassis for at least 10 days.

34. Is there any exclusion to the proposed carrier technology?

   A: There is no constraint on the bioelectronic carrier technology as long as it addresses questions in the BAA.

QUESTIONS SPECIFIC TO THE CIRCADIAN RHYTHM MANAGEMENT TRACK

35. Is the focus to achieve a relatively normal sleep/wake cycle or is there an expectation to push the human body beyond normal limits (i.e., 72-hour wakefulness for extreme missions)?

   A: Extreme missions are outside the scope of this BAA. Instead the focus is to help warfighters achieve sufficient sleep and restfulness for optimizing their natural performance. This program specifically seeks to address sleep disturbance caused by jet lag due to switching time zones and shift lag from a changing sleep/wake schedule due to shift changes (e.g., switching between day and night shifts).

36. For circadian rhythm management - do you expect to have closed loop control?

   A: No, the warfighter should maintain complete control over therapy initiation. The therapy can be automated, however, such that it occurs on a preprogrammed schedule.

37. Are we required to use melatonin, as suggested in the BAA, for one of the therapies?

   A: No, melatonin was simply presented as an example and does not represent a requirement or a reflection of our preference.
QUESTIONS SPECIFIC TO THE DECONTAMINATION TRACK

38. In the BAA, several pathogens of interest are listed, including 5 E. coli strains. The BAA calls for “five species degraded by end of Phase II.” Can these 5 species include some or all of these 5 E. coli strains listed, or is it expected that a maximum of 1 E. coli strain count against the 5 species to be degraded?

A: The primary purpose of targeting multiple strains of bacteria is to ensure that protection will be provided against a range of relevant threats; however, an important secondary purpose is to demonstrate the flexibility of the proposed approach. Consequently, with justification, proposers can select some or all of the E. coli strains listed but should carefully weigh whether this fully demonstrates the strength of their technology.

39. Is a kill switch required for naturally occurring bacteriophages?

A: Regardless of chosen therapy, it is critical that proposers can “demonstrate on demand complete termination of [therapy] production within 6 hours.” There may be rare exceptions when a kill switch is not relevant or necessary, but these should be clearly justified.

40. Is a kill switch required for naturally occurring bacteriophages?

A: Regardless of chosen therapy, it is critical that proposers can “demonstrate on demand complete termination of [therapy] production within 6 hours.” There may be rare exceptions when a kill switch is not relevant or necessary, but these should be clearly justified.

41. What role does the microbiome have in this program?

A: As described in the BAA, if following the traveler's diarrhea track, the gut microbiome must return to similar composition as pre-disease. Additionally, current literature outlines how the microbiome may or may not have direct impact on in vivo therapeutics, delivery mechanism, intervention track, etc. Thus, it is up to the performer to determine the relevance of the microbiome (if any) for the therapeutic strategy.

42. If the goal is eliminating bacteria that contribute to traveler's diarrhea, is there also potential for integration of "good" bacteria?

A: Any appropriate bacteria can be introduced; however, all must be susceptible to removal by the device.

43. What is the criteria for showing efficacy against a species since there are many different strains for each species?

A: Minimal criteria for efficacy are defined in the BAA as 99.9% reduction in bacterial number and a measured therapeutic impact. While all treatments will be required to meet the 99.9% reduction in number, proposers should address if specific species/strains targeted may require a greater reduction to impart therapeutic impact and how they will meet the threshold
required for therapeutic efficacy. Strains chosen should be DoD relevant. Examples are provided in the BAA.

ANIMAL STUDY RELATED QUESTIONS

44. What types of small animal models are acceptable? What is considered a large animal?

A: The choice of animal model(s) is at the discretion of the proposers and should be appropriately justified. The final technology will be tested in humans, so the large animal model must accommodate a system of that size and scale.

45. Does CRO/IV&V testing need to be performed in the same large animal model that investigators use for their studies?

A: All large animal testing must be performed in a single model.

46. It seems as though there is some overlap in the roles of the CRO and the IV&V team, at least when it comes to efficacy testing. Is there a clear dividing line in the roles of the CRO and the IV&V, or some specific differences you envision in how the CRO and IV&V teams will work with the performers?

A: The CRO will be identified and contracted by the performers and will work under their direction. In this capacity, the CRO will assist the performers in timely completion of all necessary tasks to meet the required milestones. The IV&V team will be selected and funded by DARPA for the purpose of providing unbiased validation of the efficacy of the integrated system. The IV&V team will not specifically evaluate safety aspects of the therapy and/or integrated system and the CRO will be responsible for all safety-related testing.

HUMAN TRIAL RELATED QUESTIONS

47. Do you anticipate requiring studies in humans? Are we expected to propose a plan for the clinical trial in the application? Will DARPA be helping to identify human populations for the safety study (e.g., military) or will that be up solely to the proposers?

A: As described in the BAA, Phase III includes safety studies in humans. All proposals should address these requirements and identify appropriate patient populations for the clinical trial.

48. Could you please delineate requirements / expectations for human testing?

A: As stated in the BAA, human trials will be performed for the purpose of evaluating safety rather than efficacy. To simplify testing, the TA1 and TA2 components may be tested for safety independently. Combined devices may be tested if the proposal outlines a path for entering trials under the timeline specified. There are no restrictions on patient populations
for the clinical trial and DARPA will not be facilitating access to patient populations inside or outside the DoD.

49. Should the human study demonstrate efficacy?

A: We do not intend for efficacy to be evaluated; instead, the purpose of the human study is to achieve a relatively minimal demonstration of safety.

50. For well-established therapies, is a human safety study required?

A: Therapies with well documented safety profiles may not require a human safety trial. However, if there is anything unique to the therapy or formulation, proposers should consult with the FDA on whether a safety trial would be warranted.

51. How detailed should studies for Phase III be given the protocols for human work might change over Phase II?

A: The Phase III proposal should be detailed enough to justify the scale and costs of the clinical study. If awarded, the statement of work can be amended to address any changes that arise.

52. Do the Phase III safety studies require that the implanted devices (or components) be “activated” during the implant period (i.e., to activate the production in the cells and/or to power the ingested/implanted bioelectronics carrier)?

A: The human trials only require safety testing. Consequently, the need to “activate” the device will depend on whether the proposed technology requires it to demonstrate safety. Specifically, if the mechanism of activation could plausibly impact the physiology or safety of the host, it should be tested through activation of a sham therapy or other appropriate process. Proposers should justify the need for device activation in the context of demonstrating the safety of their specific technology. Safety considerations also dictate that if the kill switch triggers removal or passage of the device through the body, this mechanism must be demonstrated.

53. Can an integrated system be evaluated in the human study if the therapy and carrier cannot be separated?

A: Yes. The BAA allowed separate testing of the components to simplify the path to human trials. Proposers of an integrated system should justify that it can be tested within the time frames outlined in the BAA.
54. Does the ADAPTER program provide a pathway to streamline first-in-human studies with the FDA?

A: No streamlined or fast-track process for human testing has been arranged with the FDA. Proposers are expected to work with the FDA on their own to obtain any necessary IND/IDE approvals.

55. Can you please clarify the meaning of “IND enabling studies” from the following statement under Phase 3 deliverables: “Report detailing her results of the first in-human safety study of ≥ 1 therapy or service from TA1 (or IND enabling studies).”?

A: While a first-in-human study during Phase 3 is preferred, there may be reasons why a safety trial of the therapy cannot be performed during the ADAPTER award period; if this is the case, proposers should clearly explain the reasons. In such circumstances, additional IND enabling studies in animals may be permitted if they significantly advance the technology towards human trials by addressing additional aspects of the therapy or by being more comprehensive than the studies performed in Phase 2. Please note that this does not remove the requirement of a human trial to evaluate safety of the carrier and communication method (TA2).

56. Will DARPA provide patients for the human study?

A: Proposers are responsible for planning and coordinating all aspects of the human study, including subject recruitment. Proposers should outline a plan for obtaining IRB approval at the institution where the human trial will be performed in their milestones/timelines.

CONTRACTING/BUDGET QUESTIONS

57. Is there an expected level of funding and number of contracts awarded for this BAA?

A: To avoid biasing proposals that are submitted, DARPA is not defining an anticipated budget at this time and will not predetermine award amounts; however, typical DARPA BTO program budgets range from $50-100M over 3-5 years. This is given as an average full program budget (with multiple performers), not an individual project budget and is not necessarily reflective of the specific program budget for ADAPTER. We anticipate funding more than one team. Budgets should accurately reflect the funds needed to complete the project in its entirety, there is no specific budgetary target, and budgets should not be based on your approximation of DARPA’s program budget.

58. How should we budget for IV&V? Is that a team provided by DARPA?

A: DARPA will provide the IV&V team and will fund their time/labor. Proposers should budget interaction costs, including travel for meetings with the IV&V team, and costs incurred to supply and transfer the system to the IV&V team.
59. Is it acceptable for the subcontracted laboratory assisting with large animal testing for Milestones and Metrics described in the preceding section (pages 12-13) to also be the CRO for the safety and efficacy testing?

A: As specified on Page 9 of the BAA in the section on CRO testing: "Proposals must include plans and budget for contracting third party groups to test carrier and intervention biocompatibility (e.g., acute and subacute toxicity), biofouling, and safety during Phases I and II." Given the requirement for a third party CRO, a subcontracted laboratory cannot serve as the CRO.

60. Will COVID-19 impact the contracting process?

A: We do not anticipate the proposal review and contracting process to be negatively impacted by the current COVID-19 crisis. We expect contracting to be completed in early 2021 (Q2 of FY2021).

61. The ADAPTER BAA states proposers have the option of choosing a procurement contract, cooperative agreement, or an OTA. Does DARPA have a preference for a particular type of contracting mechanism?

A: This varies by organization and proposal, hence the following language from the BAA:

“In all cases, the Government contracting officer shall have sole discretion to select award instrument type, regardless of instrument type proposed, and to negotiate all instrument terms and conditions with selectees.”

62. The BAA advises the use of templates provided for the SOW and budget. Both templates seem to suggest that TA1 and TA2 activities should be proposed and tracked separately through all three phases of the program. However, Phase II activities will mainly be concerned with an integrated system of TA1 and TA2 technologies. Is it appropriate to identify and propose activities separately for TA1 and TA2 only during Phase I and modify the templates for Phase II?

A: In Phase II, the performers will integrate the components from both TAs developed in Phase I. There is often a preference by both performers and DARPA to maintain the TA1 and TA2 designations across phases for continuity sake while adding tasks as appropriate to cover integration. In particular, it is important to outline the specific tasks and plan for improving performance to meet more rigorous TA1 and TA2 metrics and milestones. If this is not appropriate to your technology development scheme, you should adapt the templates accordingly making it clear which tasks are directed towards improving performance and what appropriate risk mitigation steps are involved. This also applies to Phase III if you plan to conduct a human trial on the integrated system.
SUBMISSION QUESTIONS

63. Do subcontractors need to create a DARPA BAA (https://baa.darpa.mil) account or just the PI of the entire project, i.e. the team leader?

A: No, only the PI/team leader needs to create an account.

64. Do we need to submit the provided MS Excel spreadsheet and fill out the R&R budget in the SF424? Specifically, where in the application do we upload Volume I, Volume 2 and the Excel spreadsheet?

A: The provided spreadsheet should be completed, but not the R&R budget. It doesn’t matter how/where the proposal attachments/volumes are uploaded – they are made available to DARPA as contents of a .zip archive regardless where (in the application) they are included.