Vascular Tissue Challenge Official Rules

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SECTION 1: EXECUTIVE SUMMARY

Objectives Summary

The Vascular Tissue Challenge (hereafter "Challenge") is a $500,000 prize purse to be divided among the first three teams who can successfully create thick, human vascularized organ tissue in an in-vitro environment while maintaining metabolic functionality similar to their in vivo native cells throughout a 30 calendar day survival period. NASA's objective for this Challenge is to produce technologies capable of creating viable thick (>1cm) metabolic tissues that can be used to advance research on human physiology, fundamental space biology, and medicine taking place both on the Earth and the ISS National Laboratory. Specifically, technology innovations may enable the growth of de novo tissues and organs on orbit which may address the risks related to traumatic bodily injury, improve general crew health, and enhance crew performance on future, long-duration missions.

Evaluation Criteria Summary

Produce an *in vitro* vascularized tissue that is ≥ 1 centimeter in thickness in all dimensions at the launch of the trial and maintains ≥85% survival of the required parenchymal cells throughout a 30 calendar day period. Tissues must provide adequate blood perfusion without uncontrolled leakage into the bulk tissue to maintain metabolic functionality similar to their in vivo native cells. Histological measurement of the quality and amount of functional performance will be required to determine survival of parenchymal tissue. Teams must demonstrate 3 successful trials with at least a 75% trial success rate to win an award. In addition to the in-vitro trials, teams must also submit a Spaceflight Experiment Concept that details how they would further advance an aspect of their tissue vascularization research through a microgravity experiment that could be conducted in the U.S. National Laboratory (ISS-NL) onboard the International Space Station. This Spaceflight Experiment Concept will be used in evaluation for the CASIS Innovations in Space supplemental award, but will not have an impact on determining if a team has won the Vascular Tissue Challenge.

Awards Summary

The Challenge will provide a First Place Award of $300,000 to the team that can first achieve all of the requirements as stated in the rules. Two runner up awards of $100,000 each will be provided to the next two teams to complete all requirements by the Trial Deadline.

SECTION 2: DEFINITIONS & ASSUMPTIONS

1. **New Organ (and New Organ Alliance):** an initiative of the Methuselah Foundation serving as a coordinating brand for all tissue engineering efforts of the foundation to help advance technologies for patients in need of replacement organs and tissues.
2. **Evaluation Criteria:** The collective group of requirements that are necessary for a team to perform in order to win the Challenge awards.
3. **Success Rate:** the percentage of trials where the engineered, vascularized tissue survives, and continues producing the stated, natural functions of that tissue.
4. **Trial**: a 30 calendar day period of in vitro testing on a single tissue sample for performance on the evaluation criteria.
5. **Survival**: a tissue is defined to have survived if ≥ 85% of the parenchymal cells have remained functioning and producing the stated, natural functions of that tissue at the conclusion of the trial with no more than 20% variability from a naturally functioning tissue.
6. **Vascular Tissue Challenge Judging Committee (hereafter "Judging Committee")**: a group of 5 or more subject matter experts who will review team trials and determine performance based on the Evaluation Criteria. Judging Committee will consist of 1 or more NASA subject matter experts, 1 or more Center for the Advancement of Science In Space (hereafter "CASIS") subject matter experts, and 3 or more New Organ Alliance subject matter experts.
7. **Trial Deadline –** teams must have an Intent to Compete submitted by September 30, 2019, and all trials completed by September 30, 2020. These deadlines have been modified from its original wording to accommodate the additional time needed to complete the Trials for the challenge.
8. **Blood Perfusion:** teams may use in their Trials any type of perfusate that can provide oxygen, remove carbon dioxide, maintain pH balance, prevent edema and oxidative damage, and maintain tissue viability and function (e.g. Wisconsin Solution, Whole Blood or similar).

SECTION 3: EVALUATION CRITERIA

Each of the following items are requirements that must be met by the team and verified by the Judging Committee in order for the team to win an award:

1. ***Tissue Survival –*** the tissue must be shown to have survived through the 30 calendar day trial as defined in Section 2. The tissue's survival must be dependent upon nutrient delivery through blood perfusion of the tissue with no other outside support such as nutrient baths throughout the duration of the trial.
2. ***Perfusion*** –tissue shall include channels comprised of endothelial cells with active Blood Perfusion throughout the tissue for the duration of the trial. Blood Perfusion must be enough to keep the tissue surviving as defined in Section 2. Histological evidence must demonstrate fluid flow in the blood vessels without uncontrolled leakage causing edema of the bulk tissue. Perfusion must be demonstrated a minimum of three times

during the trial: (1) ten calendar days into the trial, (2) 20 calendar days into the trial, and (3) 30 calendar days into the trial.

3. ***Thickness*** – The tissue sample shall be ≥ 1 centimeter minimum thickness in all dimensions at the beginning of the trial.
4. ***Cell Types, Volumes and Functionality***
   a. ***Cell Types***: In addition to endothelial cells, teams must include parenchymal cells in their tissues that demonstrate the function equivalent to a human's native (i.e., in vivo) functions of that cell type. For this Challenge, the acceptable parenchymal cell types are listed below. Teams are only required to include one type of parenchymal cell in this list. Additional parenchymal cell types may be considered acceptable if approved by the Judging Committee prior to the team's trial.
   b. ***Tissue Functions***: The functions listed in the table below must be performed within a 20% variance from the native, in vivo tissue's functional performance.
   c. ***Demonstration Requirements***: Cell types, volumes, and functionality must be demonstrated a minimum of three times during the trial: (1) 10 calendar days into the trial, (2) 20 calendar days into the trial, and (3) 30 calendar days into the trial.

Organ	Parenchymal Cell Types/functional units	Minimum Cell volume	Functional Measurement requirements
Heart	Cardiomyocytes	85% of tissue	Contractile Force
Liver	Hepatocytes	85% of tissue	Albumin & Bilirubin production
Kidney	Nephrons & collecting ducts	85% of tissue	Glomerular Filtration Rate, and Urine production maintaining a pH within 20% variance of a normal functioning kidney.
Lung	Pneumocytes	85% of tissue	O2 and CO2 Exchange
Muscle	Myocytes	85% of tissue	Contractile Force
Pancreas	Pancreatic Islets including Alpha cells and Beta Cells	85% of tissue	Insulin production

Note on addition of the Pancreas to updated rules: the addition of the pancreas to the list of viable tissue types is important to the vascular tissue challenge due to the complex nature of the pancreatic tissue. Approximately 44,000 people will die each year of pancreatic cancer. The lifetime risk is about 1 in 65. Diabetes, a disease of the pancreas, is present in about 9% of the population and is the 7th leading cause of death in the United States. Tissue cultures, such as those sought by the Vascular Tissue Challenge, can serve as an important tool for biomedical research leading to determination of causes and testing of cures for both these pancreatic disease conditions. The current state of the art is similar for pancreas as for the other tissues of interest in the Vascular Tissue Challenge.

5. **Human Cells –** All parenchymal and endothelial cells shall be human in origin.
6. **Success Rate –** Teams shall have a minimum 75% success rate in their trials with a minimum of three trials that meet all Evaluation Criteria. Examples of successful teams that will be awarded prize money are as follows:
   a. Team A: Conducts 3 trials and the tissues in each trial successfully meets all Evaluation Criteria delineated in items 1-5 above. All three trials are completed before any other team completes their 3 trials, then Team A wins the First Place

Award. Team B and C will still be eligible for the runner up awards if they can successfully meet all evaluation criteria before the Trial Deadline.

b. Team B: Conducts 3 trials and only 2 tissues meet the Evaluation Criteria. The team must conduct a 4th trial where the tissue successfully meets all Evaluation Criteria (3 out of 4 = 75% success rate) to win an award. If the 4th tissue fails to meet the criteria, the team must conduct additional trials. The award will be either First Place or a Runner Up award depending upon their date of completion of the 75% of trials successfully meeting the Evaluation Criteria.

c. Team C: Conducts 3 trials. None of their tissues survive. The team then conducts 3 more trials and all of the tissues successfully meet the Evaluation Criteria. This team will win an award after these 6 trials because the last 4 trials produced 3 out of 4 tissues surviving (meeting a 75% success rate in the last 4 trials). The award will be either First Place or a Runner Up award depending upon their date of completion of the 75% of trials successfully meeting the Evaluation Criteria.

7. **Spaceflight Experiment Concept (SEC)** – Microgravity has been shown to have potential benefits for understanding cell biology, materials, and microfluidics research that have the ability to accelerate tissue engineering technologies. To be eligible for the Challenge awards, a team must submit a written proposal for an experiment that could be conducted in the U.S. ISS-NL onboard the International Space Station to advance some aspect of their tissue vascularization research. The SEC must be submitted as an MS Word or PDF document no more than 10 pages long excluding figured and tables. It must detail the following items:

a. What knowledge would be gained through the experiment that may not be available through ground-based research (i.e., why the microgravity environment would be beneficial to further study),

b. What data would be needed to provide this knowledge and how it would be gathered (experimental design and specific aims),

c. What commercial and scientific impact related to increasing knowledge for fundamental space biology and human exploration could be attained through the experiment,

d. How the experiment would leverage the information gained through this Challenge, and

e. Proposed materials and flight hardware required for the experiment.

SECTION 4: SAFETY & CARE

All teams shall follow the proper tissue care and use policies identified by their host institution, and adhere to the requirements for cell and tissue handling and human subject welfare listed in:

1. NIH Human Stem Cell Policy: http://stemcells.nih.gov/policy/Pages/Default.aspx

2. Code of Federal Regulations Title 45 Part 46 Protection of Human Subjects http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html

SECTION 5: REGISTRATION REQUIREMENTS

Teams must officially register with the New Organ Alliance management in order to be eligible to win the award. To officially register, teams are required to:

1. **Submit an Intent to Compete –** Teams shall submit a notice that they intend to compete to the New Organ management by September 30, 2019. The "Intent to Compete" must be a written statement to New Organ expressing the team's interest in being recognized as an official Challenge Team. The statement must include:
   - ***a.*** Name and nationality of the team leader;
   - ***b.*** Names of all team members and the host institution(s) for each of the team members; and
   - ***c.*** An Executive Summary, no more than 1000 words, describing the proposed techniques to be employed in pursuit of the prize monies.
2. **Sign the Team Agreement –** Intent to Compete forms will be reviewed by the Judging Committee within 30 calendar days of submission. Teams invited to officially register for the competition based on their "Intent to Compete" will be recognized as an official team only after the Team Agreement is co-signed by the New Organ Management and the Team Leader. Teams must be invited to submit a signed Team Agreement by the New Organ Management. The Team Agreement includes all details on how the New Organ management, and the Team will interact. Among others, the Team Agreement governs the following items between New Organ and the Team:
   - ***a.*** Award Disbursement
   - ***b.*** Media and Public Relations rights
   - ***c.*** Progress Report Requirements
   - ***d.*** Intellectual Property (IP) ownership (New Organ Alliance takes no IP of the teams)
   - ***e.*** Insurance protection & liability waiver requirements for Judging Committee members.
3. **Submit a "Team Trial Application"** - This document covers the details of how the team will conduct the trials. The Team Trial Application must be submitted a minimum of 30 calendar days prior to the expected date of the first trial. The Judging Committee will review the trial application and either approve or reject the application within 30 calendar days. The Team Trial Application must be approved by the Judging Committee prior to beginning the trial in order to be eligible for the Challenge awards.
4. **Submit Team Registration Fees** – The team must submit a one-time Team Registration Fee of $1500. Fees must be submitted and received by the New Organ Alliance prior to the beginning of the team's first trial.

SECTION 6: JUDGING & TRIAL REQUIREMENTS

The Judging Committee shall conduct the review of each team's trials to ensure that all trial requirements listed below are met in determining the Challenge winner(s). The Judging Committee's determination on the success or failure of a team to meet these criteria is final. The judging process and evaluation shall be conducted in the following steps:

1. "Team Trial Application" Submission: To begin the judging process, each team shall submit a "Team Trial Application" to the Judging Committee. This document will be reviewed by the Judging Committee to ensure that the team's trial will provide adequate data for the review of all Evaluation Criteria and that the team meets all Safety and Care requirements noted in Section 4 of the rules. The "Team Trial Application" document shall be submitted to the New Organ Management a minimum of 30 calendar days prior to the proposed start of the trial. The Judging Committee will provide a determination on acceptance or rejection of the application within 30 calendar days. The Team Trial Application must include:

    a. ***Process Description:*** A step-by-step description of all details in the process generating the team's tissue(s) and in conducting the team's trials. The information contained in this Process Description shall be considered "proprietary" (in accordance with the terms of the Team Agreement) and held in confidence by the judges (all Judging Committee members will have signed NDAs with the New Organ Alliance for their participation on the Judging Committee).

    b. ***Trial Tests:*** The Team's Trial Application must include a list and description of all tests the team will perform to verify that they have met all Evaluation Criteria in these rules. The Trial Tests and Process Description combined must provide sufficient detail to allow someone skilled in the art to reproduce the experiments. The tests described in this section must provide enough data for the Judging Committee to verify whether all Evaluation Criteria have been successfully met.

    c. ***Materials list:*** The team shall submit a table listing all materials used in generating the team's tissue(s) as well as those used in the trial processes and tests. This information shall be held in confidence by the Judging Committee.

    d. ***Process timeline & key milestones:*** The team shall submit a table identifying key milestones and timing of all tests and experiments required in the team's trial.

2. "Team Trial Application" Review: The Judging Committee shall review the Team Trial Application described by the team and make one of two determinations within 30 calendar days of application submission based on their review:

    a. ***Rejection***: A team's trial application shall be rejected only if the team has not provided the information listed above or has not provided for adequate tests required in their trial processes to accurately determine whether the team has met all Evaluation Criteria by the Judging Committee. A team whose application is rejected may re-apply with an updated process.

    b. ***Approval***: A team's trial application shall be approved if the Judging Committee determines that a team has developed a process capable of meeting all the requirements in the rules, and a team has included sufficient tests to determine whether or not the team has successfully met all Evaluation Criteria.

3. Trial Oversight Procedures: Upon review and acceptance of a Team Trial Application, the Judging Committee shall submit to the Team a "Trial Oversight Procedures"

document. This document will define when the Judging committee will require on-site access to the Team's trial location for review and evaluation of the Trial. The Judging Committee will, at a minimum, conduct an on-site evaluation at the conclusion of the 30 calendar day trial period, but may also require additional visits that will be defined in this document. The team will be required to provide access for the Judging Committee according to this Trial Oversight Procedures document in order to be eligible for the awards. One additional oversight requirement is that the Team must allow 24/7 Video Surveillance of the Trial by a qualified independent company to ensure the integrity of the process and serve as proof that Challenge conditions were met throughout all phase of the Trial. These videos will be recorded for examination after the trial by the Judges and NASA Officials. The addition of video surveillance is important to insure the integrity of the challenge.

4. Final Trial Report: Upon completion of the team's trials, the team shall produce a final report for the Judging Committee including the results of all tests performed and the procedures used throughout the trial. The report must be submitted to the Judging Committee within 7 calendar days of the conclusion of the trial. The report must be submitted to the Judging Committee as either an MS Word or PDF document a maximum of 10 pages long excluding tables and figures describing the results of all trial tests.

5. Determination of Success: The team's Final Trial Report and the Judging Committee's own on-site evaluations will be used to determine whether or not the team has successfully met all Evaluation Criteria. Determination of success will be completed by the Judging Committee within 60 calendar days from the conclusion of the team's trial. Determination of success is at the sole discretion of the Judging Committee, and the review of the Committee is final.

   a. **Winning Criteria -** In order for the team to receive a favorable decision by the Judging Committee and receive an award, they must:

      i. Provide the results to all tests, measurements, and experiments agreed upon in the accepted Team Trial Application.

      ii. Be able to demonstrate and verify that their trial(s) meets all Evaluation Criteria defined in the rules.

      iii. Have submitted to the Judging Committee a valid Spaceflight Experiment Concept.

      iv. Be able to demonstrate that they have complied with all other items listed in the Rules.

   b. **Determination of Placement** – If multiple teams complete the required successful Trials, determination of placement will be by the date upon which the team's final report for all trials is submitted to the Judging Committee.

SECTION 7: TIMELINE & MILESTONES

Teams are required to complete the following milestones:

- **Submit an Intent to Compete –** Teams wishing to compete for the prize shall first submit an Intent to Compete. It must be submitted by September 30, 2019.
- **Sign Team Agreement** – Teams invited to be recognized as an Official Team competing for the prize(s) shall next submit a Team Agreement.
- **Complete Quarterly Progress Reports** – Official teams must submit to the New Organ Alliance quarterly progress reports via email noting any work done towards winning the awards including funds spent and team invested time (total not individual).
- **Submit a Team Trial Application** – Teams shall submit their Team Trial Application documents to the New Organ Alliance a minimum of 30 calendar days prior to their proposed Trial start date.
- **Submit the Team Registration Fee** – Teams must submit the Team Registration Fee prior to the beginning of their first trial.
- **Conduct Trial(s)** – Teams shall begin the trials on the date accepted in their Team Trial Application. Teams must also provide access to trial facilities as defined in the Trial Oversight Procedures provided to the team by the Judging Committee.
- **Submit Final Trial Report** – the final report on the team's trial must be submitted to the Judging Committee within 7 calendar days of completing the Trial.
- **Submit Spaceflight Experiment Concept** – within 7 days of completing the trial, the team must submit to the Judging Committee a concept for an experiment that could be flown on the international space station that will further advance an aspect of their thick tissue vascularization research. This will be utilized in reviewing the team's ability to receive the CASIS Innovations in Space Award, but will not have an impact on determining whether the team has won the Challenge.
- **Determination of Success** – the Judging Committee will provide a determination of success to the team within 60 calendar days from the completion of the trial.

SECTION 8: ELIGIBILITY, DISQUALIFICATION, & APPEAL

1. **Eligibility –** Any organization incorporated in the United States is eligible to register as a team for the Challenge. The officially recognized team shall be the organization and individual members listed on the signed Team Agreement. The Team Lead shall be limited to United States citizens or permanent residents only.
2. **Disqualification** - All teams shall adhere to the following guidelines to remain eligible for the Challenge. If at any time, a team is found to be in violation of one of these requirements, it shall be disqualified from further participation in the Challenge.
   - ***a.*** Falsification or Misrepresentation of Data – if a team is found to have falsified data that is used in any part of the Challenge, the team shall be disqualified.
   - ***b.*** Unethical Behavior – a team will be disqualified if it is found that they conducted unethical behavior during the Challenge period. Unethical behavior includes but is not limited to hampering another team's progress toward a winning solution or providing denigrating or false information about other participants. Determination

of unethical behavior is at the sole discretion of the Judging Committee.

Disqualification of teams is at the sole discretion of the Judging Committee.

3. **Appeal –** Disqualified teams may appeal to the Judging Committee for reconsideration in order to compete for the prize(s). Appeals shall be considered for each team only once. For an appeal to be successful, the team must demonstrate to the Judging Committee that the committee has been misinformed of the actual behavior or falsification of data by the team. Appeals may only be made in regards to a team's disqualification, not on the determination of success from the team's Trial. The determination of appeal by the Judging Committee is final.

SECTION 9: AWARDS

The Challenge will provide a First Place Award of $300,000 to the team that can first achieve all of the requirements as stated in the rules. A runner up award of $100,000 will be provided to each of the next two teams that complete all requirements by the Trial Deadline. Awards shall be provided by NASA directly to the winning team(s) in a lump sum payment.