The hidden questions behind the Heilmeier Questions

This document is a general guide for developing a clear program concept using the ARPA-H Heilmeier questions (HQs). The additional insights and considerations enumerate many overlooked questions underlying the fundamental HQ questions. This guide is not universal or exhaustive in the scope of considerations to address, and candidates should expect additional feedback throughout our unique application process.

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Write a vision statement

Provide a banner or vision statement: "What if we could (fill in the blank)." The vision statement should be one sentence that clearly describes the intended health impact of the program if successful.

HQ 1: What are you trying to do? What health problem are you trying to solve?

Articulate your objectives using absolutely no jargon. Clearly state the health care problem you would solve (in one sentence). Provide brief justification or need for that solution. Also clearly state what it is that you will produce by the end of the program (also, in one sentence or less).

- Explain as you would to a family member or the general public.
- The need for the program must be obvious to all (even if it wasn't before they read it). Your end objective should be obvious, a "no brainer."
- Think more about the big picture and less about the components.
- Avoid jargon. Broadly knowledgeable non-experts must understand and appreciate what you propose.
- Focus on the problem and a single phrase about what your program will accomplish, not on the details of the approaches and solutions.

Considerations: Is the end objective a clear and obvious unmet health-related need? Have you avoided developing a solution in search of a problem? Have you focused on what the program is attempting to achieve and solve rather than the how (HQ3) or the impact it would have (HQ4)? Have you described what "thing" you will deliver at the end of the program to change health outcomes (e.g., is it a device, platform, ecosystem, or method to improve health care delivery, etc.)?

HQ 2: How is it done today? What are the limitations of present approaches?

Define the status quo of today's solutions, the technical state of the art, and explain why current approaches are not solving the well-defined problem articulated in HQ1.

- Outline the full range of existing and emerging approaches. Show knowledge of state-of-the-art solutions available to the population today. Identify what technical hurdles prevent the capability needed as described in your "what if…" vision statement and HQ1.
- Sometimes it can be useful to distinguish between the state of the art and the state of practice, especially if there are technical challenges that need to be overcome to change the state of practice.
- Show examples or case studies – don't caricature, be up to date.
- Use effective reasoning, for example, "The key technical impediments to success are X, and they can't be achieved currently because of Y." (Example of poor reasoning:

"Nobody is currently doing my cool technology, which is why the problem remains.")

- Provide the metrics that quantitatively describe where today's solutions fall short (this can be used to build the success criteria and milestones for HQ8). Clear quantitative metrics are critical for driving program phase goals and timelines.
- Provide data on the effectiveness of today's solutions. These data could define the technical problems addressed in response to HQ3.
- Ideally, the limitations that you identify in H2 foreshadow the new approach that you will identify in H3.

Considerations: Are the state-of-the-art and the emerging landscape accurately represented rather than exaggerated or undersold? Is it clear why current approaches are not solving the problem? Have you fully decomposed the challenges by identifying the fundamental root-cause barrier(s) and/or tradeoff(s)? Have you included key figures, references, and data to support your assessment of the status quo?

HQ 3: What is new about your approach? Why do you think you can be successful at this time?

Describe potential solution(s) that offer an inflection point, not merely an incremental or fractional evolution beyond the state of the art. These opportunities might be a way to leverage a new scientific breakthrough or a new approach to a hard problem. The approach might demonstrate that something is possible for the first time, or it might revisit a well-known problem in a new way because today's technological advances give us reason to hope that you can succeed in a way that has not been possible in the past.

Aim to make a well-informed and convincing case that moves the concept from "impossible" to "possible." Provide detailed examples of what possible solutions to the problem would entail. Provide technical details on how enabling and emerging technologies can be combined, extended, or adapted to achieve the proposed goal. Explain why ARPA-H should do it now: why it was not possible 5 years ago, and why, without ARPA-H's involvement, will it still not have been done 5 years from now. Share figures, data, and/or references that point to enabling technologies – i.e., technologies that give reason to believe that a new innovative approach might be possible. Enabling technologies should convince the reader that the ambitious goals might be feasible after all. It can be helpful to note what type of extension to a new technology X would be needed to enable a new capability Y.

- What are your new insights? Focus on what fresh perspectives or insights you have that suggest the problem may be solvable.
    - Cite recent breakthroughs/capabilities (papers, data, etc.) that provide reason(s) to be optimistic about new possible solutions.
    - Leverage advancements from other communities that have solved analogous problems.
- How will your new approach work? Describe in technical detail how you will implement the new insights you've identified.

- For example, don't just say you will use AI to discover new therapies. Instead explain what class of AI methods or features, what data is needed, how the results of AI analysis will lead to or provide the desired solution, and what shortcomings need to be overcome to reach your objectives.
- Outline the framework or programmatic structure for implementing your approach. Describe how potential Technical Areas (TAs) of focus result in program objectives. You can think of a technical area as a component of a larger solution or alternatively as an area where you can imagine 2-4 different approaches and it's not clear from the outset which one will work best.

- Why is this overall approach appropriate for ARPA-H? Why is now the time to do it?
  - Describe why ARPA-H is the agency to fund this and not another organization, company, or entity.
  - Include evidence for emerging and enabling technology that could be extended, adapted, or enhanced to achieve your goals now.

Considerations: Have you identified novel approaches showing how the problem could be solved? Do you show what is theoretically possible, what has been practically achieved to-date, and why your revolutionary approach could bridge the gap? Have you made a clear case that your proposed approach(es) is/are "ARPA-Hard" (challenging enough that a single company or a stand-alone research effort could not support them)? Have you described the fundamental technological or scientific advance that indicates this is possible now when it wasn't ten or even two years ago? Are particular use cases presented (example cases to establish the new paradigm)? What are the new insights that are nucleating your excitement enough to launch a program around them? Are there advancements you could draw on from other communities that have solved analogous problems? What is the value-added in your solution (essentially, provide clear differentiation from existing or recent solutions)?

HQ 4: Who cares? If you succeed, what difference will it make?

Expound on scenarios of how the program would change the world. Position your approach in the framework of (or in comparison to) existing solutions outlined in HQ2. Provide data and citations supporting the need for the solution or the impact the solution would make if successful.

Considerations: How will this solution be game changing, and how will you ensure it will "survive in the wild"? Do improvements in metrics justify the investment? Is this a 2% improvement, or 10x improvement? Who are the target customers, end users, stakeholders, and transition partners? How would they be affected if the program succeeds? What potential transition partners would be interested in taking the program outcomes to the next level? Is this something they are clamoring for already, or is it a new paradigm that they haven't even considered? If the program does not meet its stated objective, what could still be learned? Are the primary barriers to adoption identified, or do other major uncertainty/challenge need to be addressed before the program concept could be implemented?

HQ 5: What are the risks?

Describe the primary reasons the program might fail to achieve its objectives. It is helpful to perform a risk analysis and distill the results to the factors with the highest likelihood and/or severity. These risks can be the basis for the milestones and metrics in response to HQ8, in that the milestones are designed to de-risk the program and mark progress against those risks.

Perform a deep dive into the **scientific or technical risks** that would impede success in solving the problem. Identify potential failure points and provide potential technical or programmatic solutions to mitigate those identified risks.

Also address some of the other risks which may include:

- **Programmatic/management risk**: Will the disparate performers work well together given their very different formalisms and terminologies? Will the results be tested independently and promptly? Will stakeholders engage, why or why not?
- **Transition risk**: Might the American Medical Association be hesitant to adopt the new approaches? Will the Center for Medicare/Medicaid Services help to make the solution affordable?

Considerations: Are the main technical and scientific risks identified and addressed? Are all other major types of risks (clinical, managerial, translational, economic, environmental) considered? Are risk likelihoods and severities estimated, and are there plans to manage or mitigate those risks?

HQ 6: How long will the program take?

Recommended practice is that programs usually last 3-5 years. Typical Programs are Phased (two or three Phases) to break an aggressive program mission into tractable pieces and allow for Go/No-Go gates where unsuccessful ideas/teams no longer continue. In relation to HQ8, consider what capabilities performers must achieve at each phase. (Responses to this HQ are often displayed in table format in combination with HQ7 and/or HQ8.)

Considerations: Is the timeline aggressive but in the realm of the possible? Have you justified the schedule for all expected phases of the program? Note that the program duration can be separated from the Program Manager's tenure. What are the main drivers that might accelerate or decelerate this timeline?

HQ 7: How much will the program cost?

ARPA-H investments can range from $50M-$150M over the course of a program. Break down costs by phase and significant task area. Provide brief justification for the expenses. (Responses to this HQ are often displayed in table format in combination with HQ6 and/or HQ8.)

Considerations: Have you used the targeted number of projects or teams in each potential area and the approximate cost for a project in each area to justify the overall program budget? Is the projected budget for each phase and each significant effort within those phases well-justified and realistic (e.g., order of magnitude)? Do you include a budget for independent verification and validation? Do the

justifications reflect an understanding of the actual costs? (If applicable) have you included various scenarios reflecting different levels of program scope (full, partial, etc.)?

HQ 8: What are the mid-term and final exams to check for success?

Mid-term and final exams should have clearly defined success criteria or metrics that can be objectively measured as completed or not. Whenever possible, metrics should be quantitative (e.g., affects 70% of the population) rather than quantifiable (e.g., calculate how much of the population it affects) or qualitative (e.g., it affects a lot of people). They should be ambitious, meaningful, and impactful. (Example: recovery time drops 4x, the cost drops 100x, patient access doubles, infection rate to zero, demonstrate GMP production and FDA IND submission.) For the Phasing outlined in HQ6, what milestones must be met to progress to each phase? When possible, metrics should be identified for the integrated solution that the program seeks to create as well as each of the technical areas outlined in HQ3. (Responses to this HQ are often displayed in table format in combination with HQ6 and/or HQ7).

Considerations: Are the milestones realistic but ambitious, and do they reflect tangible progress towards overall program goals? Are the metrics/success criteria rigorously defined, easily measured, and validated by an independent third party? What are the go/no-go or critical decision points, and have you clarified how you will use them to make decisions at critical phases of the program?