FREQUENTLY ASKED QUESTIONS

ISSUE 3

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Please note, the FAQs below are exclusive to the Healthspan track of the competition. For teams competing in the FSHD Bonus Prize, an FAQ document for the Bonus Prize will be released later this year.

HEALTHSPAN FINALS - TOP FAQS FOR TEAMS

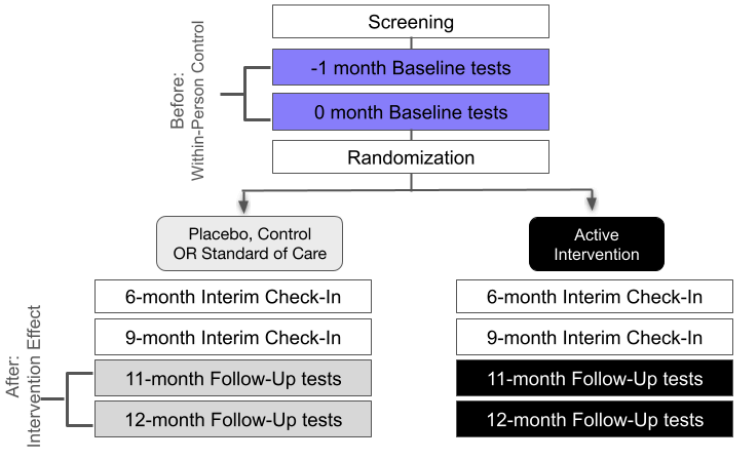
1. How to Use the Rules & Regulations Document

The Rules & Regulations document is an extension of the Competition Guidelines that is specific to the general protocols and judging required for XPRIZE Healthspan Finalists. If there is a discrepancy between the Competition Guidelines and the Rules & Regulations, then the Rules & Regulations supersede the Guidelines. The Rules & Regulations can be used by Finalist teams to structure their clinical protocols, but teams must make their protocols for approvals specific to their therapeutic, rationale, location, and regulatory requirements.

2. What trial design is required for the Healthspan Finals?

Teams are expected to conduct a randomized controlled trial (RCT) comparing an intervention group to a control group. We have removed all language from the Rules and Regulations referring to crossover designs.

Teams may choose the specific intervention strategy, dosing, and protocol details, provided the trial is designed to rigorously test whether the intervention improves healthspan-related outcomes.



Multi-site studies and different types of interventions (pharmacologic, biologic, device-based, behavioral, etc.) are permitted, provided the design allows for clear comparison between treatment and control groups.

3. What is the expected visit schedule?

In response to team feedback and consideration of participant burden, the required visit frequency has been reduced to:

- Two baseline visits, separated by approximately one month, after which participants are randomized
- Two follow-up visits at months 11 and 12 post-randomization
- Two midpoint assessments at 6 and 9 months.
    - Minimal information and biospecimen will be collected during midpoint visits. Primary endpoint assessments will NOT be required during these visits.
- = Total of 6 required visits.

The average of the baseline measurements is used in determination of each participant's personalized threshold, and the average of the follow-up measurements is used to determine whether the threshold has been met. This approach helps reduce the impact of short-term biological and measurement variability and improves the stability of responder classification.

4. **What blood samples will be required, and how often will they be collected?**

The exact blood collection schedule, volumes, and biomarker panels are still being finalized.

XPRIZE is currently working with the Central Laboratory to determine the appropriate balance between:

- scientific rigor
- participant burden
- operational feasibility for teams

We recognize that these details are important for protocol development and budgeting, and we aim to provide finalized guidance as soon as possible.

5. **What defines a "responder" in the Healthspan Finals?**

A participant is classified as a responder if they meet or exceed their personalized response threshold between baseline and follow-up assessments.

For the purposes of prize adjudication, a global responder must meet their threshold in all three domains:

- Muscle function
- Cognitive function
- Immune function

Participants who meet thresholds in only one or two domains will not be counted as global responders.

Prize eligibility is based on the difference in global responder rates between the treatment and control groups of at least 20%, evaluated using a one-sided 90% confidence interval, where the lower confidence bound must exceed 15%.

6. **How are response thresholds created?**

Personalized response thresholds define the amount of improvement each participant must achieve in muscle, cognitive, and immune function for the Team to count that participant as a responder. These thresholds are at the individual level rather than one shared cutoff for all participants. To create these thresholds:

- Annualized changes in expected age-related change will be estimated by modeling longitudinal trajectories of function. Using data from large, diverse, longitudinal cohort studies of adults, longitudinal trajectories will be modeled for endpoints in each functional domain. A detailed description of the methods along with the cohorts used for modeling longitudinal trajectories will be released in 2026. These analyses will be the result of a global research collaboration and conducted by domain and biostatistical experts.
- Expected declines over time by age and will be calculated. For each measurement, we will calculate the amount of change that would be expected over 10, 15, and 20 years, stratified by age and sex. For awarding, the magnitude of the observed improvement for each participant in each of the three domains must be equal or exceed the calculated 10, 15, or 20 year expected declines.
- Personalized response thresholds will be applied to each individual. Each participant's personalized response threshold is based on their own baseline measurements and the modeled aging trajectory for people of similar age, sex, and other relevant factors. For example, if a 70-year-old woman begins the trial with a 6 minute walk distance consistent with the average performance of a 60-year-old woman, then to exceed her 10-year threshold she must show improvement equivalent to the modeled performance of a typical 60-year-old woman.

7. What sample size should teams use for their trial?

The minimum required sample size is 40 participants per arm. However, teams are strongly encouraged to consider larger sample sizes.

Because prize adjudication depends on demonstrating a difference in responder proportions between treatment and control groups, larger studies improve the precision of the estimate and increase the likelihood that the lower bound of the confidence interval exceeds the required 15% threshold.

Teams should consider their expected responder rate and the possibility of responders in the control group when determining an appropriate sample size.