

Crohn's & Colitis Foundation IBD Ventures Initiative

Program Guidelines

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Crohn's & Colitis Foundation
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MISSION:

To cure Crohn's disease and ulcerative colitis,
and to improve the quality of life of children and
adults affected by these diseases.

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Program Policies & Instructions

Overview

The mission of the Crohn's & Colitis Foundation is to cure Crohn's disease and ulcerative colitis, and to improve the quality of life of children and adults affected by these diseases. In order to pursue this mission, the Crohn's & Colitis Foundation seeks to support and accelerate the discovery and development of research-based products with potential for positive impact for patients suffering from inflammatory bowel diseases (IBD). The Foundation hereby solicits proposals from companies and academic investigators seeking support for the discovery and development of such products. Proposals will be reviewed in order to determine whether programs are eligible for Foundation support through the IBD Ventures (IBDV) Initiative to fund the discovery and development of products with potential for benefit in the IBD field. Funded programs may be led by investigators at companies or academic institutions. The IBDV program is not a traditional research grant mechanism. Its objective is to identify and support organizations that will benefit from partnership with the Foundation in pursuit of product discovery and development. This document identifies program policies and terms, funding and resources available for fundees, eligibility, selection criteria and application procedures.

The Crohn's & Colitis Foundation also seeks to engage with companies and investigators who are not necessarily interested in or eligible for the IBDV funding at this time, but who are actively seeking to discover and develop products for positive impact in the IBD field. Such companies and investigators are encouraged to submit a Letter of Intent as an initial step in the identification of Foundation resources that may be of interest, including future funding opportunities.

Funding and Resources

Research & development (R&D) projects will be funded to advance the discovery or development of a specific product candidate with potential for positive impact in the IBD field. Funded projects should be approximately 12 months in duration, with specific intermediate and final milestones identified at project onset. Funding up to \$500,000 per project per year will be considered, inclusive of all direct and indirect expenses. Indirect expenses may not exceed 10%. Project funding may be extended past the first year if milestones are met. Projects that require lower levels of funding are also welcome. Project cost-sharing, through which Foundation funds would be complemented using additional sources of funding to achieve project goals, is encouraged. The Foundation will not request intellectual property (IP) ownership in funded technologies. In the event that the funded technology becomes commercially successful, the Foundation would receive a financial return (see Appendix C: Funding terms).

In addition to direct funding, the Crohn's & Colitis Foundation will provide accelerator resources to support for funded programs. Such support will be tailored to the specific program and may include scientific review; strategic advising; patient and clinician insights; assistance in identifying research resources; facilitation of strategic partnerships (including identification of and referral to specific potential partners); assistance with clinical trial recruitment; presentation opportunities; and consideration for future Foundation funding opportunities. Accelerator support will be provided by Foundation staff, advisors and partners.

Eligibility

The following types of organizations are eligible to apply for this funding if the following criteria are met. **Applicants not meeting the specified criteria based on the Letter of Intent (LOI) submitted will not be considered for funding.**

- **Company.** The majority of applicants in this category will be small for-profit biotechnology companies; non-profit organizations meeting the criteria may also apply. This category does not include organizations whose primary mission is education, clinical care and/or basic research (e.g. universities, academic medical centers or basic research institutes). In order to qualify as a company applicant, an organization must meet the following criteria at the time of LOI submission:
 - Independent organization with a primary focus on product discovery and/or development.
 - Business plan specifying organization's mission and projected milestones.
 - The proposed project must be consistent with the organization's business plan.
 - Funds must be available for essential company operation during the project period.
 - Full-time personnel are employed by organization.
 - Necessary infrastructure is accessible for proposed research activities.
- **Academic or research institution.** Projects led by investigators at universities, research institutes and medical centers may be proposed. **Academic applicants must demonstrate commitment to, and experience with, commercialization-oriented activities, and access to appropriate resources for commercialization.** Such resources may include SBIR award(s), intramural accelerator programs, industry-sponsored research, drug discovery

core facilities, contract research organizations, entrepreneur-in-residence programs, etc. Basic research programs are not eligible unless described work is directly related to a product discovery/development objective. Applicants are encouraged to discuss the application with relevant institutional officials (e.g. technology transfer officer). Preferably, at least one full-time staff member should be dedicated to the proposed project. Projects associated with invention disclosures, patent applications and/or other IP (e.g., proprietary assays) are preferred.

For both applicant categories, collaborative projects will be considered, including projects involving an academic investigator and an industry partner. Applications should identify one organization as the primary applicant. Collaborating organizations should also be identified at the time of application. International applicants are welcome.

In addition, the following are required for eligibility for all IBDV applicants:

- Principal investigator & key personnel with appropriate expertise
- Demonstrated commitment to product discovery/development
- Core intellectual property (IP) for the proposed product must be assigned or licensed to the primary applicant, as reasonably required for commercial development

Selection Criteria & Review Process

The selection criteria below will be evaluated by reviewers using the IBDV scorecard (Appendix F). **Please note the following when preparing LOIs and proposal:**

- **LOIs are reviewed on a competitive basis; LOIs that do not address each element in the review scorecard will be rejected.**
- **In general, a proposal must satisfactorily address each parameter in the review scorecard (average score of >2 under review) in order to be considered for funding.**

Proposal

Project should describe a specific potential product with the potential for positive impact for IBD patients. Any research-based product concept will be considered, including but not limited to:

- **Therapeutics.** Small molecules, large molecules, gene therapies, cell therapies and nutraceuticals.
- **Devices and diagnostics.** Medical devices, imaging agents and laboratory tests.
- **Healthcare technology.** Software, services and other technology-based products.

Applicants should articulate a clear, up-to-date understanding of how the proposed product would address a specific unmet need in IBD. Substantiation of the unmet medical need (for example, based on clinical research or input from patients and clinicians) is encouraged. Unmet medical needs in IBD may include, but are not limited to: Improved and less toxic therapy; improved treatment of severe, unremitting, refractory and/or recurrent disease; therapeutics for fibrotic complications; improved detection and quantification of active disease; improved prediction of inflammatory, fibrotic and/or penetrating disease; prediction of response to specific interventions; and improved management of post-surgical complications and recurrence. For reference regarding unmet needs in IBD, see the Foundation's Challenges in IBD document at: <http://www.crohnscolitisfoundation.org/research/challenges-in-ibd-research/> . The proposed solution should be differentiated from available solutions. Applicants must demonstrate an understanding of the competitive landscape for the proposed product and should articulate a barrier-to-entry strategy that should include, at a minimum, pursuing appropriate IP protection for funded activities.

The research plan and budget will be evaluated according to the following criteria: Are the proposed activities specifically focused on the development of the proposed product in IBD? Are these activities critically important to advance the product in the short term? The proposed plan and budget should include specific milestones that, if met, would increase the likelihood of successful development of the proposed product. At a minimum, milestones anticipated at six months and twelve months should be specified. The projected time and cost associated with each milestone must be described. Anticipated results should facilitate clear go/no-go decisions regarding the development of the proposed product. Alternative approaches, explicit success metrics and risk mitigation strategies should be included. Funded indirect expenses may not exceed 10% of funded direct expenses. Cost-sharing (supplementation of Foundation funds using additional funding sources to achieve project goals) is encouraged. **The proposed R&D activities should consist of critical path activities required for near-term advancement of the proposed product opportunity.**

Proposals should include preliminary evidence in support of the scientific validity and commercial potential. At all stages, validation studies and insights from patient data are encouraged. Applicants should prioritize those activities considered to be most critical for the discovery or development of the product. **Note that proposals focused on target identification or basic investigation of mechanisms of disease will not be considered under this mechanism.**

For therapeutics, the following stages of development will be considered:

- *Therapeutic target has been identified.* **Proof-of-concept experiments have been performed, demonstrating that the proposed target is relevant for IBD.** For example, such preliminary data may include pharmacological or genetic manipulation of the pathway in a relevant *in vitro* or *in vivo* model. Insights derived from human data (such as the identification of relevant biomarkers in clinical samples) are encouraged. Demonstration of a well-designed assay to screen candidates and assess *in vivo* target engagement is also encouraged. At this stage, fundable activities may include optimization of screening assays (miniaturization, etc.), high-throughput screening or design of candidates through medicinal chemistry and/or protein engineering approaches.
- *Preliminary candidates have been identified.* Preferably, projects at this stage will present preliminary data on efficacy in appropriate animal models, safety, ADME (absorption, distribution, metabolism, excretion) profile and target engagement. Fundable activities at this stage may include identification of lead development candidates, drug delivery strategies, efficacy studies (e.g. multiple disease models, dose-response, and/or route of administration consistent with the intended clinical application), safety studies (e.g. *in vivo* maximum tolerated dose studies), PK-PD studies, target engagement in tissue, identification of relevant biomarkers (e.g. for PD assessment), screening and/or chemistry for lead optimization, and elucidation of therapeutic candidate's mechanism of action.
- *Lead candidate has been nominated.* Fundable activities may include additional efficacy studies in an additional species, detailed PK-PD studies, characterization of clinical biomarkers, development and validation of assays for cGMPs or clinical biomarkers, or process development for API synthesis. More advanced activities (such as IND-enabling GLP toxicology, cGMP manufacturing, IND filing, or Phase I clinical studies) may be proposed; however, applicant should identify additional funding sources to supplement Foundation funds to reach such milestones.

For laboratory diagnostics, target biomarker must be identified and prior demonstration of feasibility of detection in clinical samples is required. For devices, software and imaging modalities, demonstration of feasibility (e.g. a functioning prototype) is required. Funded activities for diagnostics, devices and software may include assay development, prototyping and validation.

Applicant

Applicant organizations are expected to demonstrate the necessary capabilities, personnel and infrastructure to develop the proposed product. Applicants should have an operating plan and budget and the proposed project should be consistent with the organization's mission. First-time entrepreneurs are encouraged to apply; however, capabilities and prior achievements in product discovery, development and commercialization will be considered. Commitment to IBD research, for example based on a track record of contribution to the field, will be considered, but only where such expertise is critical for the proposed R&D. Organization's general resources, including a balanced team covering general management, operations, R&D and commercial functions; fundraising to date; infrastructure; IP portfolio; contractor and vendor networks; and active collaborations with academics and industry will also be considered. Prior to funding, Foundation staff will perform due diligence.

Commercialization potential

Criteria will include the unmet medical need for the proposed product; differentiation; IP; go-to-market strategy (including clarity on regulatory pathway); likelihood of early partnerships; consideration of initial clinical indication(s) and minimum requirements to reach clinical proof-of-concept. Applicant must have assignment or license to any required IP associated with the proposed product, and preferably should have evaluated freedom to operate in advance.

Review process

Proposals will be evaluated by a dedicated review committee. The review committee will include: Industry scientists; academic scientists; commercialization-oriented professionals (with experience in entrepreneurship, investing, and business development in the biomedical setting); IBD patients and caregivers; and IBD clinicians. Scientific reviewers will generally have a background in immunology/inflammation and IBD but will not necessarily be technical experts in the specific subject matter of each proposal. For proposals on specialized topics, subject matter experts may be consulted on an *ad hoc* basis. Applicants should provide adequate technical detail such that the proposal can be evaluated from a research perspective, but whenever possible, submitted materials should be accessible to a sophisticated but non-

specialized reviewer. Patient/caregiver reviewers are trained to evaluate the target product profile, and not the detailed scientific plan, based primarily on the lay abstract and slide presentation (Appendix E); those two documents should be accessible to non-scientists. Applicants with concerns regarding disclosure of confidential information, potential conflicts of interest or any other review-related issue are encouraged to contact the program manager to resolve any concerns in advance of proposal submission.

Application Instructions & Timeline

All organizations developing research-based products for IBD are invited to contact the Foundation by submitting a Letter of Intent (LOI) form. Forms will be reviewed by Foundation staff and review committee members and applicants will receive a response at least 4 weeks prior to the next deadline for full proposal submission. Applicants should indicate, at the time of LOI submission, interest in submitting a full proposal for the next cycle of review. If that does not apply, LOI submission is nevertheless encouraged if the applicant may be interested in engaging with the Crohn's & Colitis Foundation regarding development of a product for IBD. Such applicants will be considered for future funding opportunities and additional Foundation support (including advising, clinical trial recruitment assistance and presentation opportunities). An applicant organization may submit multiple LOIs for individual projects, however, not more than one project would be funded for a single applicant simultaneously.

While there is no specific deadline for LOI submission, applicants should be aware that in order to be considered for review in a given cycle, cutoff dates for each year will be applied which will be posted on the program website and on the proposal submission portal (see links below). Selected applicants will be invited to submit a detailed full proposal for project funding. Full proposals will not be reviewed without prior submission of a LOI. Applicants will have a minimum of four weeks to prepare and submit a full proposal. Full proposals will be reviewed by a dedicated committee twice per year. Following review, applicants selected for funding will be notified (generally, in mid-May and mid-October); funding terms will be proposed and negotiated; and Foundation staff will perform due diligence as needed (e.g. verification of contractual relationships and IP filings). The process from notification to contract execution is intended to take less than six weeks. Strict confidentiality will be maintained by Foundation for all submitted materials. Applicant may request a confidentiality agreement at any time in the application process. In some cases, a project may be identified with potential for funding, but for which additional information and/or revisions are required. In that case, applicants will be notified of requested revisions and will have the opportunity to resubmit. Depending on the extent of revisions required, the resubmission may be reviewed by Foundation staff or by full committee review. **Applicants should review funding terms** (see Appendix C: Funding terms) **and should indicate any potential disagreement in advance of full proposal submission.** A contract template may be provided upon request.

Dates, program guidelines and a link to the submission portal may be found on the Foundation's website at the following address:

<https://www.crohnscolitisfoundation.org/research/grants-fellowships/entrepreneurial-investing>

Application may be accessed and must be submitted through proposalCENTRAL:

<https://proposalcentral.com/>

Navigate to the 'Grant Opportunities' tab (top right) and filter by grant maker (select 'Crohn's & Colitis Foundation') to find the application link for the IBD Ventures Program.

Appendix A: Letter of Intent Questionnaire

All Letters of Intent must be submitted through proposalCENTRAL:

<https://proposalcentral.com/>

Navigate to the 'Grant Opportunities' tab (top right) and filter by grant maker (select 'Crohn's & Colitis Foundation') to find the application link for the IBD Ventures Program.

For your convenience in filling out the LOI questionnaire, questions contained in the online form are listed below.

1. Application title. (Required. Max 250 characters.)
2. Please describe how you heard about this program. (Required. Max 1000 characters.)
3. (Y/N) Would you be interested and able to submit a 5-page research proposal for the IBDV Program by the deadline for Full Proposals, if invited to do so? (Required)
4. (Y/N) Are you interested in additional resources the Foundation could provide, such as: scientific advising; clinical advising; recommendations regarding potential partnerships; access to research resources; patient/clinician insights; and/or presentation opportunities? (Optional).
5. Please describe the resources you are most interested in. (Optional. Max 3000 characters.)
6. (Y/N) Are you interested in setting up a confidentiality agreement? (Optional)
7. PI Name (Prefix, *First, Middle, *Last) (Required)
8. PI Highest Degree (Required)
9. PI Primary affiliation (Required)
10. PI Additional affiliation(s) (Required)
11. PI Position/Title (Required)
12. PI Address (Required)
13. PI Email (Required)
14. PI Phone (Required)
15. Lead Organization Name (Required)
16. Lead Organization Address, City, State, Zip, Country (Required), website (optional)
17. Choose the type of organization for the prime applicant: (Required)
 - For-profit small technology company (<25 employees)
 - For-profit medium-sized or large company (>24 employees)
 - Non-profit organization
 - Academic or research institution
 - Clinical organization
 - Other
18. Organizational Contact Name (Required) (may be same as PI)
19. Organizational Contact Position/Title with applicant organization (Required)
20. Organizational Contact Email (Required)
21. Organizational Contact Phone (Required)

22. (Y/N) Is the lead organization an independent entity with a primary focus of product discovery and/or development? (This does not include institutions whose primary mission is education, basic research or clinical services.) (Required)
23. Companies: Describe the mission, core competencies and business model of the applicant organization. Academic investigators: Describe the research and product development goals of the research group. (Max 3000 characters.) (Required)
24. (Y/N) Does the organization have full-time employees? (Required)
25. List key project personnel. Indicate role in the organization, percent time commitment at the time of application, anticipated percent time commitment during proposed project term (if applicable), date recruited to team and relevant experience. Describe experience in IBD. Company applicants may include management staff. Advisors may be included. Include weblink profile (LinkedIn or other) if available. (Max 6000 characters.) (Required)
26. (Y/N) Does the organization have operating funds for essential company activities for the next 12 months? (Required)
27. Briefly describe applicant's relevant R&D infrastructure, including laboratories, and/or information technology systems. Key collaborators or contractors may also be identified here. For academic applicants, describe access to commercialization-oriented infrastructure. (Max 6000 characters.) (Required)
28. Describe related funding and resources secured to date. (Optional. Max 3000 characters.)
29. If the company has additional marketed or investigational products, in addition to the product described, so describe. If any such products are currently in clinical testing, so describe. (Optional. Max 3000 characters.)
30. (Y/N) Are you proposing the discovery and/or development of a specific product intended to cure IBD or improve the quality of life of adults and children affected by IBD? (Required).
31. Project description. Briefly describe the proposed product for IBD. (This description is for informational purposes only; you may revise the project proposal at a later time.) Include the following information:
- The problem being addressed and relevance to specific unmet needs in IBD.
 - The specific product opportunity and how it would address the problem.
 - Description of the underlying technology and preliminary data.
 - Design of proposed studies with timeline, specific objectives and expected outcome (if applicable).
 - Anticipated milestones with metrics for success. How would milestones increase probability of successful product development?
 - Approximate funds required to reach indicated milestones.
- (Required. Max 6000 characters.)
32. (Y/N) Does the applicant have partnerships or collaborations, especially any related to the proposed product? (Required)
33. If Yes: Describe. (Optional. Max 3000 characters.)
34. Choose the product category: (Required).
- i. Small molecule
 - ii. Large molecule
 - iii. Cell therapy (including microbes)
 - iv. Vaccine
 - v. Gene therapy

 - vi. Laboratory diagnostic
 - vii. Imaging modality
 - viii. Other medical device

- ix. Software
- x. Service
- xi. Combination product
- xii. Other

If the proposed product is a therapeutic, answer questions 35-53 (Optional).

- 35. (Yes / No / Not applicable) Has a proprietary molecule been generated?
- 36. (Yes / No / Not applicable) Has a proprietary molecule library been generated or screened?
- 37. If yes, what is the size of the library and how is it being accessed? (Max 1000 characters)
- 38. (Yes / No / Not applicable) Has the therapeutic target been validated in IBD?
- 39. If yes, how? (Max 1000 characters)
- 40. (Yes / No / Not applicable) Has high-throughput screening been initiated?
- 41. If Yes describe; if not, when will screening be performed? (Max 1000 characters)
- 42. (Yes / No / Not applicable) Has a biochemical or phenotypic screening assay been developed?
- 43. If yes, what is the throughput of such assay(s)? (Max 1000 characters)
- 44. (Yes / No / Not applicable) Has a lead compound been nominated?
- 45. What is the presumed mechanism of action of the lead compound? (Max 1000 characters)
- 46. (Yes / No / Not applicable) Has an appropriate formulation been developed?
- 47. (Yes / No / Not applicable) Have experiments been performed to determine absorption, distribution, metabolism and/or safety?
- 48. (Yes / No / Not applicable) Has any GLP toxicology or GMP process development been initiated?
- 49. (Yes / No / Not applicable) Have any related biomarkers been identified?
- 50. What are the projected endpoints for in vitro and in vivo assays? (Max 1000 characters)
- 51. (Yes / No / Not applicable) Are resources available for protein engineering or medicinal chemistry?
- 52. (Yes / No / Not applicable) Is there a manufacturing process in place?
- 53. (Yes / No / Not applicable) Could the existing manufacturing process be adapted for production of clinical material?
- 54. (Yes / No / Not applicable) If the proposed product is a device, diagnostic or piece of software, has a functional prototype been generated? (Optional)
- 55. Describe, at a high level, the proposed commercialization path for the proposed product, for example, the intended regulatory pathway and how the product would eventually be sold. Explain how the development of the proposed product fits into the overall mission and business plan for the organization. If a commercialization strategy has not been generated or is not applicable, so indicate. (Required. Max 3000 characters)
- 56. (Y/N) Are there invention disclosures, patent applications, granted patents or other IP associated with the proposed product? (Required)
- 57. If Yes: Describe. (Optional. Max 6000 characters.)
- 58. (Y/N) Does the applicant believe that freedom to operate exists for the proposed product? (Optional.)
- 59. If Yes: Describe how this was determined. If No: Explain how this will be addressed. (Optional. Max 3000 characters.)
- 60. Enter any peer-reviewed publications associated with the proposed project. List publications in chronological order. Include only publications directly related to applicant's research program or IP. Limit your entries to 10 total publications. List publications in chronological order. Indicate whether author(s) are affiliated with applicant. (Max 10 citations.) (Optional)
- 61. (Y/N) Has the program benefited from accelerator resources, such as drug discovery or device prototyping accelerators? (Required).
- If yes, so describe. (Optional. Max 2000 characters.)
- 62. Attach an investor-oriented slide presentation (max 20 slides) and 1-page executive summary.

Note that the executive summary and investor-oriented slide presentation are often the first documents reviewers consult. Thus, it is advisable that the executive summary provides a succinct overview of the entire program and that the slide presentation includes key data supporting the program.

- 63. For resubmissions, attach a cover letter describing how the applicant is addressing prior critiques. (Optional)

Appendix B: Review Policies

To ensure that the business of the Crohn's and Colitis Foundation is conducted effectively, objectively, and without improper influence or the appearance of improper influence, reviewers of funding proposals for the IBD Ventures Initiative must maintain high standards of honesty, integrity, and impartiality in the performance of their duties and dealings with Foundation and with applicants submitting funding proposals. This policy is designed to help reviewers identify situations that present potential conflicts of interest and to provide Foundation with a procedure that, if observed, will allow a transaction to be treated as valid and binding even though the reviewer has or may have a conflict of interest with respect to the transaction. It is the duty of every reviewer to become familiar with and abide by this policy continuously while serving on the review committee.

Proposals will be evaluated under strict confidentiality in accordance with a confidential disclosure agreement to be executed by reviewer in advance of provision of application materials to reviewer. Application materials are intended to be used by reviewer exclusively for the stated purpose of evaluating proposals for potential funding by Foundation. Prior to each meeting, you will be sent a master list of applications. Please indicate any conflicts as they will need to be reassigned.

For purposes of this policy, the following circumstances will be deemed to create a potential conflict of interest:

1. Reviewer having a direct or indirect links to industry, such as pharmaceutical, medical device, health insurance, and healthcare related companies that have the potential to bias or appear to cause bias in the review process;
2. Reviewer serving as a board director or corporate officer for an entity developing and/or selling products/services related to Inflammatory Bowel Diseases;
3. Reviewer having a significant interest (financial or otherwise) in the outcome of any proposal under review by reviewer;
4. Reviewer having a significant financial interest in an organization that is in direct competition with an applicant entity under review by Reviewer;
5. Reviewer holding employment with a commercial entity that has a significant commercial interest in an applicant entity.
6. The PI or key personnel on the application are from the reviewer's institution.
7. Within in the past three years, the reviewer has been a collaborator or has had another significant professional relationship (e.g., served as a mentor) with any person on the application who has a major role.
8. The application includes a letter of support or reference letter from the reviewer.
9. The reviewer serves as a member of the advisory board for the project under review.
10. The reviewer has an indirect financial interest from the applicant institution or PD/PI of over \$10,000 in honoraria, stocks, and fees during the course of the last year or during the project period

It is extremely important and incumbent upon reviewers to adhere to the rules of confidentiality. These rules are critical to the integrity of the peer review system. In essence, all discussion related to the scientific merit of an application should be confined to the actual review and what occurs during the review is to be considered strictly confidential. Reviewers must feel free to openly discuss the strengths and weaknesses of an application without concern that any of that discussion might filter back to the applicant through any avenue other than the anonymous summary statement. Reviewers should have no discussion with any applicant regarding any aspect of the study section meeting either before or after the review. If you become aware of or have any concerns about such a breach of confidentiality, please notify Foundation staff.

Reviewers should disclose and, where appropriate, refrain from engaging in any activity that might reasonably conflict, or appear to conflict, with the interests of Foundation and applicants, or that might result in or create the appearance of: (i) Using one's position as a reviewer for private gain; (ii) Giving preferential treatment to any one party; (iii) impeding the efficiency or economy of Foundation's operations; or (iv) Making decisions without impartiality. Any reviewer shall recuse himself or herself from involvement in any decisions or discussions with Foundation in which the reviewer believes he or she has or may have a conflict of interest. It is the responsibility of the reviewer to disclose any such links that could

reasonably create a conflict. Final determinations regarding managements of such potential conflicts will be made by the Foundation's Chief Scientific Officer.

Reviewers also acknowledge a continuing obligation to disclose in writing when there is any significant change regarding potential conflicts of interest. In the interest of maintaining compliance with the above policy, reviewers are asked to refrain from communicating with applicants regarding proposals under review until the conclusion of the review cycle, except as may be specifically requested by Foundation staff, and to disclose to Foundation any business arrangements entered into between a reviewer and any applicant entity.

This policy is intended to supplement and be consistent full the Foundation's formal policies regarding submission and review of proposals, which can be accessed at:

<https://www.crohnscolitisfoundation.org/sites/default/files/2019-06/Guidelines%20for%20Maintaining%20Research%20and%20Peer%20Review%20Integrity%202014%20name%20update.pdf> as well as any applicable state and federal laws or governing conflicts of interest applicable to nonprofit and charitable organizations. Prior to receiving application materials, candidate reviewers must certify in writing that he or she has read and agreed to the policy above and that all information provided is complete and accurate. Foundation employees serving on the committee are considered to have committed in writing to complying with the above policy by virtue of the Foundation's standard employment and compliance policies.

Appendix C: Funding Terms

The following is an outline of certain terms and conditions that, together with additional customary terms, will be required to be included in a final Funding agreement. The Crohn's & Colitis Foundation will not take equity interest nor IP ownership in relation to funding.

1. Funding to be paid by CROHN'S & COLITIS FOUNDATION to applicant on a milestone basis during the period of the funded research program.
2. Return payment to CROHN'S & COLITIS FOUNDATION on commercialization of a product from funded invention/technology or any improvement thereto, corresponding to a multiple of CROHN'S & COLITIS FOUNDATION funding (such multiple will be determined upon agreement between applicant and CROHN'S & COLITIS FOUNDATION to account for risk and Funding amount).
3. Partial return payment to CROHN'S & COLITIS FOUNDATION on early exit event(s), e.g. option/out license and/or change of control transaction, with any remainder to be paid at commercialization.
4. Upon cessation by Applicant of active development in IBD field for business reasons (i.e., not for scientific failure) prior to commercialization or full satisfaction of point 3 above, Applicant and CROHN'S & COLITIS FOUNDATION will have agreed to one of the following: repayment to CROHN'S & COLITIS FOUNDATION with interest at a compounded rate the funding provided by CROHN'S & COLITIS FOUNDATION; substitution of a different invention/technology for development in the IBD field which will be subject to above CROHN'S & COLITIS FOUNDATION repayment terms; or outlicense funded invention/technology to CROHN'S & COLITIS FOUNDATION on mutually agreeable terms.
5. Twice yearly reports for 2 years after initiation of funding and annual reports from end of research program until full satisfaction of 2. Reports must be satisfactory to CROHN'S & COLITIS FOUNDATION and should include description of research and IP activities.

Please indicate any disagreement with any of the above in making your funding proposal. Foundation will consider alternative structures for highly competitive applicants.

Appendix D: Frequently Asked Questions

1. What is the IBD Ventures Initiative?

The Entrepreneurial Investment (IBDV) Initiative is a funding mechanism intended to accelerate the discovery and development of novel research-based products with the potential to alleviate suffering caused by Inflammatory Bowel Disease (IBD).

2. What types of potential products may receive funding?

Any research-based product with the potential to address an unmet need of IBD patients will be considered.

3. Who is eligible for this funding?

We anticipate that the majority of recipients will be companies with a primary focus on product discovery and/or development. Companies should have independent operations, appropriate capabilities and full-time staff. Investigators at academic institutions are also eligible if they can access appropriate resources for product development.

4. How can I access program information and application forms?

Application may be accessed and must be submitted through proposalCENTRAL: <https://proposalcentral.com/>. Navigate to the 'Grant Opportunities' tab (top right) and filter by grant maker (select 'Crohn's & Colitis Foundation') to find the application link for the IBD Ventures Funding.

5. Is there a deadline?

LOIs can be submitted at any time. However, proposals will be reviewed twice per year; in order to be considered for the upcoming review cycle, LOIs should be submitted by the corresponding deadline.

6. How will Letters of Intent be reviewed?

All organizations developing research-based products for IBD are invited to contact the Foundation by submitting a Letter of Intent (LOI) form. Forms will be reviewed by Foundation staff and a multidisciplinary review committee. Applicants will receive a response at least 4 weeks prior to the next deadline for full proposal submission. Applicants should indicate, at the time of LOI submission, interest in submitting a full proposal for the next cycle of review for the IBDV Funding.

7. Should I submit a Letter of Intent (LOI) even if I am not interested in or eligible for this funding?

Yes! Even if you do not intend to apply for this funding, we still want to hear from you. LOI submission is encouraged if you are interested in engaging with the Crohn's & Colitis Foundation regarding development of a product for IBD. LOIs will be considered for future funding opportunities and additional Foundation resources (including advising, clinical trial recruitment assistance and presentation opportunities).

8. How will full proposals be reviewed?

Full proposals will be reviewed by a multidisciplinary committee comprised of industry scientists; academic scientists; clinical experts; entrepreneurs; business development and venture professionals; and IBD patients.

9. Can I submit a full proposal if I have not previously submitted a Letter of Intent?

No.

10. Will the Crohn's & Colitis Foundation treat submitted materials in a confidential manner?

Yes. All submitted materials will be treated in a confidential manner and will be used only for the purpose of application review. If the applicant would like to request a confidentiality agreement in addition, a template for that can be provided.

11. Will the Crohn's & Colitis Foundation offer additional resources for fundees in addition to funding?

Yes. Accelerator resources will be provided to support ventures, including scientific and strategic advising, according to the needs of each funded program.

12. Is the IBDV funding project-based?

Yes, funding will be project-based funding with specific milestones established in advance.

13. Will the Crohn's & Colitis Foundation ask for equity in funded companies?

No.

14. Will funding be associated with a financial commitment?

Yes. If the funded technology is successfully commercialized, payment would be due back to the Foundation.

15. What should be the estimated duration of funded programs?

Approximately one year.

16. Will funded programs be eligible for extended funding beyond the first year?

Yes, especially if milestones are achieved.

17. Are there any limitations as to the type of technology that might be funded?

No, so long as there is clear potential for benefit for IBD patients.

18. Are commercial-stage or public companies eligible for the IBDV Funding?

Yes, any company meeting the eligibility criteria is eligible to apply.

19. Can applicants be located outside the US?

Yes.

Appendix E: Full Proposal Format

Applicants will be asked to submit the following documents in PDF format for full proposal consideration. Text documents should use 11-pt or larger Arial font and not less than ½ inch margins. All files should be uploaded through proposalCENTRAL.

- Cover letter addressing critiques from prior review (required for resubmissions, otherwise optional).
- Research plan (up to 7 pages, not including bibliography).
- Bibliography may be provided as a separate document or included in the research plan document.
- Summary of commercialization plan, including discussion of funding, resources & partnerships to date & projected (up to 1 page).
- Key personnel and R&D resources (up to 1 page).
- Milestones & timeline (flow chart, Gantt chart or similar) (up to 1 page). Overall project flow, timeline, milestones and go/no-go decisions should be indicated. Parallel critical path activities outside the scope of the funded proposal, but related to the proposed product, should be indicated using a different color.
- Milestone-driven budget summary table (up to 1 page). When Foundation funding would be supplemented by additional funds from another source applied towards project objectives (cost sharing), such funding may be indicated (in a separate column). Project related overhead may be included in proposed Foundation funding but must not exceed 10% of total funding provided. General overhead and costs associated with development activities occurring in parallel may also be indicated (in a separate column).
- **Lay-accessible** abstract. Please note that all funding proposals to the Foundation are evaluated by patients/caregivers. It is the applicant's responsibility to describe the target product profile in clear, non-technical language.
- Scientific abstract.
- Slide presentation (up to 25 slides). Content is at applicant's discretion, but preferably should address the selection criteria (target product profile, validation, IP, team, resources, R&D, milestones & commercialization strategy) in a **lay-accessible** format.
- Resumes/CVs for key personnel (optional).
- Letters of support (optional).

Appendix F: Review Guidelines for Stakeholder Reviewers

The technical merit (and, in the case of the IBDV program, the commercial merit) of the proposals will be evaluated in detail by professionals active in the biomedical space. The main objective of involving stakeholder reviewers - patients and caregivers - in proposal review is not to draw on their specific professional expertise. Rather, the primary, distinct and independent role of a stakeholder reviewer is to help ensure that funded research addresses a problem that is meaningful from the perspective of patients and caregivers. In this context, relevance refers to the scope of the study, which must be focused on development of research-based products addressing unresolved challenges in IBD healthcare (unmet patient needs). Significance means that the project could measurably impact the quality of life of the IBD patients and families. Innovation means that the project addresses the problem in a new and differentiated way and has a potential to improve on the solutions that have been tried before. In the case of the IBDV program, this is reflected in assessment of the target product profile (Parameter A): if successfully developed, would this actually have a positive impact relative to what was already available?

Stakeholders are encouraged to discuss the proposals with other fellow committee members; however, they should be able make an assessment based on the summary information provided by the applicants (lay Summary and slide deck) and any discussion that takes places during the review process. The stakeholder reviewers help keep the review process focused with 'eyes on the prize' of delivering meaningful solutions, as opposed to basic research projects that may be technically advanced and elegant but may not be so focused on patient needs in IBD. The stakeholder reviewers also assess the communication skills of the applicants; it is the applicants' responsibility to explain the significance of their projects using clear, non-technical language. For the IBDV program, stakeholder reviewers should score Parameter A; additional parameters may be scored at the reviewer's discretion.

Fundamentally, the qualifications for participating in proposal review as a stakeholder review is to 1) be a patient or caregiver; 2) be willing to participate actively in the review process/discussion; and 3) be willing to respect the review policies. In some cases, the stakeholder reviewer may also have relevant input based on specific professional experience.

Appendix G: Review Scorecard

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Scoring system: Eight parameters are scored on a 1 to 4 scale. A score of 1 indicates that minimum requirements are not met for that parameter; generally, if average score on any single parameter is below 2, the proposal would be not be considered fundable, regardless of how well it is scored on other parameters. 2 denotes that minimum requirements are met but not exceeded; 3 denotes 'strong'; 4 denotes 'exceptional.'

Review parameters:

Parameter A: Target product profile addresses unmet need in IBD

Specific product proposed with the potential to address a specific, important unmet need of IBD patients, which is not adequately addressed through available solutions. Specific patient population identified that could benefit from the proposed solution. Programs addressing critical unmet needs in IBD will be prioritized. For reference regarding unmet needs in IBD, the Foundation's *Challenges in IBD* publication may be considered:

1	2	3	4
Poor	Adequate	Strong	Exceptional
Proposed product not clearly described or does not clearly address unmet need in IBD	Proposed product could address unmet need that is not fully addressed by available solutions	Proposed product could clearly address an unmet need in IBD that is not addressed at all by available solutions	Proposed product could address a critical, pressing unmet need in IBD

<http://www.crohnscolitisfoundation.org/research/challenges-in-ibd-research/>

Parameter B: Validation of proposed product

Data must be presented in support of the utility and feasibility of the proposed product. Specifics of preliminary data package may depend on stage of development. Advanced programs are preferred. Validation using multiple approaches preferred. For therapeutics, therapeutic target/strategy must be validated specifically in IBD. Demonstration of efficacy in appropriate animal models, safety, ADME profile and *in vivo* target engagement is preferred. Discovery of novel targets will not be supported. For devices/software, there must be a functional prototype. For diagnostics, a biomarker candidate and means of detection should be identified. Discovery of novel biomarkers will not be supported. Demonstrated link to IBD (for example, based on clinical samples/data) is preferred.

1	2	3	4
Poor	Adequate	Strong	Exceptional
Proposed product is not supported by adequate evidence	Proposed product is supported by single line of evidence (e.g. single model)	Multiple lines of evidence (e.g. several experimental models) presented in support of proposed product	Data package includes validation studies, multiple lines of evidence and clinical samples/data

Parameter C: Intellectual property (IP)

Applicant must demonstrate existing IP and/or path to obtain IP. Specific IP strategy may depend on the project and product category. Research activities should have the potential to result in additional IP. Freedom-to-operate should preferably be demonstrated. Core IP must be assigned/licensed to applicant for commercial development.

1	2	3	4
Poor	Adequate	Strong	Exceptional
No defensible IP presented, and no clear strategy presented to develop IP; or, core IP not assigned/licensed to applicant	Proprietary methods, and/or provisional patent application(s) with specification. Funded R&D has the potential to generate IP	Proprietary methods that would be difficult to replicate, and/or patent applications with claims directly related to product. Funded R&D is likely to generate strong IP	Granted international patents with commercially defensible claims, and proprietary methods that would be difficult to replicate

Parameter D: Research & development team

Team must have the appropriate expertise, experience and time commitment required to execute the proposed R&D plan. Full-time employees must be in place. Consultants/contractors may be contributors. Project management approach should be described. If the project involves collaboration between multiple R&D sites, roles and coordination of efforts should be documented. Prior expertise in IBD research is not required, except where such expertise is necessary for proposed R&D activities.

1	2	3	4
Poor	Adequate	Strong	Exceptional
Team is not qualified to execute R&D plan, or lacks adequate commitment, or collaborations not explained	Team has the minimum required experience; collaborations are described and supported	Team has strong relevant experience for the proposed R&D as demonstrated by track record	Team has unique, world-class expertise for the proposed R&D and for commercialization, based on recent track record

Parameter E: Resources & funding

Applicant must have ready access to appropriate facilities/resources required to execute the proposed R&D plan, including supplementary funds, if applicable. Funds for essential overhead must be available for at least 1 year. If work is performed by contractors or collaborators, capabilities should be described. Supplementation of Foundation funds (cost sharing w/ matching funds) preferred.

1	2	3	4
Poor	Adequate	Strong	Exceptional
Access to resources is not demonstrated, or adequate funds not available to sustain operations during project period	Minimal required resources accessible. Funding in place for essential activities/overhead secured	Ready access to appropriate resources; applicant will supplement Foundation funds to support project	Immediate access to unique, best-in-class resources; significant commitment of supplemental resources towards R&D objectives

Parameters F, G and H are intended to score distinct stages of product development. F is intended to score the specific research plan proposed for funding. G is intended to score the longer-term product development program. H is intended to evaluate the commercialization strategy that will be supported by the R&D activities.

Parameter F: Research plan

Research plan must be scientifically rigorous, feasible and milestone-driven. Funding should be used for critical path activities for product development. Important R&D parallel activities funded through other sources may be described and considered. Appropriate technology should be applied. Risks should be discussed with mitigation strategies including alternative approaches. Budget should be milestone-based and reasonable for the proposed activities. Indirect expenses (e.g. general & administrative costs) must not exceed 10% of total funding.

1	2	3	4
Poor	Adequate	Strong	Exceptional
Experimental approach is unclear, not related to milestones or lacks scientific rigor; or budget is not reasonable for proposed work	Experimental approach is scientifically sound, with a reasonable budget, but lacks validation activities & alternative approaches	Experimental approach is well-designed, milestone-driven and includes validation strategy, alternative approaches and milestone-driven budget	Experimental approach is well-designed and milestone-driven, includes validation strategy & alternative approaches, and employs best-in-class technology

Parameter G: Development plan & milestones

Tractable long-term product development plan must be described. Milestones for funded activities with explicit metrics for success and timeline. Milestones linked to decision points (go/no-go) for product development activities. Funded activities should have the potential to significantly de-risk and accelerate program from research and commercialization perspective. Must address regulatory approvals (e.g. IND) as applicable for the specific product.

1	2	3	4
Poor	Adequate	Strong	Exceptional
Development plan is unclear, or not linked to specific milestones and decision points	Plausible development plan described with milestones, but activities are not on critical path, or lack explicit metrics	Development plan with defined milestones & explicit metrics for critical path activities	Validated development plan with metrics, critical path decision points & potential to reach a major value inflection point

Parameter H: Commercialization potential

Commercial potential (differentiation) must be justified. Plausible path to commercialization (go-to-market strategy) must be described. Major commercial risks (e.g. reimbursement, competition) must be addressed. Potential for applicant to access resources/partnerships for commercial development preferred. Commercial strategy must be consistent with organization's mission and capabilities. Commercialization plan expected to be commensurate with the stage of development.

1	2	3	4
Poor	Adequate	Strong	Exceptional

Applicant does not have clear plan/resources for commercialization, and has not demonstrated ability to secure adequate resources	Minimal resources for commercialization; commercialization strategy described, but major risks not addressed	Appropriate commercialization strategy addressing major risks; dedicated resources (incl. personnel) in place	Clear, validated go-to-market strategy; commercialization resources in place; track record of advancing related products
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