DARPA-PS-25-04 Simulated Microbial Systems Questions and Answers (Q&A) as of 2/12/2025

Updates HIGHLIGHTED below

GENERAL INFORMATION

- Q: Will the Industry Day slides be posted online?
 A: Yes; information relayed during the Industry Day will be made available on the SMS
 Program Page: https://www.darpa.mil/research/programs/simulating-microbial-systems
- Q: My research is not geared specifically to meet the SMS program goals. Is there an alternate solicitation that I can respond to?
 A: Yes. DARPA/BTO has an office-wide solicitation, HR001124S0034, for this purpose.
 (https://sam.gov/opp/5fff3c4c76c341a4a6b1d2010211c793/view
- **3. Q:** What is the expected team makeup? A: Please see Section 4.1.3 of DARPA-PS-25-04.
- 4. Q: Does the assembled team need to have a track record of working together? A: No, teams are not required to have worked together in the past.
- 5. Q: Is there a limit to the role of non-US performers (with respect to budget allotted to performers, etc.)?

A: No. As stated in DARPA-PS-25-04, "Non-U.S. organizations and/or individuals may participate to the extent that such participants comply with any necessary nondisclosure agreements, security regulations, export control laws, and other governing statutes applicable under the circumstances. Specifically, since SMS is anticipated to be a CUI-level program, any non-U.S. organization would be expected to possess capabilities to ensure the protection of U.S. DoD CUI level information.

6. Q: Can a performer or individual participate on more than one team?

A: Yes. Proposers may join any number of teams as a subcontractor and still submit a separate proposal as the Principal Investigator (PI) (with or without subcontractors). The proposer should be very clear as to how hours will be charged in each proposed effort and describe what safeguards are in place to ensure that time is not double billed.

CONTRACTING/COST

7. Q: What and when are the milestone payments? Can additional or alternative milestones be provided than what is in the template for the Schedule of Milestones and Payments?

A: Please see Section 1.6.5 of DARPA-PS-25-04.

- 8. Q: What date is anticipated for start?A: DARPA anticipates awards in Spring 2025.
- **9. Q: How many awards will be given?** A: Multiple awards are anticipated.
- 10. Q: What are abstract and proposal evaluation processes and guidelines?

A: Please see Sections 4.3, 4.5, and 4.6 of DARPA-PS-25-04.

11. Q: DARPA/CMO mentioned there is no guarantee for any continuations after the 18 months, but is it a possibility? If a program is highly successful, could it go beyond 18 months?

A: Please see Section 1.11.3 of DARPA-PS-25-04.

- **12. Q: Is DARPA considering Grants for this effort?** A: No. The types of instruments that may be awarded are Other Transactions for Prototype.
- **13. Q: Will SMS be funded by 6.1 or 6.2 money?** A: SMS is categorized as 6.2.

14. Q: Should my budget only include direct costs?

A: No. Please see Sections 4.2.G, 4.3, and 4.4.E.

15. Q: Are national labs/ FFRDCs (ex: DOE national labs) are allowed to submit abstract? If yes what type of documentations or approval would be required?

A: DARPA encourages technical solutions from all responsible sources capable of satisfying the government's needs. To ensure fair competition across the ecosystem, DARPA prohibits contractors/performers from concurrently providing Systems Engineering Technical Assistance (SETA), Advisory and Assistance Services (A&AS), or similar support services and being a technical performer, unless the DARPA Deputy Director grants a written waiver. DARPA extends this prohibition to University-Affiliated Research Centers (UARCs) and Federally Funded Research and Development Centers (FFRDCs) including National Labs, who because of their specialized expertise and areas of competencies, are able to accomplish integral tasks that cannot be met by government or contractor resources. Therefore, these entities are highly discouraged from proposing against this (and other BTO) solicitation(s), as awards to a UARC or FFRDC will only be made by exception. UARCs and FFRDCs interested in this solicitation (once published), either as a prime or a subcontractor, should contact the Agency Point of Contact (POC) listed in the Overview section prior to the proposal (or abstract) due date to discuss potential participation as part of the government team or eligibility as a technical performer.

16. Q: Does the funding cover 100% of the expenses or is industry matching needed? A: Please see Section 4.4.a of DARPA-PS-25-04. 17. Q: Are the costs required to be broken out between Simulate & Predict and Measure & Inform, or can the costs be combined?

A: The costs can be combined (both research thrusts are addressed by some milestones).

18. Q: In connecting our milestones to budget, are milestones evaluated every 6 months and funding for the next phase based on completely meeting the prior 6 months goals or is there a different evaluation window?

A: 10. While there are natural 6-month evaluation periods that shake out from the program related to CDs, workshops, etc., most milestones in the provided Attachment E are suggested and may be edited, including the timing thereof. SMS is only requiring milestones for a kickoff, CD, workshops and final deliverables, and the timing for these should conform to the program schedule. Proposers are encouraged to use these milestones as a baseline for creating their own.

Each milestone represents a distinct, completed event with accompanying deliverable(s) and payment amount, and negotiated prior to contract award. Please refer to Section 2.1 of the PS.

PROGRAM STRUCTURE

19. Q: How do we balance the need to take risks and think big with the need to provide deliverables on schedule?

A: DARPA explicitly seeks transformational change instead of incremental advances. Proposals that do not involve significant or fundamental advances on state-of-the-art approaches may be considered non-conforming.

20. Q: For the pressure test, will we know or select the PT category or specifics? For example, PT for oxygen versus temperature requires different parameters and variables in the model as well as different experimental data sets. Would there be any other conditions?

A: Details of each PT will be provided after capability demonstration 1 (CD1). Please refer to Section 1.5.3 of DARPA-PS-25-04.

21. Q: Do we need to request permission for alternative compounds or antibiotics prior to submission of the abstract or does that occur after selection of proposers.

A: As stated in Section 4.2 of DARPA-PS-25-04: "SMS suggests limonene or violacein, although proposers may suggest alternative compounds with appropriate justification. DARPA reserves the right to review and approve alternatives. Final assignments are to be determined at time of award negotiation."

22. Q: Once the anti-microbial is assigned, is there a possibility to get that changed?A: The government does not anticipate changing antimicrobials once assigned during award negotiation.

PROPOSALS

23. Q: What dates are anticipated for the proposals?

A: Oral Proposal Package (OPP) Due Date & Time: February 25, 2025, 1200 Eastern

24. Q: How much existing / new data are proposers expected to leverage / generate? Are there minimum requirements?

A: Proposers are free to leverage as much existing data as they like and should include descriptions and justifications for their plans to use existing datasets. Proposers should also include a significant data generation effort. Proposals that do not describe efforts to generate data during the program will be considered non-responsive.

25. Q: Should proposals directly address and budget for Independent Verification and Validation (IV&V)?

A: Yes, please outline a plan and create a budget for sending material to and interacting with the IV&V team for testing.

26. Q: Are there limits to the number of participants, both in-person and virtual/hybrid?
 What is the process for inclusion of virtual participants?
 A: We strongly prefer that representative(s) from the prime attend in person. We anticipate
 1-3 presenters per team in person. Others (e.g., subcontractors) are welcome to attend virtually.

- 27. Q: The Task Description Document, Schedule of Milestones and Payments, and Property/Equipment are listed in the OPP Document Checklist as OT Attachments (1, 3 and 5, respectively) and as separate checklist items. Should these documents be submitted as part of the OT, separately, or both? A: Either is fine.
- 28. Q: Are we free to add to or modify the SOW template to meet the BAA SOW requirements? Can we modify the task numbering to accommodate our own work breakdown structure? A: Yes.
- 29. Q: Are we free to add to or modify the SOW template to meet the BAA SOW requirements? Can we modify the task numbering to accommodate our own work breakdown structure? A: Yes.

TECHNICAL - GENERAL

- 30. Q: What is your attitude towards (fill in the blank) technology?A: Proposed technologies and approaches should fit within the boundaries and spirit of the SMS Program.
- 31. Q: Who is supposed to generate measurement data, the proposing teams, or IV&V and the proposing team is only on computation? Will the SMS program fund data generation efforts?

A: The proposing teams should consist of unified activities across both research thrusts, simulate and inform and measure and predict.

As described in DARPA-PS-25-04, "The SMS program will be composed of two complementary research thrusts: (1) Measure & Inform; and (2) Simulate & Predict. Proposals must describe credible plans to conduct research in both research thrusts simultaneously... Technical abstracts and oral presentations should present innovative approaches in each research thrust and a cohesive workflow that integrates them. Proposers are expected to be comprised of dynamic, interdisciplinary, and potentially multi-institutional teams with expertise that collectively spans both research thrusts." The research thrusts are described in more detail in the solicitation. Separately, IV&V will generate ground truth data.

32. Q: Can you verify that all proposals are intended to fulfill the full scope of the call (identified metrics for Measure & Inform, Simulate & Predict; use cases, capability demonstrations, and pressure tests)? Or will proposals with a more limited scope, but more development and innovation be considered?

A: Yes, proposals should fulfill the full scope of the program solicitation (PS). The SMS program will be composed of two complementary research thrusts: (1) Measure & Inform; and (2) Simulate & Predict. Proposals must describe credible plans to conduct research in both research thrusts simultaneously. Please see Sections 1.4, 1.5, 1.6, and 4.1.3 of the PS.

33. Q: As described, it appears that each team is not responsible for including every reaction in E. coli, but rather needs to include in the model what is necessary to meet their stated milestones. Is this a correct assumption and should we expect that other teams may be developing complementary models that cover other parts of the metabolic map?

A: This is an incorrect assumption; teams are responsible for all aspects of their own simulation of an *E. coli* cell. Each team's simulation must be sufficiently comprehensive to create a generalizable simulation of E. coli that will address all metrics in Sections 1.6.1 of the PS. Per 1.6.1, the number of properties and behaviors simulated is a program metric. While performer teams may develop different types of simulations during the program, individual teams should NOT assume they will have the ability to incorporate aspects of other teams' simulations to meet program goals.

34. The solicitation requires measure and predict >4,000 gene transcripts and >400 metabolites and proteins, this suggests that we generate predictions for a subset of the system, is this correct? Are we required to predict all 4,000 genes even if some of the genes may not impact our selected 400 metabolites or proteins? A: Simulation outputs (predictions, forecasts, etc.) should not be for a subset of the measured system – all of a team's measurements should inform the team's simulations. Please see Table 3 in the PS.

Further, per Section 1.5 of the PS, DARPA will reveal evaluation specifics of capability demonstrations and pressure tests during the program. Should a performer choose to create a simulation capable of only a subset of predictions, revealed specifics may or may not overlap with the chosen subset of capabilities, which could negatively impact simulation performance.

35. Q: What combinations of techniques would DARPA like to see in terms of grey, black, and white box models? Are there any explainability requirements?

A: The DARPA team is open to any combination of black, grey, and/or white approaches that can meet the goals of the Simulate & Predict thrust of SMS. It is up to the proposers to choose the right foci to fulfill the program goals and justify the decision. There are no explicit explainability requirements.

36. Q: Could you elaborate on simulation extensibility?

A: Please refer to the description of Simulation Generalizability and Compatibility with Specific Use Cases (1.4.2) in the solicitation.

37. Q: How are the simulations expected to be different from previous whole cell models? Is it just that they will handle lot more data and stochasticity associated with a more complex organism, or do they need to have additional technical novelties? A: The SMS program shares the goal of whole-cell modeling – namely the creation of computational simulations to predict the behavior of a cell such as a bacterium. However, SMS seeks radical new approaches to redefine the art of the possible in single-cell simulations. SMS also then seeks to apply these simulations to forecast the behavior of a bacterium for DoD-relevant use cases.

Proposals that prominently feature incremental improvements of approaches will be considered non-responsive.

38. Q: While both use cases described in the PS should be addressed, do the two prediction outputs come from the same simulation, or can we build multiple simulations with multiple outputs?

A: Performers should use the same software to simulate both use cases as well as generalizable properties and behaviors. Tuning this single simulation for different applications is acceptable. Proposals that plan for individual, independent, or otherwise unlinked models for predicting each property or behavior will be considered non-responsive.

39. Q: Solicitation mentions multiscale simulations to address higher order properties. Does SMS desire the prediction of structural phenotypes (biofilm formation)? A: SMS simulation metrics are described in section 1.6.1. Teams are welcome to propose additional metrics (see Section 1.6.4). Final metrics are to be determined at time of award negotiation and are subject to DARPA approval. Proposers should note that program metrics may serve as the basis for determining whether satisfactory progress is being made.

40. Q: Are we allowed to leverage parts from previously developed models?

A: Yes, however proposals that prominently feature incremental improvements of approaches will be considered non-responsive.

41. Q: Are models we develop allowed for public release to complete the existing work in this area.

A: Please see Section 1.12 of DARPA-PS-25-04.

- **42. Do we share our models, data, etc. with other teams or only the Government partners?** A: The initial plan is for teams to share simulations and data solely with Government partners. As the program progresses, if it is determined by the Government that additional sharing of data will be needed to achieve the goals of the program, DARPA may also facilitate formalized Associate Performer Agreements (APA) for performers sharing data with other performers. Please see section 4.1.4 of the PS.
- 43. Q: Does a single team need to address all aspects of the simulation (e.g., intracellular diffusion all the way up to multicellular behavior) or would it be responsive to define the scales we plan to simulate and highlight limitations of our simulation.
 A: Proposals should describe credible plans to meet the metrics and simulate the properties and behaviors listed in the PS. Please refer to Section 1.6 of DARPA-PS-25-04.
- 44. Q: The solicitation mentions predicting 100s of proteins (concentrations, regulation, etc.) in 2 different networks. Does this mean that proposers should select 2 subnetworks to simulate (e.g., glycolysis/TCA/ETC cycle and amino acid biosynthesis) or are proposers expected to simulate all pathways in E. coli?
 A: As stated in Table 3, Section 1.6 teams are expected to simulate all measured mRNA, protein, and metabolite dynamics over time and should plan to simulate at least two (2) different protein interaction networks each comprised of >100 proteins.

45. Q: What level of quantitation is expected for concentrations of mRNA, protein, metabolites? Do we need to predict absolute concentration or relative <mark>concentrations?</mark>

A: We would ideally want as much information as possible. To that end, absolute concentrations would be preferred, but relative concentrations are also acceptable so long as they are able to use the same simulations to complete all the CDs and PTs.

46. Q: Is the goal to generate software for single cell simulation and measurements?

A: SMS seeks to create comprehensive, generalizable, and extensible computational simulations to predict the stochastic properties and behavior of *E. coli* K12 at a single cell level.

47. Q: How will simulation results be evaluated?

A: As stated in the solicitation, progress and ultimately success will be determined when data created through *in silico* simulations are statistically equivalent to data generated through *in vitro* experiments conducted by IV&V. Proposals will be asked to include methods

of establishing equivalence. Progress will also be tracked via the number of properties and behaviors able to be simulated and measured. See Section 1.6 of DARPA-PS-25-04.

48. Q: Can additional metrics be added by the proposer?

A: Yes; please refer to 1.6.4 of DARPA-PS-25-04.

49. Q: Is there a specific goal or timeframe for each simulation run?

A: DARPA is seeking proposals that address the goals as outlined in the solicitation. In the solicitation, there are descriptions of program metrics that are used to assess technical progress, and separately (Section 1.7.2) there are statistics DARPA will collect. Statistics include things like training time and retraining time.

- 50. Q: The solicitation also highlights a preference for measurements that minimize human-in-the-loop, which is more difficult to achieve for some large-scale, brute force omics methods. Would it be responsive to propose non-omics based methods that can generate similar biochemical information that informs the model? A: While successful approaches for Measure & Inform are anticipated to include high-throughput "human out-of-the-loop" experiments, the Measure & Inform thrust should "generate large datasets that describe the dynamics of *E. coli* K12 properties with the goals of filling in these gaps in data and informing simulation development, parameterization, training, and testing." Teams are free to propose using any methods that meet SMS goals and metrics. Per the PS, proposals should describe how their [Measure & Inform] approaches: will properly parameterize and inform simulations; create relevant data including relevant metadata. Proposals that do not plan to generate significant datasets but instead leverage only pre-existing datasets will be considered non-responsive. Please see Sections 1.4, 1.6, and 4.
- 51. Q: As single cell omics (transcription, metabolite, proteins, protein-interactions etc.) are costly and have sensitivity challenges, are alternative approaches to capturing measurements acceptable? Is the expectation that the required >10e6 measures per time point comes from single cell measurements? Do single cell measurements need to measure all genes, or a subset of RNAs that are detectable at the single cell level? A: Single cell measurements are strongly preferred; however, teams may propose alternate approaches to meet the measurement goals of the program. If alternate approaches are used, teams should explain how the data captured will accurately reflect the stochasticity inherent in biological systems and will enable the predictive accuracy required by program metrics.
- 52. Q: Are there specific metabolite classes that should be prioritized in the >400 target?
 What validation requirements will be expected to demonstrate single-cell resolution?
 A: No specific classes should be prioritized. Teams should indicate their validation strategy when describing the accompanying measurement approach.

53. Q: Section 1.4.1 of the RFP states that "The Government team will furnish an E. coli K12 to performers which will serve as the standard for the SMS program. Alternatively, performers may describe their own *E. coli* K12 strain with justification(s). DARPA reserves the right to review and approve alternatives.". For the biomanufacturing use case, can we use our own K12 strain?

A: Proposers may describe an alternative K12 strain with justification. Please refer to Section 1.4.1 of DARPA-PS-25-04.

54. Q: Will K12 strains that produce limonene or violacein be provided for the Biomanufacturing portion of the work, or is it the responsibility of the performer to engineer the chosen strain as necessary for production as part of Biomanufacturing use case?

A: Performers are responsible for engineering strains to produce their selected compound (limonene, violacein, or a proposed alternative) as part of the biomanufacturing use case. Teams may propose to engineer production into the SMS-provided K12 strain or may propose an alternate K12-derived source.

55. Q: What are the criteria for choosing target compounds for bio-manufacturing? Why were the target compounds (limonene and violacein) chosen?

A. Limonene and violacein are selected because they fulfill the intellectual goals of the program and are of interest to DoD stakeholders. Proposers may suggest alternative compounds with appropriate justification. DARPA reserves the right to review and approve alternatives.

56. Q: Do we need to predict the target of the antibiotic/small molecule as well as the response of the system to the antibiotics? Or will we be given information that specifies which protein it targets?

A: Explicit identification of the target is not necessary; however, the simulation should capture the response of the system to antibiotics including the information detailed in Section 1.5.4. The Government will specify the antimicrobial to be used, not specific targets of the antimicrobial.

57. Q: What are the expected final deliverables?

A: SMS aims to deliver a beta version of simulation software that addresses the goals as outlined in the solicitation, along with data and other technical deliverables. Please refer to Section 1.9 of DARPA-PS-25-04.

58. Q: Are there requirements or expectations regarding algorithm runtimes and other simulation progress statistics (Section 1.7.1)?
 A: No – there are no requirements or expectations regarding any simulation progress

statistics (Section 1.7.1). Performers should plan to collect and report these statistics to DARPA, and performers may collaborate with IV&V to do so.

59. Q: Is there a particular scale or range of scales being targeted in terms of HPC resources required or expected for simulators developed within the SMS program? For

example, is distributed computing at scale a requirement versus merely demonstrating the capacity to scale?

A: Distributed computing at scale is not a requirement in SMS. Proposers should describe the computational resources required for their approach (see Section 1.4.1) and should plan to report simulation progress statistics (see Section 1.7.1).

60. Q: What are the expectations for usability of the containerized platform? What is the level of expertise (computational and microbiology) of the anticipated user of the platform?

A: Performers may use packaging mechanisms such as containerization for the simulation platform to better facilitate interoperability. Anticipated users of the simulation platform would be skilled in relevant areas of computational and microbiological research. Please see Section 1.7 of DARPA-PS-25-04.

TECHNICAL - INDEPENDENT VERIFICATION AND VALIDATION (IV&V)

- 61. Q: Can you be specific about the role of the IV&V partners? Can you explain or give an example how the performers will engage or work with the IV&V partners?
 A: The IV&V team will consist of subject matter experts (SMEs) from Government and/or other relevant domains. Please see Section 1.7 of DARPA-PS-25-04.
- 62. Q: How frequently do we interact with the IV&V partners? Is there a time frame to complete travel and work with IV&V partners or should we plan for a continuous flow of communication and visits as needed? Can IV&V partners travel to our institutions to learn our workflow and if so, do they have their own travel budget?

A: It is up to proposers to describe credible plans for engagement with IV&V partners that aligns with the program timelines. Capability demonstrations and workshops serve as deadlines for performers to facilitate IV&V evaluation; please see section 1.10 of the PS for corresponding activities.

Given the program's desire for interoperability and compatibility with the computing platforms of Government partners and stakeholders, IV&V partner travel to performer institutions is not anticipated. IV&V partner travel should not be included in proposers' budgets.

63. Q: Do performers need to identify an IV&V research partner ahead of time?

A: No. Performer teams will directly engage with Independent Verification and Validation (IV&V) partners, coordinated by DARPA, during the program. However, performers should budget for interactions (e.g., shipping samples, code and supporting data transfer, travel to testing sites, sharing protocols) with IV&V partners.

64. Q: Can you please provide the number of IV&V tests that will be performed for validation?

A: There will be at minimum four (4) interaction points for each performer team – capability demo one, capability demo two, and one pressure test evaluation for each use case. Proposals may include a plan to build up to more advanced combinations to be discussed and approved by DARPA, should the testing schedule and their success allow.

65. Q: Will the IV&V team share the expected growth conditions for the cell? (i.e., batch vs continuous growth, flask vs. bioreactors, etc.)?

A: IV&V will be prepared to share data and metadata from experiments and evaluations, including protocols and expected growth conditions.

66. Q: Will the independent IV&V partners need to be able to replicate all experimental as well as computational outcomes? If so, do we need to budget for equipment they may need to setup experiments?

A: IV&V partners will independently evaluate simulations and produce their own ground truth data they will share with performers. IV&V will compare performers' in silico and in vitro results to these ground truth data. Performers do not need to and should not budget for IV&V or other government partner equipment, materials, etc.

SECURITY

67. Q: Do individuals/PIs need to have a permanent residence?

A: No, Individuals and PIs may be foreign nationals that are not otherwise prohibited from participating in US Government (USG) funded projects and they are compliant with export control regulations, security regulations, and applicable governing statutes.

68. Q: Are teams of non-US citizens (academics in US institutions) eligible and are there other restrictions on composition?

A: Yes, non-US citizens are eligible and may participate. If technical information is generated that the USG would consider "controlled" due to export control, subject to ITAR/USML regulations, or other controls, then that information is protected at the CUI level and all foreign national participants are required to sign a non-disclosure agreement and implementation of IT system controls are required.

69. Q: Are foreign national proposers eligible? How about foreign national proposers as prime organizations?

A: Yes, foreign nationals and foreign corporations, and academic institutions are allowed to participate as prime or sub-contractors. If controlled technical information, export controlled or ITAR/USML information or other categorized CUI is to be generated then NIST 800-171 controls apply to the performer IT system to protect USG CUI information. Please refer to NIST 800.171 - <u>https://csrc.nist.gov/pubs/sp/800/171/r3/final</u>

70. Q: How does DARPA typically work with universities in terms of CUI?

A: DARPA understands that most of the program work may be fundamental research. However, because of potential sensitivities of the research that may require protection because of "unknown advancements" we are requesting that the program work be controlled by the university until formally allowed to be released by DARPA. We do have several universities nationwide that do work in the CUI levels. They use the controls in NIST 800-171 to configure their network architecture that allows them to process CUI data. Other options have been to have isolated workstations that are configured with controls to restrict access through the university domain, restrict access to the workstations by authorized persons only, encryption of the data "at-rest" and "in transmission," and other similar restrictive controls to ensure that the data is properly protected.

71. Q: Similarly, with respect to our model and multi-scale modeling framework, we typically make all our work available on GitHub automatically and have done so for years. Is DARPA asking us to take this offline?

A: Information already shared on GitHub for previous DARPA programs or work may remain online. Any new information/data for modeling and simulation for the SMS program may not be published on GitHub (DARPA will likely recommend an alternative repository to avoid GitHub auto-upload) until approved by the DARPA team for public release.

72. Q: The OTP template agreement terms also seem to impose a dissemination restriction that requires DARPA approval prior to any public release or dissemination of any information and data. Our institution would very likely not be able to agree to this either. Is there an expected time for reviewing new information to determine if it qualifies as CUI?

A: DARPA has worked with numerous universities on this issue. DARPA complies with the National Security Decision Directive 189 (NSDD 189), 21 Sep 1985, as fully as practicable. As defined in NSDD 189: "'Fundamental research' means basic and applied research in science and engineering, the results of which ordinarily are published and shared broadly within the scientific community, as distinguished from proprietary research and from industrial development, design, production, and product utilization, the results of which ordinarily are restricted for proprietary or national security reasons." Because SMS is exploring novel scientific modeling of cellular behavior that will simulate molecular processes, there's a potential that "technologies" developed in SMS may fall under intellectual property/proprietary restrictions, export control regulations, or even national security restrictions. With recent policy changes in the AI/ML and cybersecurity research areas within the government, we have decided to impose a publication restriction on the program information and data until after it's been reviewed by DARPA. To the extent possible, we will gladly allow publishing of the scientific discoveries as we fully understand the necessity of contributions from our academic performers. Before any information/data is deemed "not publishable," DARPA will convene a panel to discuss the decision and input from the academic institution will be requested and considered. Typically, public release reviews are completed within 2 weeks from date of submission to DARPA.

73. Q: The draft RFP states the following: "Performers will need to operate at the Controlled Unclassified Information (CUI) level. This includes prospective individual researchers and all information technology (IT) systems, including but not limited to data analysis, storage, networking and data transfer, cloud, high-performancecomputing (HPC), and document systems." Does this apply to all subcontractors' IT systems even if subcontractors are compartmentalized to nonsensitive research? (I assume this is for BTO Security) A: It is possible for CUI level IT protection to not apply to a given subcontractor. A subcontractor may receive approval for exemption by DARPA if all the following statements apply:

- i. A sub must be conducting only unclassified fundamental research.
- ii. A sub must be isolated from the rest of the program by the Prime Contractor.
- iii. The Prime Contractor's proposal must indicate how they will isolate the sub from CUI level information.
- iv. The Program Manager & Program Security Officer must validate that the sub's Task Description Document (TDD) is all fundamental research (if selected for award).

Additionally, NIST SP 800-171 Rev.3 (May 2024), is the baseline guidance for a fully compliant system. However, we realize that most universities' IT systems are not fully 800-171 compliant. There are alternate solutions that can be utilized based on discussions with the institution's IT and research security departments, if the IT system does not meet all the controls listed in 800-171. These are uniquely based on the institution, their current IT architecture and configuration, and the program's requirements. These alternatives will be discussed if selected for award. See Section 1.11.2 of the Program Solicitation for additional details.

74. Q: Does the equipment used to process the samples and generate data also need to be in a NIST 800-171 compliant environment?

A: Standard lab equipment is typically not required to be compliant with 800-171. RAW data generated by lab equipment is UNCLASSIFIED until processed so it does not require CUI controls.