

REQUEST FOR APPLICATIONS (RFA)

MSCRF Clinical Program

INTRODUCTION:

Stem cell research offers extraordinary promise for new medical therapies and a better understanding of debilitating human diseases, injuries and conditions. The development of new medical strategies for the prevention, diagnosis, treatment and cure of human diseases, injuries and conditions through human stem cell research is a high priority for the State of Maryland.

FUNDING OBJECTIVES

In this Request for Applications, the MSCRF is soliciting Clinical Stem Cell Research Grant Applications from organizations that wish to conduct clinical trials in the State of Maryland using human stem cells to advance medical therapies.

ELIGIBILITY INFORMATION

Organizations that meet the in-State eligibility requirements specified below, and evidence the skills, experience, resources and support necessary to carry out the proposed research may apply for a Clinical Research Grant.

Maryland-based, for-profit, public or private research Companies of all types are eligible for this Award (i.e., those affiliated with universities, colleges, research institutes, medical centers and laboratories as well as those that operate independently). A Company is considered based in Maryland if its primary location of operations is in [Maryland](#).

Companies eligible for Clinical Research Grants must conduct all MSCRF-funded work in the State of Maryland.

Companies conducting Clinical research may be based outside of Maryland, in the United States, but the work funded by the MSCRF must be conducted at a site in Maryland.

Companies and/or PIs that have received **prior MSCRF funding may apply for this Award** on a related or different topic. A summary of the research progress and any publications and/or presentations that resulted from the former MSCRF funding must be included in the Appendix.

Each Application for an Award funded by the MSCRF shall have only one (1) PI, but may have multiple Co-PIs, Investigators and/or collaborators. PIs may participate as collaborators in any number of MSCRF-

funded Projects in the same funding cycle. However, they may apply to the MSCRF as the lead PI for only one new Award in any given year.

PIs, Companies and at least one contact from each Company who will be responsible for Grant administration must be registered in the [TEDCO on line submission system](#) at least one month before the Grant Submission Deadline. Companies owned by women, underrepresented minorities and individuals with disabilities are encouraged to participate in this program.

ELIGIBLE RESEARCH AND CELL TYPES:

Only Applicants requesting funds for Projects with clearly defined achievable milestones will be considered.

All research funded by the MSCRF must involve human stem cells. All types of human stem cells, as defined in the Stem Cell Act, are eligible without preference. The Stem Cell Act defines eligible human stem cells as follows: A human cell that has the ability to: (1) divide indefinitely; (2) give rise to many other types of specialized cells; and (3) give rise to new stem cells with identical potential. The full text of the Stem Cell Act is available on the MSCRF Web site (see www.MSCRF.org).

OTHER ELIGIBILITY CRITERIA

Applications that involve a *clinical trial* must have an IND or IDE, cleared by the FDA for the therapy or device under study, **before the Application is submitted to the MSCRF for review.**

Awardees shall receive MSCRF funds only after providing documentation to TEDCO confirming that the research to be conducted with MSCRF funds has been approved by the relevant Institutional Review Board ("IRB"), Institutional Animal Care and Use Committee ("IACUC") and, for Projects involving human embryonic stem cells ("hESC"), a Stem Cell Research Oversight Committee ("ESCRO/SCRO").

AWARD INFORMATION

AVAILABLE FUNDS

The MSCRF is currently budgeted to commit up to \$9 million. The number of Grants awarded will depend upon the quality, size and mix of Applications received.

AWARD SIZE, DURATION & TERMS

Under this RFA, the total direct costs proposed may not exceed \$750,000 for a maximum of 2 years.

Clinical Projects shall require a 1:1 match of non-state money. In-Direct-Costs are not allowed under this RFA

Because the nature and scope of the proposed research will vary from Application to Application, the size and duration of Awards also will vary. Approved Projects may be funded at or below the requested/proposed amount.

Under this RFA, MSCRF Grant Award funds may be used for the following direct costs, commensurate with the time dedicated solely to the proposed research:

-  Salary and fringe benefits for the PI and essential personnel
-  Equipment
-  Supplies
-  Consultant costs
-  Contract services

-  Collaboration expenses
-  Travel and conference expenses
-  Publications and miscellaneous costs

MSCRF funds may not be used to cover personnel costs of Investigators who are located and conduct the work outside the State of Maryland, regardless of whether such out-of-State Investigators are employed or retained by a Maryland-based or non-Maryland based organization.

Purchase of equipment and supplies, publication costs, conference expenses, contract manufacturing and services and other non-personnel costs may be incurred outside the State of Maryland, in accordance with customary practices of researchers.

Once a Grant has been awarded, up to ten (10) percent of funds can be reallocated between budget categories without prior TEDCO approval (e.g., from salaries to supplies). However, reallocations in excess of ten (10) percent must be approved in advance by TEDCO.

SHARING RESEARCH RESULTS AND PUBLISHING

Applicants must commit to make the results of their MSCRF-funded research readily available to others, through publications (preferably), public presentations or other accessible means.

COMPLIANCE

A Company and/or PI not in compliance with the reporting obligations under the Clinical Research Grant shall not be eligible to apply for continued or subsequent MSCRF funding.

APPLICATION AND SUBMISSION INFORMATION

CONTENT & FORMAT OF APPLICATION

All Sections of the Application must be submitted through the [TEDCO on line submission system](#). The document must be formatted using point size 12 Arial font, with margins no smaller than one-half (0.5) inch on all sides. Uploaded file must be limited to 5 (five) megabytes (MB).

The Application must include the following Sections:

A. Project Summaries - *Limited to one (1) page each*

A Project Summaries describing the proposed research and its potential contribution toward the goals of the MSCRF and this RFA, as set forth in this document. One Project Summary shall be nontechnical and directed to a lay audience.

B. Clinical Research Plan - *Limited to six (6) pages, including all tables, figures and charts*

An overall plan for development of the therapeutic candidate, including (1) A description of the targeted disease, condition or injury and the potential impact that the proposed therapy will have, if successfully commercialized, on the treatment or progression of that disease, injury or condition, or on medical practice; (2) An explanation of why human stem cells are necessary or advantageous to the proposed research; (3) The Research Design, including the Scientific Rationale, Experimental Approaches, Methods and Technique proposed for accomplishing the Project goals within two (2) years.; and (4) If applicable, a Target Product Profile for the therapeutic candidate. Each of the following aspects of a TPP should be

addressed: (a) description; (b) significance; (c) indication(s); (d) activity (in vitro/in vivo) and efficacy endpoint (in patients); (e) safety; (f) route; (g) regimen; (h) risk versus benefit and (i) clinical competitiveness. For proposed allogeneic cell therapies, immune tolerance or immunosuppression strategies should be addressed in the above sections.

C. Clinical Potential and/or Plan - *Limited to one half page not included in the page count*

An explanation of (i) how clinical practice and treatment of human diseases, conditions or injuries will be advanced by the proposed research; (ii) how the proposed research may contribute to new medical treatments or interventions; and/or (iii) how the proposed research will translate prior research results into new medical therapies or test new therapies in human patients, and the projected time line for accomplishing such clinical application(s). This section is required for all Applications.

D. Key Project Personnel - *(A table format, not included in the page count)*

A list of the names, affiliate organizations, and roles of all key personnel, defined as the PI and individuals in addition to the PI, who contribute to the scientific development or execution of the Project in a substantive way, and devote measurable effort (in person months) to the Project, whether or not salaries are requested.

E. Budget & Budget Justification - *(A table format, not included in the page count)*

A detailed yearly budget and budget justification, including salaries that are within the current NIH salary range and commensurate with the time allotted to the proposed research. This budget will be used if the Application is funded. Make certain that it is complete and accurate. Applicants should request only the funds needed to complete the proposed Project. Requests for less than the maximum allowable amount will not be considered as a weakness. Applicants must provide matching funds details in the budget.

F. Resources and Environment - *Limited to one half page not included in the page count*

A description of the facilities in which the work will be conducted and how the scientific environment will contribute to the probability of success, including such things as collaborative arrangements involving on-site resources, unique features of the subject population and support from the Applicant.

G. Impact on Biotechnology in Maryland - *Limited to one half page not included in the page count*

A description of how the proposed research should contribute to the development, expansion or improvement of biotechnology operations or capabilities in the State of Maryland. Examples (for illustrative purposes only) include the introduction of improved, streamlined or automated processes involving stem cells; expansion or improvement of stem cell production or storage; training of stem cell researchers, technicians and related personnel and the like.

H. Bioethics - *Limited to one page not included in the page count*

A description of the ethical issues relevant to the proposed research and how these issues will be addressed, including, but not limited to, a discussion of the ethical issues related to the cell type(s) and cell line(s) to be used; animal welfare (i.e., IACUC); IRB review and related concerns regarding human subjects.

I. **Appendix - Limited to 25 supplemental pages (Upload in the same file as the application)**

The Appendix shall include (in this order):

(1) Literature in Support of the Application

(2) Biosketches and Publications - **Limited to four (2) pages each relevant to the application**

Short Biosketches, and up to five (5) relevant Publications, for key personnel, collaborators and pertinent others. Include online publicly accessible links.

(3) **Response to Reviewer Comments, if Applicable - Limited to three (1) page (not counted in the Appendix page limits)** - For Applicants Resubmitting an Application that was previously reviewed under any MSCRF funding mechanism, but not funded: An Introduction to the revised Application, including the Application Number of the previous MSCRF submission, and a point-by-point response to the prior scientific review.

(4) **You must include the subjects consent form for the clinical trial.**

(5) Letter(s) of Collaboration, if Applicable - *Limited to one (1) page per collaborator*

(6) **Other Current Support** - The Project Number(s), Title(s) and Funding Source(s) of all currently supported research, and a short paragraph summarizing each Project.

The Appendix may not be used to circumvent the length limitations of the Application. Applications that are incomplete, do not meet the format and/or content requirements, exceed specified length limits, are non-responsive to this RFA or are from ineligible Applicants will not be reviewed.

The uploaded document must include all sections. The Appendix may not be used to circumvent the length limitations of the Application. Applications that are incomplete, do not meet the format and/or content requirements, exceed specified length limits, are non-responsive to this RFA or are from ineligible Applicants will not be reviewed.

SOURCE FOR APPLICATION INFORMATION

Application information will be available electronically on the MSCRF Web site (see www.mscref.org).

SUBMISSION DEADLINES & REVIEW DATES

Application Submission Deadline: January 24, 2017, by 5:00 p.m.

Peer Review Date(s): March 2017

Commission Review Date(s): May 2017

Earliest Anticipated Start Date: June 2017

METHODS OF SUBMISSION

Grant Application

PIs, must register in the TEDCO on line submission system at least one month before the Application Submission Deadline. Grant Applications must be submitted through the [TEDCO on line submission system](#) by January 24, 2017, no later than 5:00 p.m.

One signed paper copy of the Application must be submitted by mail to the Maryland Stem Cell Research Fund (see address below). The paper copy of the Application must be postmarked no later than January 25, 2017. All submissions must be received by their respective due dates. Late submissions and hand deliveries will be NOT be reviewed.

Paper copies should be sent to:

Maryland Stem Cell Research Fund – Clinical Program
Maryland TEDCO
7021 Columbia Gateway Drive, Suite 200
Columbia, Maryland 21046

REVIEW INFORMATION

AWARD DECISION CRITERIA

The Scientific Peer Review Committee will review all Applications and rank them based on scientific merit. Scoring system of 1-9 will be used to rate the overall impact/priority of the proposed research. In this system, “1” indicates the highest impact/priority and “9” indicates the lowest impact/priority. The Commission will then review the ranked Applications and make recommendations to the TEDCO Board, which will make the final funding decisions.

To receive a high scientific priority score, an Application must be judged strong in all of the following categories:

-  **Meeting the Overall Objectives of The MSCRF Program:** Do the proposed studies broaden and advance the knowledge of human stem cells? Does the Project address problems in regenerative medicine, as defined by the Commission? Are the studies relevant to the development of clinical application(s) to treat human diseases, injuries or conditions? Will these studies enable, support and expedite such clinical application(s)?
-  **Clinical Impact:** Can the proposed research result in a therapeutic candidate that meets an unmet medical need and/or offers a competitive advantage over other therapies or devices currently in practice or in the development pipeline? Does it have the potential to significantly impact clinical treatment or medical practice?
-  **Scientific Rationale:** Does the Application adequately address the scientific basis and rationale for the therapeutic candidate?
-  **Readiness:** If applicable, does the data presented follow the FDA Target Product Profile TPP Guidelines, as required by the MSCRF? Does the Application adequately characterize the key product under investigation and describe in detail the production tasks required for this specific phase of development?
-  **Objectives, Strategies and Milestones:** Does the research plan include appropriate, achievable objectives, feasible strategies and clearly defined milestones? Does it define and address key issues in all areas critical to the successful progression to the next phase of the research, trial, product development or other Project objective described in the Application? In *pre-clinical* Proposals, if the Applicant does not already have FDA clearance for the therapeutic candidate, do

the goals include preparing and filing an IND or IDE? Does the research plan describe IND- or IDE-enabling studies?

 **Likelihood of Success:** Are there limitations of the proposed studies that will make it difficult to apply findings or strategies in the clinic? Are there completed or on-going clinical trials that will impede or accelerate the proposed research?

 **Use of Human Stem Cells:** Does the proposed research use adult, embryonic, iPS or other human stem cell lines? Does the PI justify the use of human stem cells in the proposed research as necessary or advantageous as compared to other approaches?

 **Impact on Biotechnology in Maryland:** What is the potential impact of the proposed research on the advancement of biotechnology in Maryland's academic, business and/or non-profit sector(s)? Will this Project help create new biotechnology jobs and grow Companies and/or program opportunities in Maryland?

 **Budget and Budget Justification:** Is the requested period of support appropriate for the scope of the Project? Is the effort listed for all personnel appropriate for the proposed work? Is each budget category realistic and justified in terms of the aims and methodology? If equipment is requested, is it justified, cost effective and budgeted appropriately? Is the Applicant's match adequate and appropriate for the Project? Does the Applicant provide justification for any and all proposed in-kind matches that involve existing equipment, including cost and date of acquisition as well as current usage?

 **PI and Team Leadership:** Is there evidence that the Investigators are adequately trained and well suited to carry out the Project? Is the proposed Project appropriate to the experience level of the PI and other Investigators? Does the research team bring complementary and integrated expertise to the Project?

 **Resources and Environment:** Does the scientific environment in which the work will be conducted contribute to the probability of success? Do the proposed studies benefit from any unique features of the scientific environment or subject population? Do these studies employ useful collaborative arrangements involving on-site resources or personnel? Can the Applicant provide the support and personnel necessary to complete the research?

 **Bioethics:** If an existing stem cell line is to be used, what are the justifications for that line? If new lines are to be created, what measures will be taken to comply with the Stem Cell Act as well as existing stem cell research bioethics guidelines? If animal subjects are to be used, what measures are taken to comply with IACUC guidelines? If human donors are involved, have they been properly consented? If human subjects are involved, what protections will be in place to ensure their rights and welfare? If human embryonic stem cells are involved, has the Proposal been approved by an ESCRO/SCRO Committee?

For Applications that involve **clinical trials:** Does the Applicant have an IND or IDE cleared by the FDA for the therapeutic candidate or device under investigation (as required by the Commission prior to submission of this Application)? Has the Proposal been approved by an IRB responsible for oversight at the Maryland facility where the trial will be conducted (as

required before any MSCRF funding shall be disbursed)? Is there an independent Data Safety Monitoring Board?

 **Collaboration Plan (if applicable):** If the proposed research involves collaboration(s) among scientists and/or clinicians from for-profit and/or not-for-profit Companies and/or other organizations, is there a demonstrated commitment from each entity and a realistic management plan that addresses all potential obstacles (i.e., how the Company and collaborator(s) will communicate, handle confidential information, use milestones to determine resource re-allocation and Project re-direction, share data and resources, prepare required reports and handle geographic separation, if applicable)?

If the PI's work was previously funded by the MSCRF, in whole or in part, the Application will be evaluated on the following additional factors: Did the Investigator make significant scientific progress towards the goals of the previously funded research? Were results of the previously funded Project reported in scientific publications and/or presented at conferences? Did the previously funded research result in new collaborations, inventions or Project-generated resources as proposed in the original Application? Did the previous Project generate subsequent funding from non-MSCRF sources?

Project Selected For Review: All Clinical applicants who score high enough to move on to the full review committee will be required to present in person at the MSCRF Review Meetings.

- The PI and or the CEO (if not the same person) listed on the Clinical Application must plan to present on the stated review dates. Other team members may attend; however, the PI and or the CEO must attend.
- All presentations will be scheduled as part of standing MSCRF review days listed below. Due to the number of applications on any given review day, presentation times will be assigned by MSCRF.
- The PI will need to hold the review day open until the time is assigned. This may be confirmed as close as a week before the review day, so PI's will need to remain flexible during this process.
- The Commercialization company applicant will be allotted a 10 minute timed presentation, followed by 20 minutes for Q&A. We recommended no more than 10 slides. Following are the required slides for the presentation:
 - What is the Problem?
 - What is the Solution?
 - Technology Outline
 - Target Market?
 - Segmentation Analysis
 - Target Product Profile
 - Clinical Process
 - Timeline and Costs
 - Risks and Mitigation Plan
 - Finances
 - Cost Projections
 - Financing Needed for the MSCRF Project?
 - Follow-on Financing for the Next Steps, Beyond MSCRF?
 - Management and Clinical Team
 - Advisors? Board of Directors?

After presentation of the preliminary scores and discussion of applications at the MSCRF Review Committee Meeting, applications will receive a final score based on an average of all the overall scores provided by the MSCRF Review Committee Members.

Applications will be ranked by average final score and submitted to the Commission for review and final approval.

AWARD ADMINISTRATION INFORMATION

NOTIFICATION

Potential candidates will be notified whether or not they are invited to submit a full Application approximately one month after the Pre-Application deadline. Applicants will be notified electronically when their full Applications have been received. After the TEDCO Board has approved the Commission's funding recommendations, a formal notification, in the form of a Notice of Award ("NOA"), signed by the MSCRF Director, will be sent via email to successful Applicants.

Selection of an Application for Award is not authorization to charge costs to the MSCRF. Except as stated in **Section C**, in regard to pre-Award costs at the Applicant's risk, Applicants may not charge costs or assume they will receive funds until an MSCRF Grant Agreement has been signed by someone from the Company responsible for administering the Grant and TEDCO. A template for the MSCRF Grant Agreement will be posted on the TEDCO Web site before the Awards are announced (see www.MSCRF.org).

POST AWARD REPORTING

Clinical Program awardees must submit the following reports to the MSCRF Program including:

- a. **Award Manager Meeting** – each applicant is required to meet with the MSCRF Award Manager at least once, prior to the mid-term. This is to assist each awardee in understanding and meeting expectations for the program. This is also an opportunity for the awardee to share feedback, discuss ideas and ask for additional assistance.
- b. **Mid-Project Reports**, (in-person PowerPoint presentation at TEDCO's offices) which must include a description of project activities and results to date, the progress toward meeting mid-term milestones, an accounting of expenditures charged to the award, and details on the proposed Commercialization Plan and budget;
- c. **Final Reports**, which must provide an overview of all activities undertaken during the course of the funded project, a description of the results of the project, the impact on commercialization, the success with achieving the proposed milestones, jobs created, follow-on-funds raised during the project, and a full accounting of all expenditures charged to the award, and suggestions for ways to improve the Program;
- d. **Symposium presentation** - The MSCRF will conduct an in-State Annual Symposium to report to the scientific community and the public the progress of the MSCRF program. All PIs must present, orally or in poster format, their on-going or completed MSCRF-funded research at each Annual Symposium, during and immediately following their Grant period.

AGENCY CONTACTS

Questions about this RFA must be submitted by email to: mscrfinfo@tedco.md. Telephone inquiries will not be accepted.