BIOlogical, Integrated, Novel, Silicon Photonics for Efficient Characterization and Testing (BIO INSPECT)

Call for Proposals
FAQs

Q1. Who can apply?
A1. This call is open to organizations that are full, active AIM Photonics members in good standing, and organizations that pledge to become full, active members of AIM photonics after a successful proposal notification.

> **Note:** To avoid extensive delays in commencing the project, a grace period of **1 month** after the tentative award will be given for organization(s) to become members**.** After the grace period the Government/AIM Photonics team reserves the right to withdraw its tentative award selection and make an award to a different proposer, who responded to the original solicitation.

Q2. What is the process to apply for AIM Photonics Membership?
A2. Information on how to join AIM Photonics is available on the AIM Photonics website: https://www.aimphotonics.com/become-a-member.

Q3. Is cost share required, and if so, what is the ratio?
A3. No specific cost matching has been identified for this project; however, cost matching is always desirable.

Q4. How do I apply?
A4. Start by **reviewing the attached proposal call**. Proposals with the completed budget template must be sent electronically to Maria Halepis at mhalepis@aimphotonics.com on or before **June 12, 2024 at 11:59pm ET**.

Q5. Will there be extensions or exceptions for late or partial proposals?
A5. No extension or exceptions will be made for this call. Only proposals in a complete and final iteration submitted on or before the deadline will be considered for funding.

Q6. Do projects need to include both academic and industry partners?
A6. It is not required, but a mix of participation (academic, industry and government partners) is preferred.

Q7. Is a Technology/Manufacturing Readiness Level expected/required?
A7. In line with the AIM Photonics' vision and mission, for this call initial Technology Readiness Level (TRL) is anticipated at 2 or higher and initial Manufacturing Readiness Level (MRL) anticipated at 2 or higher with final – with a desirable TRL at 4 or higher, and final, desirable MRL at 4/5 or higher at the end of the project.

Q8. Is there a project term limit?
A8. There is a maximum **18-month limit**.

Q9. When will successful proposals be selected and when will projects be funded?
A9. Successful proposals will be selected in the **July 2024 timeframe**. Additional instructions on the specifics and timing of the funding will be provided at that time.

Q10. Who do I contact with additional questions?
A10. Contact Maria Halepis at mhalepis@aimphotonics.com.

> **Note:** that questions about the proposal call topic or submission logistics, should be submitted before **May 28, 2024** to ensure there is reasonable time for the Government/AIM Photonics teams have time to respond accordingly.

Q11. We understand you are looking for a diagnostic system that measures the inputs to the differentiation protocol shown in Figure 1, and that there is a requirement to take multiple samples without human intervention. We are unsure about where or how the differentiation protocol is contained and how we are expected or allowed to retrieve fluid samples from it. Can you please clarify with words, photos, or videos what the physical setup of the differentiation protocol looks like so that we can plan for how to interface with it? In particular, how do people currently take samples and measure them?
A11. The ultimate goal of this effort would involve interfacing with a specific system, but the current call-for-proposal only focuses on developing a capability that addresses the technical objectives without overly specifying or constraining the interface. As such, proposers can envision the differentiation campaign to be contained within a system that offers a 1-inch sample access window at the top of the system for which liquid can be exchanged by whatever means the proposer favors (provided it meets the threshold objectives and ideally would offer a path to address the program's goals in the future). If it helps performers focus their efforts/proposal it could be envisioned that the proposed solution should be able to pull a sample through a cap or through a swabable port with a septum that a syringe needle can be pushed through to sample but this is not a requirement of BIO INSPECT.

Q12. The metrics have both a Sample Volume and a Volume Lost. Does this mean we are expected to remove a Sample Volume (<100 µL/measurement for threshold metric), analyze the component concentrations in that sample, and then return most of the volume (>90 µL for threshold metric) to where it came from?
A12. The sample volume was provided as a way to note that the sensor system could be expected to work with a volume of material as large as the sample volume, but the objective is for the sensor system to consume no more than the "volume lost." As such, when focusing on the

threshold objectives, the sensor could intake 100 µL/measurement and then consume 10 µL/Measurement. This would imply that 90 µL/Measurement remains in the differentiation protocol or is "returned" to the system. Alternatively, a solution could extract 10 µL/Measurement and consume all the material and still address the threshold objectives.

> **Note:** There is a subtlety that depends on the proposed solution. A sensor solution that would remain immersed in the differentiation protocol and provide many real-time insitu measurements would NOT be constrained by the 100 µL requirement and could interact with the entire volume of the sample. This metric was provided for solutions whose sensors may exist outside of the differentiation protocol over the concern that repeated measurements could eventually extract large volumes of material which could alter the protocol itself. We apologize for not better clarifying this distinction in the original call-for-proposals.

Q13. 12 Media Components of interest are specified but only one Sensitivity metric is specified. Is the goal a qualitative measurement that reports whether each concentration exceeds that Sensitivity metric? Or is the goal a quantitative measure of the concentration of each Media Component?

A13. The call-for-proposals requires a solution that can monitor no fewer than 4 of the 12 components listed in the example differentiation protocol. Note: It is most desirable to use a single system to measure all the components of interest in a specific differentiation protocol as noted in the goal.

While it is true that the call-for-proposals could have provided specific metrics for each component, the call-for-proposals also provided some flexibility by noting that proposers could identify a different differentiation protocol to explore. As a result, we needed to keep the metrics in this call-for-proposals somewhat generic. To provide some flexibility, but still provide a sensitivity metric, we selected a single generic metric. The goal is to provide a quantitative measure of the concentration of each media component. Based on how these differentiation protocols are conducted, i.e. "sequentially" vs. "in parallel," it is anticipated that only a single component needs to be monitored at any one time.

To provide some additional information, proposers may want to consult the references associated with the BIO INSPECT call-for-proposals. In particular, Tables 4 and 9 (from Ref. 4) one of which is provided below for convenience.

Table 9 | SC-β-cell differentiation schedule

	Day of Differentiation	Base medium	Factor	Final concentration	Dilution from aliquots
Stage 0	1	mTeSR1	Y-27632	10 μM	1:1,000
Stage 1	2	BE1	Activin A	100 ng/mL	1:1,000
			CHIR99021	3 μM	1:10,000
	3–5	BE1	Activin A	100 ng/mL	1:1,000
Stage 2	6–7	BE2	KGF	50 ng/mL	1:1,000
Stage 3	8–9	BE3	KGF	50 ng/mL	1:1,000
			TPPB	0.2 μM	1:10,000
			SANT1	0.25 μM	1:4,000
			RA	2 μM	1:5,000
			LDN	0.2 μM	1:5,000
Stage 4	10–13	BE3	KGF	50 ng/mL	1:1,000
			TPPB	0.2 μM	1:10,000
			SANT1	0.25 μM	1:4,000
			RA	0.1 μM	1:100,000
			LDN	0.2 μM	1:5,000
Stage 5	14	S5	XXI	1 μM	1:10,000
			Alk5i II	10 μM	1:10,000
			T3	1 μM	1:10,000
			SANT1	0.25 μM	1:4,000
			RA	0.1 μM	1:100,000
			Latrunculin A	1 μM	1:237.2
	15–20	S5	XXI	1 μM	1:10,000
			Alk5i II	10 μM	1:10,000
			T3	1 μM	1:10,000
			SANT1	0.25 μM	1:4,000
			RA	0.1 μM	1:100,000
Stage 6	21–27	ESFM	-	-	-
Stage 6 (after aggregating into clusters)	28–34+	ESFM	-	-	-

Table 9 from: N. J. Hogrebe, K. G. Maxwell, P. Augsornworawat, and J. R. Millman, “Generation of insulin-producing pancreatic β cells from multiple human stem cell lines,” Nat. Protocols 16, 4109-4143 (2021).

Q14. If the goal is a quantitative result, can you please specify the minimum and maximum concentrations of interest for each Media Component?

A14. The concentration levels of interest range can be found in the table provided above for the highlighted differentiation protocol. While there is variability in the concentrations of the components this number was selected as what was expected to be a reasonable target that would provide value back to those working in the field of regenerative medicine.