



Male Contraceptive Initiative 2023 RFA

Letter of Intent due:	June 1st, 2023
Notification from MCI of invitation to submit:	July 7th, 2023
Research Applications due:	September 1st, 2023
Review, evaluation, decision, and award notification:	Q4, 2023

Section I: Funding Opportunity Description

Purpose: This opportunity provides two funding tracks that support research projects with application in the development of reversible non-hormonal contraceptives delivered to men.

Background: Nearly half of all pregnancies worldwide are unintended. Furthermore, contraceptive users who produce sperm are limited to condoms and vasectomy, which do not provide adequate variety in characteristics to meet the needs of all users.

Male Contraceptive Initiative (MCI) is a US-based 501(c)3 nonprofit, funding agency, and advocates for safe, effective, and reversible contraceptive solutions for those that produce sperm.

This Request for Applications (RFA) contains two separate funding tracks in order to support research ranging from mechanistic target-based studies to late preclinical development. Further details and award scope can be found within the RFA. It is envisioned that this funding mechanism, in conjunction with MCI's program-related investment mechanism, can provide end-to-end support for male contraceptive studies through Phase I clinical studies.

The emphasis for this funding opportunity is encouraging the development of safe and effective contraceptives that are distinct from existing methods and have profiles that appeal to a broad base of users.

Award Details

	David Sokal Innovation Awards	Development Awards
Scope	Projects in discovery or exploratory phases of contraceptive development, including hit-to-lead optimization.	Projects in early-to-late stages of contraceptive development, including preclinical studies and beyond.
Maximum Award Budget	\$200,000 in total project costs; over two years at maximum \$100,000 per year.	\$400,000 in total project costs; over two years at maximum \$200,000 per year.
Indirect Costs / Overhead	Institutional indirect costs / overhead shall not exceed 10% of the total award costs listed above in the Maximum Award Budget and are to be included as a part of the Maximum Award Budget.	
Award Project Period	Awards may have a maximum Project Period of two years.	
Available Funds	MCI may commit up to \$1.4M to fund multiple awards in association with this announcement.	

A. The David Sokal Innovation Awards provide a maximum award of \$200,000 over the project period and are intended to spur novel contraceptive research pathways. They are named after the co-founder of Male Contraceptive Initiative, David Sokal, MD, who has consistently advocated for contraceptive innovation over a long career in contraception and global health. Sokal Awards are designed to enable projects in the early stages of contraceptive discovery and development with demonstrated Proof of Concept (see below) to de-risk and move closer towards or into active contraceptive development.

Sokal Award applications may focus on, but are not limited to, inquiries into biological mechanisms of validated contraceptive targets, discovery of agents with potential contraceptive application, early development of contraceptives for men, as well as tools, techniques, and delivery devices that expand contraceptive research capabilities. Objectives for past Sokal Award applications have included small molecule compound screening, the development of enzyme or cell-based assays needed to assess inhibition of a specific target, and other efforts that provide a pathway for specific compounds, devices or mechanisms to reversibly block male fertility.

B. Development Awards provide a maximum award of \$400,000 over the project period and are intended to support projects in active contraceptive development with activities up to and through regulatory approval for first-in-human studies. This funding category requires both Proof of Concept (see below) and demonstrated progress towards a specific, marketable contraceptive compound or device. Demonstrated progress may include lead compounds with suitable pharmaceutical properties for downstream development, *in vivo* or other pre-clinical data of relevant compounds or devices, or a clearly articulated pathway towards regulatory approval.

Development Award applications may focus on, but are not limited to, refinement of specific compounds to improve selectivity, potency and drug-like properties, refinement and testing of device modifications, in vitro and in vivo preclinical studies such as pharmacokinetics / pharmacodynamics (PK/PD), absorption, distribution, metabolism, and excretion (ADME), toxicology studies, and other evaluations required to progress into clinical stages of development. Preference will be given to compounds or devices with demonstrated promise for development as a male contraceptive (such as evidence of specificity and effectiveness of a compound or device in animals, target druggability, evidence of reversibility). The ideal application will have a clear pathway established towards regulatory approval and precisely outline how a funded application will move towards that goal in the US and / or other regulatory markets.

Project Eligibility

This application is open to academic institutions, for-profit organizations, and other entities, foreign and domestic. Any individual(s) with the skills, knowledge, and internal or external resources necessary to carry out the proposed research as a Principal Investigator (PI) is invited to work with their organization to develop an application for support.

Generally, projects exploring the feasibility of a contraceptive target, identifying potential contraceptive compounds, or are otherwise early-stage are eligible for David Sokal Innovation Awards, whereas projects in active contraceptive development that have identified a lead compound or series, are in pursuit of or have achieved regulatory approval for first-in-human studies, or are otherwise well-positioned for downstream development are eligible for Development Awards.

The following chart broadly illustrates project types and their eligibility for individual awards. Applicants with questions regarding eligibility should contact the appropriate MCI official listed at the end of this announcement at the earliest available opportunity.

	David Sokal Innovation Awards	Development Awards
Small Molecule Therapeutics	Proposals can include activities such as hit identification, hit-to-lead optimization, and in vitro / in vivo assessments of potency and / or specificity, as appropriate.	The compound is at the lead optimization or preclinical stage. The target is known, and/or there is some method or assay to determine its modulation.
Biologics or Cell Based Therapies	Applications should lead to new molecular entities and include some measure of assessment of efficacy in an in vitro / in vivo model.	The biologic has been identified and there are established in vivo efficacy and target engagement data.
Interventional Medical Device	The proposal includes prototype development and testing, either on	The device is in a stage of active development and the proposal

	the bench or in animals. Physiologic experiments have been conducted or reported in the literature, providing rationale for prototype development.	includes activities such as manufacturing certification, design optimization, and other preclinical or possibly early clinical work
Tool, Assay, Delivery Device, Diagnostic, or Other Research Focus	Applications should be aimed at developing methods, techniques, assays, or devices that provide new or enhanced diagnostic, screening, or delivery capabilities. Practical application and dissemination of information should be included in the scope of work.	Tools must be at an advanced stage of development and offer significant access and upside to the scientific community. Applicants seeking a Development Award for this application should contact the appropriate MCI official at the earliest opportunity.

For both David Sokal Innovation Awards and Development Awards, applications focusing on specific methods of achieving a contraceptive effect in men must provide Proof of Concept that the proposed mechanism of action will block male fertility. Proof of Concept in an animal model is preferred.

Examples of **Proof of Concept** may include, but are not limited to:

- Targeted deletion of a gene that results in complete male infertility in an animal model without other observed adverse phenotypes
- Inhibited expression of the gene encoding the target through RNAi or another gene silencing method that results in infertility as demonstrated by a secondary method such as mating studies or *in vitro* fertilization
- Clinical evidence that a target is, at minimum, strongly correlated with infertility in men
- Administration of a contraceptive agent in an animal model, resulting in reversible male infertility

Applications seeking to develop male contraceptives that do not act through a pharmacological mechanism must demonstrate Proof of Concept through other evidence that the proposed research project will generate an effective contraceptive method. Applicants seeking further discussion regarding this section are encouraged to consult the appropriate MCI official listed at the end of this announcement.

For both David Sokal Innovation Awards and Development Awards, applicants focusing on the development of male contraceptives are encouraged to submit projects aligned with **MCI Priority Research Areas**, which include the following:

- Approaches that target the post-meiotic phase of spermatogenesis
- Approaches that target sperm functions required for normal fertilization, such as sperm motility and the acrosome reaction

- Approaches that target post-testicular processes required for fertility, including epididymal maturation and sperm transport in the excurrent ducts
- Approaches that could lead to on-demand or otherwise fast-acting, reversible male contraceptives
- Approaches that repurpose existing chemical entities for contraception which may be currently approved by the FDA or other regulatory agencies for other indications.
- Approaches with the potential to result in Multipurpose Prevention Technology (MPT) products that prevent pregnancy and act against sexually transmitted infections such as HIV.

Applications not within MCI Priority Research Areas but fulfilling other eligibility criteria are reviewed alongside applications aligned with MCI Priority Research Areas using the same criteria and evaluative process.

Applicant organizations may submit more than one application, provided that each application is scientifically distinct.

Current MCI grantees are eligible to apply for funding through this mechanism. Applicants may submit proposals covering new or existing projects, as long as the work proposed is scientifically distinct from previously funded work.

MCI values representation and diversity in the scientific community. Applications from women, people of color, the LGBTQIA community, and other historically marginalized groups are encouraged.

MCI will not accept applications that are duplicate or highly overlapping grant awards from other funding agencies. Applicants should ensure submissions to MCI are scientifically distinct, and not duplicate or highly overlapping with submissions currently under consideration by other funding agencies.

Applications seeking to identify new male contraceptive targets are not responsive to this announcement.

Applications in the following areas are considered outside of MCI interests and will not be reviewed:

- Approaches developing contraceptives that are delivered to female users
- Approaches that permanently inhibit fertility, e.g. cause sterility or other defects in reproduction after cessation of treatment
- Male or female barrier development, e.g. condoms
- Approaches involving the administration of steroid hormones
- Approaches that induce active immunity
- Applications focused on molecular targets for which there is no human ortholog

Section II: How to Apply

Letter of Intent:

Prospective applicants for all award types in this announcement must submit a Letter of Intent (LOI) to apply by **June 1st, 2023** to grants@malecontraceptive.org. Applicants seeking a Development Award should apply with the subject line: "MCI Development Award LOI." Applicants seeking a Sokal Award should apply with the subject line: "MCI Sokal Award LOI."

The LOI should concisely outline the proposed research project to be considered. The LOI is a non-confidential document.

Submit letter as a one-page PDF document (single-spaced, 11 point Arial font, at least 0.5 inch margins). The letter should include:

- A. Applicant's name, title, institution (or private sector organization), and contact information
- B. Project title
- C. Overview of proposed research and its relevance to the development of novel male contraceptives

Letters of Intent will be reviewed using criteria based on the program requirements and goals described in this RFA. Successful LOIs will be invited to submit a Research Application. All applicants will be notified by **July 7th, 2023** whether they are invited to submit a Research Application.

Research Application:

Invited Research Applications from successful LOIs are to be submitted by **September 1st, 2023** to grants@malecontraceptive.org. The application must be in PDF format, 11 point Arial font, with at least 0.5 inch margins.

Subject line must be: "MCI Development Award Application" for Development applicants, and "MCI Sokal Application" for Sokal Award applicants.

Applications must include the following information, organized into the following hierarchy with the following page restrictions:

Part 1: Title Page (one page):

- a. Applicant's name, title, institution, and contact information
- b. Collaborator's (if any) name(s), title, institution, and contact information
- c. Signature of institutional official verifying approval of MCI conditions for award
- d. Project Title
- e. Research Abstract

Part 2: Research Proposal (not to exceed 6 pages, excluding references):

- a. Specific Aims: Concise summary aims, their underlying rationale, novelty of compound or target or population being studied, questions to be addressed, hypotheses, and predicted outcomes.
- b. Background: Key published and unpublished data underlying the proposed studies and the relevance of the methods and approaches to be used.
- c. Research Plan: Describe design and sequence of studies to address Specific Aims. If focused on contraceptive development, how proposed studies will validate and refine the usefulness of the potential male contraceptive under study; address evaluation of the safety, reliability and reversibility of its use; propose potential alternative approaches.
- d. References: No specific citation format is required. Many style guides with guidance for citations are acceptable.

Part 3: Project Management (up to 2 pages)

- a. Applicant's role and responsibilities in performance of proposed research
- b. Roles of key collaborators or contract research organizations (if any)
- c. Novel or essential facilities, equipment, and resources available for the proposed studies or how they will be accessed if not available
- d. **Milestones**: Expected outcomes and deliverables with quantifiable goals

All projects must clearly define milestones, or deliverables for each specific aim of the project with quantifiable metrics that define success. To be measurable, each milestone should define success as a specific target value or metric. These target values or metrics should allow for objective evaluation and be structured as go / no-go decisions for each stage of the project.

Illustrative examples: Express and isolate 10mg of a target protein with a purity of 99%; develop a cell-based assay that can screen 5,000 compounds per week with a Z' of at least 0.8; screen of a commercial library of 5,000 compounds with a Z' of greater than 0.5 and a signal to noise ratio of at least 4; develop at least 5 compounds across two scaffolds with a sub-nM IC50 value as measured by a valid assay; fertility studies at 5mg/kg will demonstrate 90% efficacy at 6 weeks; achieve a 50x therapeutic safety window between hERG IC50 and target potency.

Timelines are to present objectives and milestones in a written format that details specific activities performed during each quarterly period, as well as displayed visually in a Gantt Chart.

	2024				2025			
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
Specific Aim 1								
Milestone 1.1								
Milestone 1.2								
Specific Aim 2								
Milestone 2.1								
Sub-objective 2.1								
Milestone 2.3								
Specific Aim 3								
Milestone 3.1								
Milestone 3.2								
Milestone 3.3								

Example Gantt Chart. Chart may be adapted in any way to fit the submitting project. Milestones may be further divided into sub-objectives and other categories as needed such that they provide detailed activities that can be related directly to the milestones to be achieved.

Part 4: Requested Budget: (Itemized by the following categories, when applicable. Include other categories such as Open Access publication fees as appropriate. Divide costs per year, and include total costs. Two pages maximum)

- a. **Personnel:** names, roles in project, percentage of salary and benefits to be covered for each
- b. **Reagents:** cost for general categories, except for unique compounds and reagents
- c. **Animals:** institutional cage costs, number and species to be used. Include IACUC-approved protocol numbers when appropriate
- d. **Contractors, consultants, and sub-awardees:** names, roles in project, brief justification, and studies to be performed. Attach quotes in Part 6d of the Research Application
- e. **Equipment:** essential equipment not available and required for project, manufacturer, cost based on bid from supplier (up to a maximum of \$50,000 for Development Awards, and \$25,000 for Sokal Awards). Attach quotes in Part 6d of the Research Application.
- f. **Overhead:** maximum of 10% of total award amount. Overhead is to be included as an

itemized budget line as part of total award amount, which is not to exceed the applicable total listed in the RFA.

- g. Cost sharing: Voluntary committed cost-sharing, or matching funds from the applicant or other sources are allowed as part of the requested budget and is voluntary on the part of the applicant. If proposing cost sharing, use this section to illustrate non-MCI sources of funding, clear delineations between costs that are covered by project funds and costs that are covered by other sources of funding, and any related information such as institutional cost-sharing policy. Projects utilizing effective cost-sharing are encouraged.

Part 5: Curriculum Vitae (up to five pages each for awardee and key collaborators; NIH biosketch format is preferred)

- a. Education, current and prior positions and appointments
- b. Current and prior research experience, source and amount of current and prior research support
- c. Publications relevant to application

Part 6: Appendix (up to 3 pages total for Parts 6a-6c, up to 5 pages for Part 6d - Supporting information)

- a. Continued development statement: Use this space to describe how a successful outcome will feed directly into the next stage of male contraceptive development and how the applying program plans to continue development, with consideration given to the current environment, available expertise, and planned future studies. Examples include but are not limited to:
 - o For projects in the screening phase, a description of potential partnerships to carry out hit-to-lead studies and advance into preclinical development.
 - o For projects that are in or have completed the chemical optimization phase, a description of potential routes of delivery/administration.
 - o For projects in late preclinical development, a description of planned regulatory interactions and early clinical studies
 - o For MPT projects, discussion of the anti-infective strategy, the proposed delivery method, and the potential impact on public health.
- b. (Optional) Intellectual property statement: Information about intellectual property (IP) position of the compound(s), device(s) or process(es) described in previous sections may be provided here.
Potential topics for an intellectual property statement include, but are not limited to:
- c. (Optional) University or company IP policy: Summary of any patents, copyrights, trademarks, licenses or other intellectual property owned; Documentation relating to the transfer of any technology to the Company or any employee, consultant or other party; Proprietary Information and Invention Agreements signed by past or present employees and consultants
- d. (Optional) Supporting information: Examples of supporting information include but are not limited to:

- Data, figures, or unique methods and materials
- Letters of Support from key collaborators or institutions
- Quotes or other documentation from vendors
- Target Product Profile (TPP) of the proposed product in development, with minimally acceptable and target criteria defined

Section III: Review

Process and Confidentiality

All information submitted as part of the Research Application is treated as confidential unless explicitly stated otherwise.

Applications will be reviewed for scientific and technical merit by an appropriate review panel assembled by MCI. Reviewers will certify adherence to the Conflict of Interest and Nondisclosure Rules adopted by the National Institutes of Health. Reviewers will be advisory to the MCI Board of Directors which has the final responsibility for funding decisions.

All reviewed applications will receive a written critique, which will be anonymized and provided to the applicant as constructive feedback.

The following considerations will be taken into account with funding decisions:

- Relevance of the proposal to the vision and mission of the organization
- Scientific and technical merit as evaluated by the review panel
- Availability of funds
- Relevance of the proposal to the goals and priorities outlined in the RFA description
- Readiness of the proposal and project to move into later stages of contraceptive development
- Relevance of the proposal to MCI Priority Research Areas
- Relevance of the proposal to a balanced MCI funding portfolio

During the review, MCI may share non-confidential information provided either orally or in writing - such as in the Letter of Intent - with third parties, including key partners and potential co-funders.

MCI is required by the IRS to publish a list of awarded grants. MCI also provides general descriptions of its awards on its web sites, in press releases, and in other marketing materials. Awardees may be asked to participate in promotional efforts by MCI, which can include interviews, outreach, and other publicity. These efforts are voluntary, and will not impact the terms of the grant.

Review Criteria

- Response to RFA: How well does the proposal address one or more of the research areas identified?
- Demonstrated promise: Is there a strong scientific premise for the project? Is there evidence of specificity and effectiveness in animals?
- Research plan: Are the studies well-focused and is the scope of work, overall strategy, methods and approaches appropriate to achieve the specific aims of the study within the budget and time available (first and subsequent years of support)? Are potential problems and alternative strategies considered?
- Contraceptive development: Is the proposal based on a target or compound well-positioned to continue development towards a male contraceptive? With respect given to the current state of the project, does the proposal provide suitable plans for extending current and future studies to the next stage of contraceptive development?
- Investigator: Does the applicant have the knowledge, training and experience needed to perform the research? Will the investigator be able to devote sufficient time and effort to the project for it to be successful?
- Environment: Are the facilities, equipment and institutional support available to the applicant sufficient for the proposed studies to be successful? Is the support plan to facilitate the proposed research well-conceived?

Section IV: Award Administration

A formal notification will be provided to the applicant organization for successful applications. The notification will be signed by the MCI awards management officer and will be sent via email to the grantee.

Applicants are advised to target a project with a start date in Q1 2024. Later start dates are possible. Contract negotiations between MCI and the parent institution may prolong proposed start dates.

MCI expects applicants selected for funding to work with MCI staff in establishing a final milestone plan which will be used to evaluate progress of the award.

Any costs incurred before formal notification of award are at the risk of the awardee, and are not reimbursable.

Other grantee benefits associated with awards include access to MCI resources, promotional outlets such as webinars and meetings, connection to experts and key opinion leaders, networking opportunities, and other support from MCI staff.

Progress Reports & Monitoring

Continuation of funding beyond the first year is contingent upon satisfactory progress and availability of funds. MCI may arrange for confidential meetings with consultants with relevant expertise to facilitate the development of products resulting from funded projects. MCI may also contract with a third-party monitor to evaluate progress and provide consultation on the project, including evaluation of quarterly benchmarks as indicated in Part 3 of the proposal.

Grantees are responsible for adhering to the approved project proposal. Should changes in project objectives or key personnel be necessary, grantees must contact their MCI awards officer at the earliest possible opportunity to discuss changes and impact on award, as changes may require review from MCI.

Budget variances of more than 10% in any budget subcategory must be approved by MCI. MCI reserves the right to audit any of the relevant records of grantees.

Awardees are responsible for adhering to the Grant Progress Reporting Guide, which will be provided after award notification to successful applicants and can be provided to prospective applicants on request. The Grant Progress Reporting Guide outlines a quarterly update structure through informal email exchanges, written reports, and virtual meetings.

Ongoing funding is to be determined yearly by the MCI Research Committee. The decision of the Research Committee is reached using the quarterly updates detailed in the Grant Progress Reporting Guide and an annual written report, which details progress on proposal-specific milestones. The annual written report will be due 30 days before the end of the funding year to grants@malecontraceptive.org. Both Development and Sokal Award awardees will be provided with a grant code, and should use the subject line “[Grant code] Research Grant Progress.” The Progress Report will be a confidential document and should be submitted in pdf format. It is to include:

Research Narrative (Two pages minimum, five pages maximum, include figures when appropriate):

- List the major goals and objectives of the project for the current year and what was accomplished for these goals.
 - Include key outcomes or conclusions (both positive and negative), and a discussion of goals not met.
- Compare research progress against specific milestones and target dates against targets outlined in the project proposal and / or approved by MCI. List the specific milestones for the current year, if / when they were met, and the evidence of successful research progress.
- Explain any changes to original goals and objectives that require modification of research plans. Note that whenever possible, changes in goals, research scope,

approaches, or methods should be communicated to the appropriate MCI contact at the earliest opportunity.

- Describe, in detail, any problems or delays that impacted the project, or potential problems for the upcoming reporting period.

Budget (two pages maximum):

- Provide a proposed budget for the coming year and justify amounts and purposes of planned expenditures. Include a reporting of expenditures to date, and compare against original estimates.

Appendix (optional - no page limit)

- The appendix may be used to provide any additional information that is relevant to the progress of the project. Examples include:
 - Structures of chemical compounds mentioned in the Research Narrative, additional images or figures, relevant data tables, etc.
 - Publications, presentations, media outreach, or other public representations
 - Personal or professional accomplishments from the awardee or staff during the reporting period
 - Inventions, patents, or licenses that have resulted from the award
 - Opportunities for training and professional development
 - Meetings with regulatory authorities, new partnerships, business developments, or leveraged / newly awarded funding

Informal updates and unscheduled communications from the awardee to MCI are welcome and greatly appreciated especially in the event of unexpected challenges, recent accomplishments, or other opportunities.

Open Access

MCI is committed to dissemination of published research resulting from project funds to enable unrestricted access and reuse of all peer-reviewed publications (“Open Access”). Grantees shall publish all publications in a manner that will permit all users of the publication to have Open Access so that any reader may have access to an article without further permission or fees being required.

Applicants are encouraged to include Open Access publication fees in a prospective budget when applying.

Global Access

MCI requires that grantees establish a Global Access strategy for the products generated, if any, under the Project. Grantees will make a good faith effort to conduct and manage all Project research, product development, technologies and innovations in a manner, consistent with global access commitments, to disseminate knowledge gained during the conduct of the Project

to the scientific community, subject to a limited delay to seek intellectual property protection where such protection would best facilitate the achievement of the Project's charitable objectives, and to work collaboratively to ensure that any products developed from Project Funds are made accessible (with respect to cost, quantity and applicability) to the people most in need within the developing countries and public sector markets in developed countries of the world.

Section V: Contact

Questions regarding any aspect of the award or award process are encouraged. Please contact:

Logan Nickels

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logan@malecontraceptive.org

Or:

grants@malecontraceptive.org