
# Cancer Therapeutics Innovation Pipeline

# Request for Applications
## *Early Accelerator and Late Accelerator*

## Version 1.0

## June 2021

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# 1. INTRODUCTION

## 1.1. Purpose

This document is intended to aid Investigators wishing to apply for a Cancer Therapeutics Innovation Pipeline (CTIP) award to support the translation of Ontario discoveries into therapeutic assets with the potential for improving the lives of cancer patients.

## 1.2. OICR vision and mission

OICR was established in 2005 to mobilize and reinforce Ontario research excellence in the fight against cancer, realize the local economic value of cancer discoveries, and make Ontario a major global address for cancer research and innovation. As Ontario's facilitator of translational cancer research, OICR brings together researchers, clinicians, patients and caregivers, health system partners, industry, and funders to drive solutions to cancer needs and accelerate the advancement of discoveries to improve cancer prevention, detection, diagnosis, and treatment.

Vision

Cancer solved together

Mission

Partner with the oncology community to translate cancer research discoveries, transforming cancer care to benefit patients, and strengthening the Ontario economy.

Values

Excellence | Innovation | Collaboration | Impact | Responsibility | Community

OICR invests resources in three areas:

1. Strengthening Ontario's capacity to undertake world-class cancer research;
2. Driving collaborative, translational cancer research; and
3. Working with partners to facilitate the advancement, commercialization, and adoption of cancer innovations into clinical practice.


***Figure 1:** OICR's Research Themes and Enablers*

OICR's research portfolio is grouped under three integrated Themes, as outlined in Figure 1:

- **Adaptive Oncology**: Developing knowledge and approaches to detect and monitor cancer over its life cycle in order to enable precise and proactive clinical management;

- **Clinical Translation**: Advancing Ontario cancer discoveries through early clinical validation, partnering with industry and the health system for downstream development and implementation; and
- **Therapeutic Innovation**: Validating novel cancer drug targets and advancing selective therapeutic candidates to clinical development.

To date, OICR's investments have cultivated a collaborative, world-class cancer research system that has yielded a rich pipeline of discoveries poised for translation and clinical impact. As part of its 2021-2026 Strategic Plan, OICR seeks to capitalize on Ontario strengths and successes to develop and implement transformative, next generation solutions to cancer with a focus on early cancer detection, intervention, and the development of precision medicine biomarkers for patient monitoring for improved clinical management.

### 1.3. Cancer Therapeutics Innovation Pipeline (CTIP)

In 2017, OICR established the CTIP Program to capitalize on Ontario's expertise in cancer biology and drug discovery. The goal of the CTIP Program is to create a pipeline of validated cancer targets and first-in-class (FiC) or best-in-class (BiC), novel, selective lead molecules (small molecules or biologics) that would attract partnerships and/or investment for further preclinical and clinical development. To generate a sustainable pipeline, CTIP will support projects that aim to provide increasing evidence of target validation and disease association using functional assays and drug screening in relevant *in vitro* and *in vivo* models of the cancer type of interest.

CTIP funds projects in three stages of preclinical drug discovery as shown in Figure 2:

- **Early Accelerator (EA)**: An EA project must deliver a validated primary assay to enable initial screening of molecules against a defined target. Entry into the EA stage requires evidence of target validation and association to the cancer of interest, and minimal expectations for portfolio entry are outlined in section 1.4.1;
- **Late Accelerator (LA)**: An LA project focuses on screening, using validated primary, secondary and orthogonal assays and must deliver confirmed Hit[1] molecules against a defined target supported by evidence of disease association. A confirmed Hit molecule should possess features that support its potential to become a Lead[2] molecule. When appropriate, additional target validation will be required using newly generated tool compounds using cell lines, 3D cellular systems or *in vivo* models; and
- **Lead Generation (LG)**: An LG project must deliver high-quality Lead molecules (small or large), with demonstrated *in vivo* efficacy, ideally accompanied by a pharmacodynamic biomarker that correlates with target modulation. Lead molecule profiles should be sufficiently mature to attract partnership/investment for further development and ultimately commercialization. In addition, a clear path for development of defined biomarkers to guide patient selection is required together with evidence that a Target Product Profile (TPP[3]) is under development.

[1]A minimal definition of a Hit is a molecule series with an understood Structure-Activity Relationship (SAR) and selectivity profile in relevant *in vitro* models.
[2]A minimal definition of a Lead is a molecule series with an understood SAR and selectivity profile in pharmacologically relevant *in vivo* models.
[3]A TPP outlines the desired profile or characteristics of a drug that is aimed at a particular disease. In addition, a TPP states the intended use, target populations and other desired attributes of a drug, including safety and efficacy-related characteristics.

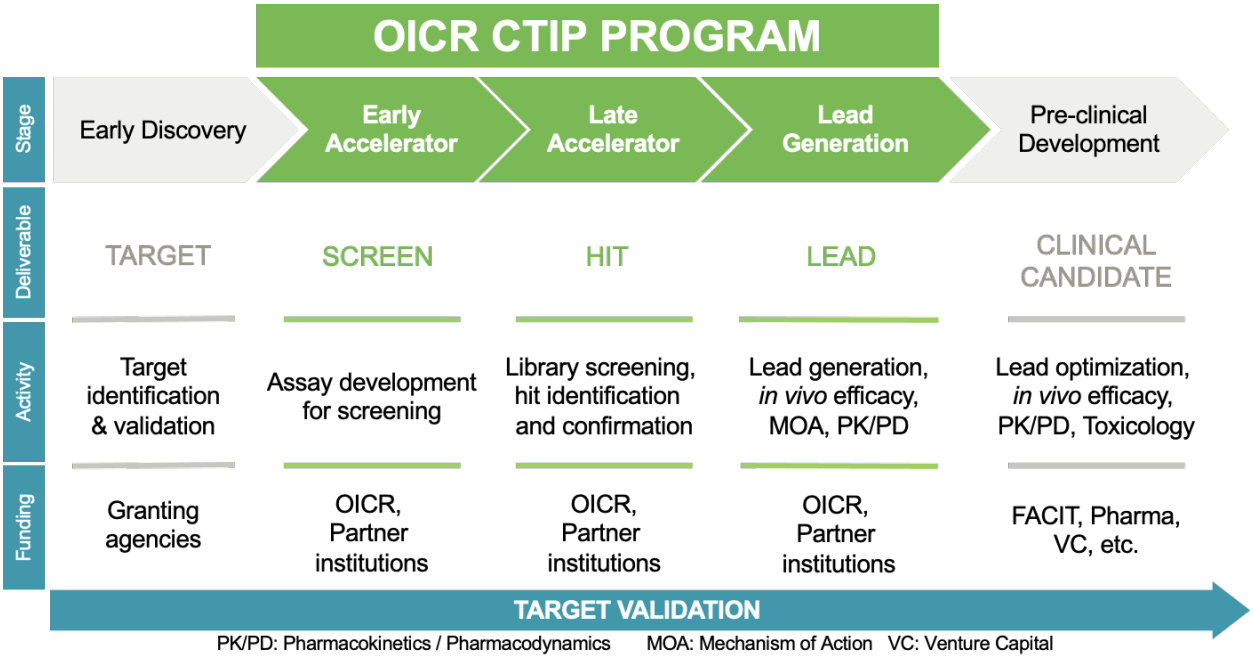


***Figure 2**: The Cancer Therapeutics Innovation Pipeline: Stages, deliverables, major activities and funding sources.*

A project can enter at any stage and can advance across stages as deliverables are met based on a go/no go decision aligned with industry standards. Expert and strict stage-gated strategic and scientific review is provided by the Therapeutics Pipeline Advisory Committee (TPAC), a group of highly qualified academic and industry experts with years of experience in drug discovery, systems biology and clinical trials.

### 1.4. CTIP projects

Understanding the role of a target in the pathophysiology of disease is repeatedly cited as the most critical factor in predicting the therapeutic value of modulating the activity of a putative target. During a drug discovery and development campaign, there is an absolute need to continually interrogate a target in the context of its biological function within a pathway(s) using functional assays, systems biology informatic tools and drug screening in increasingly complex *in vitro, ex vivo* and *in vivo* models that recapitulate the phenotype, genotype and systems of the cancer type of interest. The generation of robust evidence of target validation and disease association, and a reasonably clear ultimate target clinical indication(s), are essential requirements of projects that enter and continue in the CTIP portfolio. These parameters will be assessed together with feasibility, safety and strategic considerations in the evaluation of a proposal's suitability for CTIP funding (Appendix I).

With advances in science and technologies such as informatics, multi-omics (genome, epigenome, transcriptome, proteome, etc.), artificial intelligence, disease modelling and nanotechnologies, CTIP projects are expected to couple traditional target validation/disease association and screening approaches with state-of-the-art strategies such as querying of genomic and functional knowledge bases, selective perturbation of targets using genomic tools, pharmacogenomic screening, patient-derived 3D or organoid modelling, biomarker identification, and machine learning-inspired drug hunting, to name a few. Recently, it has also

been realized that the experiences of patients and their families/friends bring much value to disease knowledge creation and to the conversation as to how their health should be managed. It therefore follows that the establishment of a drug discovery team should involve a collaboration of talent from different branches of science that includes, but is not limited to, biologists, chemists, protein scientists, bioinformaticians, systems biologists, pharmacologists, biomarker experts, functional genomics experts, artificial intelligence scientists, imaging scientists, clinicians who regularly treat patients with the cancer of interest and data scientists. Furthermore, teams should endeavour to capture the voice of the cancer patient and their support in the design of their drug discovery campaign.

Applicants are encouraged to reach out to the research community, preferably within the province of Ontario, as well as to the Collaborative Research Resources (CRR) offered by OICR. CRR helps to enable research in Ontario by providing expertise, advice and access to research services on a cost-recovery basis. Researchers can benefit from OICR's high-end technology infrastructure, world-leading research knowledge, high-quality services and support. In addition, OICR funds major research initiatives in Clinical Translation and Adaptive Oncology and teams are encouraged to seek collaborations with investigators in these areas as they may be able to assist in buttressing the therapeutic target hypothesis and potentially contribute complementary expertise towards the achievement of CTIP deliverables, such as robust target validation.

Although this **RFA is limited to EA and LA applications only**, since successful projects have the potential to advance through the CTIP pipeline, the three stages of EA, LA and LG are described herein.

### 1.4.1. EA projects: Primary screen development

The goal of an EA project is to deliver a validated primary assay to enable initial screening of molecules against a defined target.

Entry into the EA stage requires demonstrable evidence of disease association to the cancer of interest, which **at a minimum** should include supportive data from:

1. Queries of genomics and functional knowledge bases to ascertain the relevancy of the target in the cancer of interest as well as other cancer types;
2. Application of systems biology tools to:
   a) reveal redundancies and crosstalk within pathways;
   b) identify potential correlative biomarkers and anti-targets; and
   c) expose any known potential off-target effects on molecules of similar molecular structure; and
3. Perturbation of the target in relevant cell-based models or higher order systems using genomic (e.g., knockout/knockdown or upregulation/overexpression) and/or tool compounds to support target validation and disease association. Efforts must be made to demonstrate the effects in several cell lines which differentially express the target at the protein level and in a normal cell line control. In addition, the evidence must include results from control experiments using inactive or unrelated vectors. In knockdown or knockout experiments, rescue data supportive of target function is highly desirable. In addition, evidence from more complex 3D culture systems or existing animal models is encouraged.

EA projects will be funded up to $150,000 for a maximum of one year. Funding will be provided in two tranches:

1. Tranche 1 will be used towards funding of experiments to generate additional target validation/disease association evidence. It is emphasized that **this funding is intended to generate translational, target validation** data to support the subsequent step of developing a primary screen. TPAC and OICR will provide guidance to the successful applicant as to the set of experiments that are most appropriate given the context of what is already known about the target and pathway(s), available reagents/tools and the cancer type to prepare for primary assay development. The budget for tranche 1 will not exceed 50 per cent of the requested budget for the entire EA proposal;
2. Tranche 2 will be used towards development and validation of the primary assay for screening. Target validation/disease association evidence from work accomplished with tranche 1 funds, and from existing supportive data, will be assessed by TPAC and OICR prior to the release of tranche 2 funds. A validated primary screening assay is the ultimate deliverable of an EA project.

A no-cost extension can be granted to complete tranche 1 or tranche 2 activities at TPAC's discretion.

It is highly recommended that EA applicants identify a bioinformatics or systems biology collaborator or consultant to participate in the project. In addition, EA applicants are strongly encouraged to solicit the advice of a clinician in the relevant disease area to begin to define the target clinical indication(s) and the corresponding patient population.

### 1.4.2. LA projects: Hit generation

The goal of an LA project is to deliver confirmed Hit molecules against a defined target using validated primary and secondary assays for screening. To achieve this goal, the project must describe an integrated testing cascade of experiments focused on achieving target validation and target engagement in cell-based models coupled with medium-to-high-throughput screening for Hits. Applications into the LA stage must fulfill the prerequisites for EA projects as described above and must have a validated primary screening assay to a defined target established. LA projects should consider, when appropriate, the incorporation of more complex biological systems than cell lines (e.g., 3D cultures, organoids) to further validate target-drug effectiveness and identify any off-target effects as well as potential toxicities.

LA projects will be funded up to $250,000 per year for a maximum of two years.

LA applicants should identify a bioinformatics or systems biology collaborator or consultant to participate in the project. In addition, LA applicants should engage a clinician in the relevant disease area to define the target clinical indication(s) and the corresponding patient population.

#### Eligible EA and LA project activities:

Both an EA and an LA project can include the following activities so long as they represent components of an integrated testing cascade that leads to a validated primary assay to enable screening against a defined target (for an EA project) or confirmed Hit molecules against a defined target (for an LA project):

- Functional genomic screens (e.g., knockdown experiments using RNA interference or CRISPR);
- Medium-to-high-throughput screens for large and/or small molecules;
- Development and validation of biochemical and cell-based target modulation assays for screening and orthogonal target validation. Cell-based assays should clearly demonstrate

whether perturbation of the target by leading molecules induces the death of cancer cells or only arrests cell proliferation;
- Structure-activity relationship (SAR) assessments to define minimum pharmacophores that demonstrate potential for further optimization;
- X-ray structure generation;
- Cross-target and cross-species selectivity assessments;
- Characterization of *in vitro* pharmacokinetic properties (absorption, distribution, metabolism, excretion, ADME) and toxicology;
- Computational approaches (e.g., virtual screening);
- *In vivo* pharmacokinetics for representative molecules; and
- Assessment of the viability of candidate Hit molecules to support an LG effort.

### 1.4.3. LG projects: Lead molecules with demonstrated *in vivo* efficacy

***At this time, OICR is not inviting applications for LG projects.***

The goal of an LG project is to deliver high-quality Lead molecules (small and/or large), with demonstrated *in vivo* efficacy, ideally accompanied by a pharmacodynamic biomarker that correlates with target modulation. Lead molecule profiles should be sufficiently mature to attract partnership/investment for further development and ultimately commercialization. To achieve this goal, the project must describe an integrated testing cascade of experiments which advances confirmed Hits into quality Lead series, coupling efficacy with target modulation. There must be an emphasis on establishing a connection between *in vitro, ex vivo* and *in vivo* assays, and biomarker modulation (or other surrogate measure of efficacy). Applications for the LG stage must fulfill the prerequisites for EA and LA projects as described above and must have confirmed Hit molecules to a defined target. In addition, LG proposals will require a preliminary biomarker plan and possible biomarkers for patient selection for drug therapy.

LG projects will be funded up to $1,000,000 per year for a maximum of two years. It is recognized that LG projects may require funding in excess of what OICR can provide to achieve the Lead molecule series deliverable. In such situations, applicants will need to identify leveraged funding or describe a plan to secure additional support from OICR or an external partner(s) during the funding period. Co-funding may be particularly important during the latter stages of an LG project when costs exceed OICR support, prompting the need to secure funds from other academic centres (e.g., host institution) or commercial partners, including FACIT Inc., OICR's commercialization partner, based on commercial interest in the Lead molecule.

It is critical that the proposed LG project possesses a well-articulated hypothesis for modulation of the target as a treatment for the cancer type in the intended patient population. An LG application must contain a TPP which summarizes the desired characteristics of the therapeutic asset, clinical development goals regarding safety and efficacy, and strategic elements that would confer a competitive advantage on the asset. MaRS has developed some excellent resources to help develop a TPP scheme, which can be accessed at https://learn.marsdd.com/article/defining-your-target-product-profile-therapeutics/.

LG proposals must identify a bioinformatics or systems biology collaborator or consultant to participate in the project. In addition, LG applicants must engage a clinician in the relevant disease area to define the target clinical indication(s) and the corresponding patient population.

### Eligible LG project activities:

Projects entering the LG stage will possess Hit molecules characterized by a range of supporting evidence as described in the EA and LA stages. LG projects can include the following activities:

- SAR studies exhibiting a sufficiently broad dynamic range that would allow for optimization in potency, selectivity and safety, within chemical space where there is legal freedom to operate and the opportunity to generate intellectual property (IP);
- Experiments demonstrating differentiation in the context of the expected therapy in the target patient population (e.g., mechanism of action studies);
- Protein engineering studies (for large molecule therapeutics);
- Cell line generation and biophysical characterization for large molecule therapeutics;
- Bioavailability studies using the intended route(s) of administration;
- Pharmacodynamic (PD) or efficacy animal model development;
- Dose ranging PD, PK and efficacy;
- *In vivo* proof of concept or efficacy in a relevant biological system (model species) that will be used for margin of safety calculations; and
- Assessment of the viability of candidate Lead molecules to support a lead optimization effort.

## 2. REQUEST FOR APPLICATIONS

This Request for Applications (RFA) is specific for investigators wishing to apply for funding support for an EA or LA project. Submissions for LG projects will not be considered under this RFA.

### 2.1. Eligibility

OICR invites applications from investigators at Ontario academic centres, hospital research institutes or other government research institutions. **CTIP funding is only tenable in Ontario and can only be disbursed to not-for-profit entities.**

Investigators are eligible to participate on and submit multiple CTIP submissions via this RFA.

OICR is focused on developing and supporting the next generation of cancer researchers, and strongly encourages applicants to include early career investigators/clinicians as part of the study team.

### 2.2. Term

The funding term start date for a funded CTIP application is December 1, 2021.

- The award term for **EA projects** is up to one (1) year (December 1, 2021 - November 30, 2022); and
- The term for **LA projects** is up to two (2) years (December 1, 2021 - November 30, 2023).

## 2.3. Funding available

**EA projects** will be funded to a maximum of $150,000, inclusive of overhead, for a maximum of one year. Funding will be provided in two tranches:

1. Tranche 1 will be used towards funding of experiments to *generate additional target validation/disease association evidence*. The budget for tranche 1 will not exceed 50 per cent of the requested budget for the entire EA proposal (see section 1.4.1 above for additional information); and
2. Tranche 2 will be used towards *development and validation of the primary assay for screening*. The budget available for tranche 2 is up to $150,000 **inclusive** of any funding provided for tranche 1. For clarity, the maximum budget that can be requested for tranche 1 and 2 activities is $150,000.

**LA projects** will be funded to a maximum of $250,000 per year, inclusive of overhead, for a maximum of two years.

## 2.4. Eligible expenses

Appendix II outlines OICR's guidelines for eligible expenses. CTIP funding is intended to provide support to cover salaries and benefits of research personnel over the funded term. Other expenses, including consumables, external research services, etc. are also eligible. Budgets should include thirty per cent overhead on eligible direct research expenses to cover institutional overhead (Appendix II). Overhead must be accounted for in the budget requested which cannot exceed the maximum amounts stated in section 2.3.

**Annual funding is contingent upon available funding from the Government of Ontario via the Ministry of Colleges and Universities.**

## 2.5. Deadlines

CTIP applications are a three-step process, including an NOI, LOI and full application.

| | |
|---|---|
| Information session: | June 15, 2021, 1-2 p.m. ET* |
| Notice of Intent (NOI) submission**: | No later than July 7, 2021 at 5 p.m. ET |
| Letter of Intent (LOI) deadline: | July 7, 2021 at 5 p.m. ET |
| LOI results communicated: | No later than August 17, 2021 |
| Pre-full application stage meeting with TPAC***: | August 23, 2021 |
| Full application deadline: | September 15, 2021 by 5 p.m. ET |
| Notification of results: | By December 2021 |
| Funding start date: | December 1, 2021 |

**Register here. This session will be recorded and posted on OICR's funding opportunities website.*
***The NOI form must be submitted prior to receiving access to the LOI and will be used for competition planning purposes. Information collected at the NOI stage **is editable** at the LOI stage.*
****LOIs selected to move forward to the full application stage will be invited to participate in an optional, virtual discussion session with OICR and the TPAC (Therapeutics Pipeline Advisory Committee) to discuss the development of their full application. Times will be confirmed with teams following notification of LOI results.*

**Late submissions will not be accepted.** Figure 3 displays the RFA process indicating the points of interaction with TPAC and OICR.

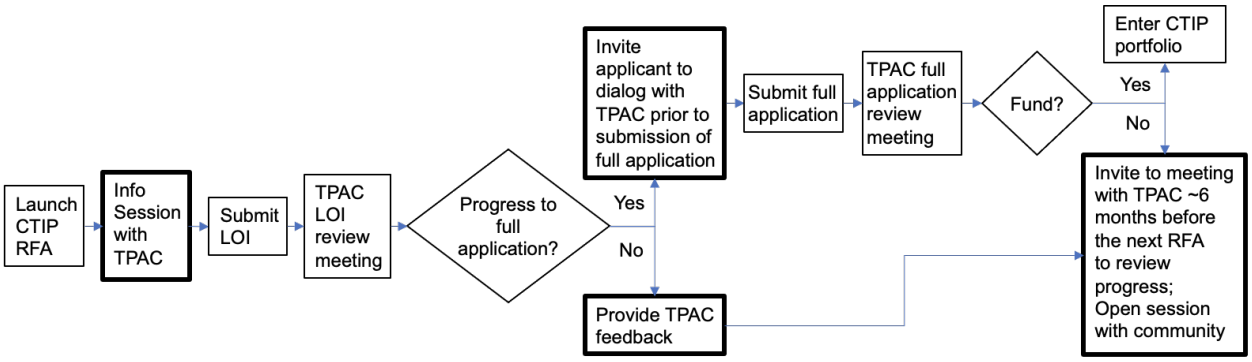


***Figure 3:*** *CTIP RFA process with multiple points of interaction with TPAC (bolded boxes): pre-LOI, pre-full application and before the next RFA.*

For any questions, please refer to the FAQ page before contacting the OICR Scientific Secretariat office (ScientificSecretariat@oicr.on.ca).

## 2.6. Application requirements

**IP, commercialization plan and recipient obligations**

If invited to submit a full application, the research plan must include a brief, non-confidential description of any project-related IP, and any restrictions or third-party rights impacting the IP development in Ontario. No commercialization plan is required for an EA or LA application beyond a description of the use of proceeds for the proposed Accelerator project. It is strongly suggested that this IP and commercialization section of the RFA be reviewed together with institutional Technology Transfer Officers.

Since the ultimate goal of this program is to support translation of new cancer therapies to the clinical setting, the creation and protection of IP that will make drug candidates attractive to potential licensing and commercialization partners is a significant consideration in prioritizing projects for funding. CTIP is structured so that the awardee Host Institution(s) retains background IP rights. In line with OICR's "Ontario First Policy" (see Appendix III), which requires that reasonable efforts are undertaken to commercialize and manufacture a project's arising IP in Ontario, applicants will contractually agree to oversight by FACIT Inc., OICR's commercialization partner, to finalize the commercialization planning, rights and obligations, with an emphasis on Ontario-based development.

Award agreements will include an Option for FACIT to act as the commercial agent for any arising IP. In order to balance academic commercialization freedom and to be in line with other similar programs, the Option will be restricted to the period during the EA or LA project and a three-month period following the completion of the project. Further, should an LA project evolve into a LG project, OICR funding of EA and LA research activities will be added to any investments made by OICR during the LG stage in the determination of OICR's total contributions to the project.

**Patient partners**
Patient perspectives and insight can be transformative to research planning and execution. Applicants should address how patient partners and communities are being, or could be, engaged throughout the life cycle of the proposal. Throughout the funding period, and as early as possible, applicants are encouraged to contact Justin Noble (Justin.Noble@oicr.on.ca), OICR's Patient Partnerships and New Initiatives Lead, to explore how to better involve patient partners and communities into the research process. OICR's Patient and Family Advisory Council (PFAC) may participate in the FR and progress reviews to provide ongoing guidance over the funding term.

**Equity, Diversity and Inclusion**
The Proposal is expected to embrace the principles of Equity, Diversity and Inclusion (EDI) in order to:

- Ensure research serves cancer patients from all communities, in particular those that are historically underrepresented;
- Foster a more diverse and inclusive research community; and
- Create an environment where all can thrive and feel included.

## 2.7. Overview of application requirements using the online submission system

NOIs, LOIs, and full applications are to be submitted using OICR's online submission system, ReportNet.

Applicants who have not used ReportNet (OICR's online system for managing grants and awards) before must register by visiting https://oicr.factorial.ca/s_Login.jsp and selecting 'Register' under 'New User?'. Once an account has been created, applicants can login to their account to view OICR funding opportunities and the associated RFAs (at the bottom of the screen under 'Funding Opportunities').

Applicants who have used ReportNet before (for OICR's Key Performance Indicator reporting process), have had their profiles automatically updated to provide access to the Applicant dashboard. Login to your account at https://oicr.factorial.ca/s_Login.jsp and toggle to the Applicant dashboard by clicking 'Researcher' on the menu at the top right hand side of your screen, and selecting 'Applicant' from the dropdown menu (refer to Figure 4). If you do not see this option, please contact the OICR Scientific Secretariat office at ScientificSecretariat@oicr.on.ca.

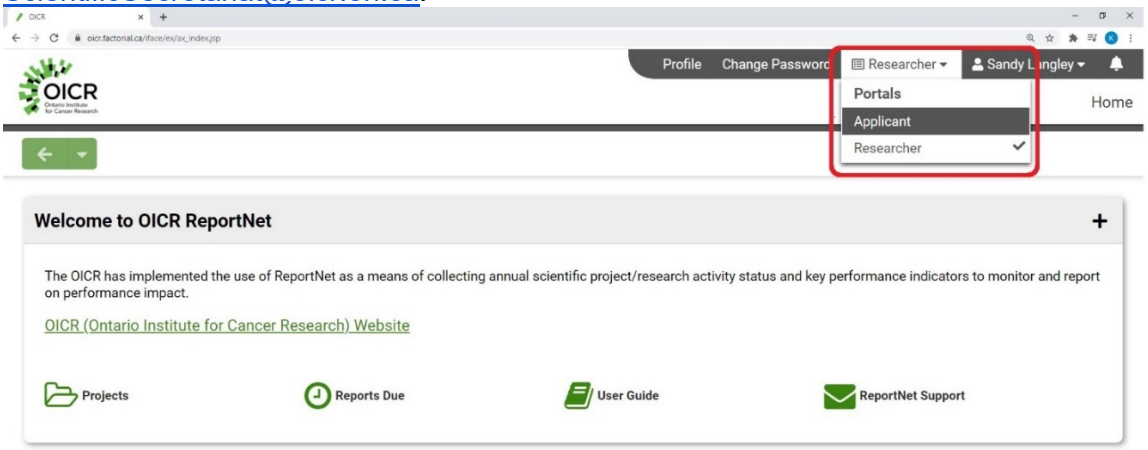


***Figure 4:*** *How to toggle between the Researcher dashboard (for KPI Reporting) to the Applicant dashboard (to apply for funding opportunities)*

Applicants and all team members are invited to complete their profiles, including the section on Demographics, within ReportNet to assist the Institute with metric reporting. The OICR Scientific Secretariat is available to help with any questions regarding the online process. The information below provides an overview of the various sections that make up a CTIP application.

Note that the textboxes in ReportNet will accept basic formatting only (no bolded or italicized text, etc.).

### 2.7.1. Completing a Notice of Intent

The NOI collects basic application information and will be used by OICR for planning purposes. **An NOI must be submitted prior to gaining access to the LOI form**. The information provided in the NOI can be updated prior to submitting the LOI. The deadline for submission of the NOI is the same as the deadline for LOI submission, however, applicants are encouraged to submit their NOI as early as possible to assist with planning.

#### Application information

The system will pre-populate the PI's information from their ReportNet profile. Additional information, outlined below, is to be provided by the applicant(s). Required fields are marked with a red asterisk in ReportNet. Word counts, where applicable, are noted.

- **What project category are you applying for?** Only EA or LA projects are eligible under this RFA; select the appropriate category for your proposal;
- **Title:** Once a title for your application has been provided, use the 'Save Draft' button at the bottom of the screen to activate the 'Invite Contacts' function (see below);
- **Invite Contacts**
  - Co-PIs, Co-Investigators, Collaborators, and/or PI Delegates are to be added using the '**Invite Contacts**' button:

    *Principal Investigator* (PI): Has responsibility for the intellectual direction of the project, as well as the technical and scientific content, the budget, deliverables and milestones, and supervision of members of the research team carrying out the activities of the project. If there is more than one PI, the PI is the individual who initiates the application and *Co-PIs* can be added subsequently. The PI can submit the application once complete.

    *Co-Investigator:* Carries out research activities related to the project. Co-Investigators are not able to submit the application on behalf of the PI(s).

    *Collaborator*: An individual whose role in the proposed activities is to provide specific expertise or access to resources (e.g., access to equipment, reagents, specialized knowledge (including techniques and statistical analysis), access to patient populations, patient partners/advocates etc.). Collaborators are not able to submit the application on behalf of the PI(s).

    *PI Delegate*: Provides an administrative role that can assume the duties of the PI, including editing and submitting the application on behalf of the PI(s).

  - Note: You must **first** provide a **project title** and hit '**Save Draft**' for the 'Invite Contacts' button to appear;

    - All PIs/Co-PIs, Co-Investigators, and/or Collaborators involved in the application **must** be invited;
    - **Note**: Before inviting contacts to your application, contact them to confirm if they have a ReportNet account, and if so, which email address they are registered with. Please use their registered email address when inviting them to your application. Invited contacts will receive an email to join the application. Please advise them to check their junk/spam folders if they do not receive the invitation within 30 minutes. While not *mandatory*, we encourage all investigators to accept the invitation and create their profile in the system.
- **Start date:** Enter a funding start date for the application, no earlier than December 1, 2021;
- **End date:** Enter a funding end date for the application. EA projects can be a maximum of one (1) year; LA projects can be a maximum of two (2) years;
- **Application type:** Indicate whether this is an initial application for this proposal or a re-application.
    - **Note:** If '*Re-application*' is selected, additional information will be requested at the full application stage, including a requirement to upload the Scientific Officer (SO) and reviewer reports from the initial application;
- **Cancer type:** If the cancer type(s) is non-specific, select 'All' at the top of the list. If there is more than one cancer type, select, 'Multiple' at the bottom of the list. If the cancer type(s) is not listed, select 'Other' at the bottom of the list;
- **Lay summary:** Provide a lay summary, using simple, easy to understand, non-technical language. This summary may be shared with external parties for communications and reporting purposes, and with reviewers to identify expertise and potential conflicts of interest. Maximum 250 words; and
- **Other:** Additional materials are not requested at the NOI stage; do not upload any additional files in this field.

Once you have completed all required fields, select the green '*Submit and Continue to LOI*' button at the bottom of the screen. You will immediately be provided with access to the LOI form.

### 2.7.2. Completing a Letter of Intent

Information provided in the NOI will be carried over to the LOI form and is editable. The *'Contacts'* will also be editable at this stage.

- **Has this work been published/patented?** If *'Yes'* is selected, you will need to describe how the proposal builds upon the published/patented work. Maximum 200 words;
- **Target and/or pathway**: Indicate the target or pathway that will be explored in this proposal. Maximum 25 words;
- **Molecule type**: Select from the options provided;
- **Target class**: Indicate the target class that will be investigated in this proposal. Maximum 25 words;
- **Scientific summary:** Provide an executive summary of the proposal. Maximum 500 words;
- **Proposed budget**: Describe the high-level budgetary requirements and any current funding allocated to the project. For EA projects, as appropriate, outline funding requested for tranche 1, which must not exceed 50 per cent of the requested budget for the entire EA proposal, and for tranche 2. Maximum 250 words;
- **Research plan - LOI**: Using the following headings, address the items below. Maximum 2500 words, excluding figures and tables, testing cascade, and references, which will be uploaded separately.
    - **Target validation and disease association**

- Define the project hypothesis, specifying the desired mechanism of modulation (e.g., inhibitor, agonist, etc.) and the intended modality (e.g., small molecule, biologic, etc.);
- Provide bioinformatics and systems biology queries of relevant knowledge bases (e.g., DepMap, TCGA, cBioPortal, MalaCards, etc.) showing clear disease indication association and/or target dependency of the disease area;
- Describe the target's function and interactions with other players in the pathway(s);
- Provide the scientific and clinical evidence supporting prosecution of the target for the treatment of the cancer type in the intended patient population. This must contain the minimal requirements for portfolio entry as an EA project described above; and
- Describe gaps or uncertainties related to target validation and disease association, and research plans to address these.

- **Safety**
  - Describe any known or potential toxicology considerations and plans to monitor these liabilities;
  - Provide data on published knockout models indicating safety and little or no off-target effects; and
  - Describe any known or suspected toxicity with other previously developed drugs hitting the same pathway of the proposed target.
- **Feasibility**
  - Describe the primary screening assay(s) that the team plans to validate (for EA proposal) or has validated (for LA proposal) and the status and performance of the assay(s);
  - Provide information on the resources available to the applicant to support target enablement and primary screen development (e.g., recombinant target protein, cell lines, controls, etc.);
  - Describe all secondary and orthogonal assays (e.g., target engagement, selectivity, cell-based, etc.) to be used for confirming Hit molecules (LA stage deliverable) and the status and performance of the assays;
  - Provide information on the resources available to the applicant to support development of all secondary and orthogonal assays;
  - Describe the chemical collections to be used for primary screening;
  - Describe the Hit generation strategy and the tools needed to execute on that strategy (e.g., crystal structure or homology models);
  - Specify the biomarkers to be measured and if they have been validated or a plan to address validation;
  - Describe the team composition and collaborations, planned or in place, and the expertise that will be contributed to the project by each PI and collaborator; and
  - Separately upload a testing cascade. The testing cascade must not exceed one page. Refer to Appendix IV for an example.
- **Strategic considerations**
  - Describe the unmet clinical need, identifying the current standard of care for the disease indication, and its limitations;
  - Describe the competitive landscape and the differentiation features of the proposed therapeutic approach;
  - Describe issues with contemporary efforts with the same or related target including reasons for successes or failures based on biologic, pharmacologic or toxicity concerns; and
  - Indicate if molecules identified from this effort have the potential to be FiC or BiC potential.

- **LOI uploads**: The following items should be attached to the LOI

- Figures, tables, and references in PDF format as a single document; and
- Testing cascade (must not exceed one page; refer to Appendix IV).

- **Other:** Additional materials are not requested at the LOI stage; do not upload any additional files in this field.

Once you have completed all required fields, select the green '*Submit LOI*' button at the bottom of the screen.

### 2.7.3. Completing a full application

Information provided at the NOI and LOI stage will be carried over to the full application form and, with the exception of '*Research plan - LOI*', will be editable. Only LOI applicants invited to submit a full application following the LOI review will be provided with access to the full application form.

#### Application information

PI attestation: The PI submitting the application must agree to the statement on research integrity prior to submission of a full application.

#### Administrative authority contact information

Information will be collected for the PI and any Co-PIs. The administrative authority is an individual who can legally bind the institution. Typically, a Vice President of Research, or similar.

#### Project details

- Re-application: Response to reviewer feedback
  - If you are submitting your proposal as a re-application, complete this section and indicate what modifications have been made as a result of the critiques. If you choose not to address reviewer feedback, the application will be reviewed as an initial application.
- SO and reviewer reports from the initial application
  - If you are submitting your proposal as a re-application, upload the SO and reviewer reports from the initial application.

#### EDI considerations

Applicants should outline how the research team and proposal will align with the principles of EDI. EDI considerations will be discussed during the review process. Feedback regarding the appropriateness of the approach(es) being undertaken, including areas where the team is doing well, and opportunities for improvement, may be provided to applicants.

Several excellent EDI resources have been developed that are available, free of charge, for training and information purposes. OICR requires that teams complete, at a minimum, the CIHR Sex and Gender Training Modules (https://www.cihr-irsc-igh-isfh.ca/) in advance of submitting their application. **The Lead PI will have to attest to the completion of these training modules prior to submission.**

Among others, OICR supports EDI resources that have been made available by CIHR (https://cihr-irsc.gc.ca/e/51709.html). These resources address many topics, including:

- EDI in research design and practices;
- EDI in the research environment; and
- EDI and research excellence.

Additional resources on including sex and gender in research can be found at: (https://cihr-irsc.gc.ca/e/50836.html)

### Regulatory requirements

When applicable, certification requirements may be used in the process of developing funding agreements, should the application be approved for funding. Certificate numbers are not required but are encouraged for projects being conducted at OICR.

### Common Scientific Outline

The applicant must select a primary classification for the research. Secondary and tertiary classifications may also be selected if applicable but **are not required**. CSO codes should reflect the main aim of the project that is achievable within the lifetime of the award. Coding should NOT include potential or future applications of the research findings. Information on selecting an appropriate code can be found in the International Cancer Research Partnership (ICRP) Coding Guidelines.

### Research proposal

**Research plan:** Using the headings indicated, provide details on the proposed research. The research plan must expand upon the content provided at the LOI stage (black bullets below) as well as address the additional full application requirements (blue bullets below). Maximum 5,000 words.

- **Target validation and disease association**
  - Define the project hypothesis specifying the desired mechanism of modulation (e.g., inhibitor, agonist, etc.) and the intended modality (e.g., small molecule, biologic, etc.);
  - Provide bioinformatics and systems biology queries of relevant knowledge bases (e.g., DepMap, TCGA, cBioPortal, MalaCards, etc.) showing clear disease indication association and/or target dependency of the disease area;
  - Describe the target's function and interactions with other players in the pathway(s);
  - Provide the scientific and clinical evidence supporting prosecution of the target for the treatment of the cancer type in the intended patient population. This must contain the minimal requirements for portfolio entry as an EA project described above;
  - Describe gaps or uncertainties related to target validation and disease association, and research plans to address these;
  - Describe the intended route of administration; and
  - Describe the mechanism of action and related pathway pharmacology.
- **Safety**
  - Describe any known or potential toxicology considerations and plans to monitor these liabilities;
  - Provide data on published knockout models indicating safety and little or no off-target effects; and
  - Describe any known or suspected toxicity with other previously developed drugs hitting the same pathway of the proposed target.
- **Feasibility**
  - Describe the primary screening assay(s) that the team plans to validate (for EA proposal) or has validated (for LA proposal) and the status and performance of the assay(s);
  - Provide information on the resources available to the applicant to support target enablement and primary screen development (e.g., recombinant target protein, cell lines, controls, etc.);

- Describe all secondary and orthogonal assays (e.g., target engagement, selectivity, cell-based, etc.) to be used for confirming Hit molecules (LA stage deliverable) and the status and performance of the assays;
- Provide information on the resources available to the applicant to support development of all secondary and orthogonal assays;
- Describe the chemical collections to be used for primary screening;
- Describe the Hit generation strategy and the tools needed to execute on that strategy (e.g., crystal structure or homology models);
- Specify the biomarkers to be measured and if they have been validated or a plan to address validation;
- Describe the team composition and collaborations, planned or in place, and the expertise that will be contributed to the project by each PI and collaborator; and
- Separately upload a testing cascade. The testing cascade must not exceed one page. Refer to Appendix IV for an example;
- Describe plans to address issues associated with primary, secondary and orthogonal assay development including the acquisition of key assay components and reagents;
- Specify any interactions with OICR's Collaborative Research Resources or other research areas under OICR's Clinical Translation and Adaptive Oncology themes;
- Describe the desired selectivity profile, including any intentional polypharmacology; and
- Summarize host/partner institution facilities and resources available to support research execution.

- **Strategic considerations**
  - Describe the unmet clinical need, identifying the current standard of care for the disease indication, and its limitations;
  - Describe the competitive landscape and the differentiation features of the proposed therapeutic approach;
  - Describe issues with contemporary efforts with the same or related target including reasons for successes or failures based on biologic, pharmacologic or toxicity concerns;
  - Indicate if molecules identified from this effort have the potential to be FiC or BiC potential;
  - The research plan must include a brief non-confidential description of any project-related IP, and any restrictions or third-party rights impacting the IP development in Ontario (see section 2.6);
  - Describe patient selection opportunities;
  - Provide an estimate of the size of the target patient population; and
  - Describe any known or anticipated hurdles associated with regulatory approval, adoption of the therapeutic by patients or clinicians, and reimbursement of the medicine.

### Additional information

**Differentiation:** Provide a description on what makes this research unique, better and/or disruptive compared to what other researchers are working on in your field (i.e., what is distinguishing about this research that makes it more attractive than other existing work). This information may be shared with FACIT Inc., OICR's commercialization partner, should the proposal be funded. Maximum 250 words.

**Data management plan:** Applicants must provide a data sharing and access plan, as well as a data storage requirements and retention plan, specifying how much data will be generated or transferred into OICR (if applicable) during the course of the project, and the plan for retaining/archiving with the ability to restore the data for the five-year period following its conclusion. See Appendix V for additional information. Maximum 500 words.

## Attachments

The following items should be attached to the application:

- Figures, tables and references as a single PDF document;
- Testing cascade (must not exceed one page; refer to Appendix IV).
- Host institution commitment letter: Must outline the institutional commitment to facilitate and support the research, assign space and resources, and provide other administrative support for the duration of the proposed research. The letter should describe how the institution maintains accountability for promoting scientific excellence and fiscal responsibility with awarded funds. Importantly, the letters must declare that the signatories have read and acknowledged OICR's "Ontario First Policy" and agree to abide by the policy through a funding agreement in the event of a successful application. Letters should also be included from the Host Institution of any Co-PIs;
- Deliverables and milestones, using the Excel template provided
    - Deliverables are pre-defined outputs or outcomes that describe what success looks like for the project. When achieved, deliverables must provide meaningful impact towards achieving the goal of the proposal. Milestones are points in the research plan that facilitate measurement of progress towards the achievement of the deliverable. These deliverables and milestones will be used to measure research progress during progress updates;
    - Specify high-level deliverables that are projected to be achieved during the funding term;
    - For each deliverable, specify at least two associated milestones. Milestones will be monitored to assess progress towards achievement of the deliverable. **Include milestones that specify go/no go decision points** whenever applicable; and
    - Both deliverables and milestones must be measurable and possess a target date for completion (provide the quarter and fiscal year of projected achievement).
- Budget, using the Excel template provided
    - **PLEASE BE AWARE:** If you need to update your budget after it has been uploaded to the system, please contact the OICR Scientific Secretariat for assistance;
    - Download the budget template provided in the application, complete budget request details (see Appendix II for eligible expenses) and upload the completed budget in Excel format;
    - Line item justifications must be **unique***. They should be brief and provide a high-level explanation of why the expenses are necessary and how they are calculated; and
    - The template will automatically calculate overhead at 30 per cent for non-MaRS based institutions. The overhead rate can be adjusted on the 'info and instructions' tab. Please contact the Scientific Secretariat with any questions regarding overhead. **Overhead must be accounted for in the budget requested which cannot exceed the maximum amounts stated in section 2.3.**
      ** Line item justifications must be unique from one another for recognition by the system. If justifications must be the same, please use a unique character at the end (*,^, etc.)*
- Biographical sketches
    - Compile CVs (**abbreviated CVs are encouraged**) for the following individuals and submit as a single, bookmarked PDF package:
        - PIs and Co-PIs; and
        - Co-Investigators.
    - CVs can be in any format so long as it addresses:
        - Education/training;
        - Employment;
        - Honours and awards;
        - Professional affiliations;

    - Research funding in the past five years; and
    - Research outputs (e.g., publications, IP, presentations, etc.)
- Other
    - Include a list of all current and pending funding applications, highlighting any overlap with the present application, as a PDF;
    - Co-funding letters (if applicable), submitted as a single, bookmarked PDF: Provide evidence of co-funding through a letter of support from the funder. Include whether funds are cash vs. in-kind, and whether they are secured vs. expected. Co-funding should also be captured in the Excel budget template.

Once you have completed all required fields, select the green '*Submit*' button at the bottom of the screen.

## 3. REVIEW PROCESS

### 3.1. LOI review

LOIs will be reviewed by TPAC, and *ad hoc* experts, if required, along the four themes of target validation/disease association, safety, feasibility, and strategic considerations (Appendix I). Projects will be reviewed by a primary and secondary reviewer who will provide feedback and an overall recommendation ('Yes to full application', 'No to full application', or 'Requires discussion'). Reports will be submitted online using OICR's ReportNet system. Anonymized reports will be circulated to the review panel in preparation for the review meeting, where the panel will meet to discuss LOIs prior to making a final recommendation.

LOIs that receive a 'No' recommendation from both reviewers will be triaged prior to the panel discussion. LOIs that receive a 'Yes/No' recommendation or a 'Discuss' recommendation will be discussed at the panel meeting. Only applications that are ranked 'Yes' by both primary and secondary reviewers, after the panel discussion, will be invited to submit a full application.
If the number and quality of LOIs received far surpasses the number of applications that can reasonably be reviewed at the full application stage, TPAC will be asked to score proposals in order to establish a cut-off that will be used to triage applications.

### 3.2. Full application review

#### Administrative review

An administrative review will be completed by the Scientific Secretariat in order to assess the submission for conformity with the guidelines. Relevant points from the administrative review will be shared with applicants.

#### External peer review

**Review panel**

Full applications will be reviewed by a panel consisting of TPAC and *ad hoc* experts, if required. The panel's mandate will be to evaluate the merits of the applications. Panel members will be assigned to applications as primary and secondary reviewers and will provide a brief preliminary report outlining their feedback on the proposal. Reports will be submitted online using OICR's ReportNet system. Anonymized reports will be circulated to the review panel in preparation for the review meeting.

**Patient and Family Advisory Council (PFAC)**
Applications may be shared with the OICR PFAC, or their delegates, who will review application materials and provide written feedback to the review panel in advance of the review meeting, which patient partner reviewers may attend. The SO report that will be provided to teams following the review meeting may include feedback from PFAC to aid teams in improving their plans.

**Reviewer reports**
Reviewers will receive the full applications approximately four weeks before the reviewer report deadline and will be tasked with providing scores and a brief report discussing the following criteria (see Appendix I for additional information):

- Target validation/disease association;
- Safety;
- Feasibility; and
- Strategic considerations.

Reviewers will be asked to indicate whether the proposal should be in contention for funding and evaluated further at the full application review meeting (Yes, No, or Undecided)

**Review meeting**
Depending on application pressure, and with the approval of the TPAC Chair, applications may be ranked by overall score prior to the review meeting so that only the top applications in contention for funding are discussed. The panel will have an opportunity to review the rankings in advance of the meeting, and, if appropriate, revise the order.

The meeting will be moderated by the TPAC Chair with support from OICR's Scientific Secretariat and will include representatives from OICR and PFAC (if appropriate). The Chair will invite primary and secondary reviewers to provide their feedback and will oversee a discussion of the application by the panel. The evaluation rubric and scoring guide can be found in Appendix I. Following open discussion, reviewers will be provided with an opportunity to revise their initial scores and comments and will be asked to provide a final overall score. The panel will then recommend a consensus overall score by which the application will be ranked. Highly ranked applications, which are deemed meritorious for funding, will be recommended for approval to OICR leadership.

## Notification of decision
A meeting report summarizing the review discussion and recommendation will be prepared by the SO and distributed to applicants, along with anonymized reviewer reports, as part of the Notification of Decision (NOD) from OICR.

OICR intends to provide NOD letters to all applicants by early December 2021. Successful applications will receive a Notice of Award outlining next steps in order to accept the award and establish a funding agreement.

## 4. ESTABLISHMENT OF AGREEMENTS

Following approval of the proposal, OICR will establish a funding agreement with the Host Institution of the Lead PI and Partner Institutions (if applicable). The agreement will cover the general principles regarding the conduct of research activities, eligible research expenses, terms and conditions regarding the disbursement of funds, agreements with third-party funders, financial and progress reporting, PI/Co-PI covenants, IP, commercialization, publications, and communication policies. In addition, OICR will establish a commercialization framework, which will require the recipient and OICR to set up an IP co-management plan, where applicable.

Note that delays in execution of research agreements may impact OICR's ability to disburse funds. **Funding is contingent upon available funding from the Government of Ontario via the Ministry of Colleges and Universities.**

## 5. REPORTING REQUIREMENTS

### Financial and operational status reporting

The following schedule (Table 1) will be used for financial and operational status reporting. Note that the deadlines indicated are moved to the next business day if they fall on a non-working day. A quarterly reporting template and instructions will be available on the OICR online financial reporting system, CaAwardNet.

Financial Officers of the Lead Institution will be required to provide quarterly updates on budget versus actual expenditures as per the table below. When reporting on the operational status of a project, an explanation of variances of greater than ±15 per cent and mitigation plans to address the budget gaps should be provided.

***Table 1**: Financial and operational status reporting*

| Period covered | Responsible party and action | |
|---|---|---|
| | **Financial Officer** | **PI at Lead Institution (or designate)** |
| Q1<br>April-June | Quarterly financial report<br>Due: July 31 | Review and submit quarterly financial and operational status report<br>Due: August 15 |
| Q2<br>July-September | Quarterly financial report<br>Due: October 31 | Review and submit quarterly financial and operational status report<br>Due: November 15 |
| Q3<br>October-December | Quarterly financial report<br>Due: January 31 | Review and submit quarterly financial operational status report<br>Due: February 15 |
| Q4<br>January-March | Quarterly financial report<br>Due: April 30 | Review and submit financial and operational status report<br>Due: May 15 |
| Q1-Q4<br>April-March | Annual fiscal year financial report: Due May 31 | N/A |

### Progress and Key Performance Indicator (KPI) Reporting

All projects will be included in OICR's annual reporting process, as required by the Ministry of Colleges and Universities according to the schedule below (Table 2). Note that the deadlines indicated are moved to the next business day if they fall on a non-working day.

***Table 2**: Reporting requirements*

| Report | Period covered | Due date | Person(s) responsible | Action |
|---|---|---|---|---|
| Progress update | Q1-Q2 | Q3 | PIs/Co-PIs | Provide status updates on Deliverables and Milestones (D/M), progress update to TPAC. |
| Progress update | Q3-Q4 | Q1 | PIs/Co-PIs | Provide status updates on D/Ms, progress update to TPAC. |
| KPI report | Fiscal year: April-March | April 30 of the subsequent fiscal year | PIs/Co-PIs | Provide quantitative KPIs using ReportNet (OICR's online submission system) |

## 6. COMMUNICATION WITH OICR

The obligations of the investigators to advise OICR of anticipated public dissemination, publications, and media announcements will be outlined in the research agreement.

## 7. ACKNOWLEDGEMENT AND RECOGNITION OF SUPPORT

All investigators and recipient institutions must acknowledge and credit the contribution/support, in whole or part, of OICR and the Government of Ontario in any promotional material, including, without limitation, scientific publications of whatever nature or kind, and in any communication materials or publications supported by OICR funding by referencing the projects/subprojects with the following statement: "This study was conducted with the support of the Ontario Institute for Cancer Research through funding provided by the Government of Ontario."

## 8. CONTACT INFORMATION

Questions related to these guidelines should be forwarded to the OICR Scientific Secretariat at scientificsecretariat@oicr.on.ca.

## 9. APPENDIX I: EVALUATION RUBRIC AND SCORING CRITERIA

LOIs and full applications will be assessed by the Therapeutics Pipeline Advisory Committee (TPAC) using an evaluation rubric developed along four themes of inquiry:

- Target validation/disease association;
- Safety;
- Feasibility; and
- Strategic considerations.

The rubric below is meant to provide *guidance* for discussion and feedback to the teams. If additional guidance is required, reviewers should reach out to the Scientific Secretariat for assistance. The application will be discussed and evaluated against the listed criteria, where applicable.

***Table 3:*** *Evaluation rubric for CTIP proposals*

| Target validation/disease association | Safety | Feasibility | Strategic considerations |
|---|---|---|---|
| Human disease altered by drugs hitting target and/or target pathway from Phase II, III or post-marketing decision clinical trial data | Toxicity liabilities can be tracked and are manageable | Relevant *in vivo* models with and efficacy endpoints | Clinical need |
| Promising Phase I-IIa clinical trial data with other drugs hitting the target and/or target pathway or similar biology | Toxicity profile of known ligands understood | Relevant *in vivo* models with pharmacodynamic endpoints | Clinical delivery |
| Biomarker for target dependence understood in the disease | Toxicity liabilities in genetically modified animals is understood | Relevant organoid-based assays with relevant endpoints | Target patient population |
| Preclinical, dose-dependent efficacy modeling predictive of human efficacy, with human genetic evidence | Toxicity liabilities of the pathway, anti-targets and isoforms understood | Relevant patient-derived cell-based assays with relevant endpoints | Market opportunity |
| Intervention at target in pathway using selective tool compounds demonstrates preclinical efficacy | Toxicity assays are available and affordable for the stage | Relevant cell-based assays (immortalized cell lines) with relevant endpoints | First-in-class or Best-in-class potential |
| Transgenic or knockout animals have disease phenotype | Toxicity liabilities can be measured reproducibly | Biomarker(s) identified and validated | Competitive landscape and history of successful or unsuccessful targeting of the major pathway or organelle under question |

| Target validation/disease association | Safety | Feasibility | Strategic considerations |
|---|---|---|---|
| Data implicating target in disease state pathogenesis and/or demonstrated pharmacology in pathway | | Selectivity assays (target class and target-specific isoforms) with no undue risk that required recombinant proteins or protein complex cannot be synthesized | Freedom to operate |
| Pharmaceutical intervention at the target unproven but suggestive research | | Availability of computational expertise | Regulatory considerations |
| Transgenic or knockout (including shRNA or CRISPR *in vivo* models) animals demonstrate linkage to physiology and/or disease | | Availability of crystal structure or homology model | Reimbursement |
| Loss or gain of function in patient-derived organoids shows disease phenotype | | Feasibility of structure-based drug design | |
| Loss or gain of function in patient-derived cell-based assay shows disease phenotype | | Confirmatory/binding assays | |
| Target function linked to pathway which is abnormal in the disease based on cell biology research | | Biochemical inhibition assays | |
| Loss (e.g., shRNA, CRISPR, partially selective tool compounds) or gain (e.g., overexpression) of function phenotype in immortalized cell lines | | Feasibility of protein complex assembly suitable for screening | |
| Target function linked to disease progression and/or poor prognosis | | Availability/feasibility of key screening reagents (e.g., target, recombinant proteins, functional domains, inactive constructs, selectivity reagents, etc.) | |
| Target tissue distribution known | | Availability of chemical collections for screening | |
| New therapeutic hypothesis or disease association of target by clinical genetics (e.g., mutation, amplification, translocation) | | Team composition and collaborations | |
| Disease hypothesis based on pathway or related protein biology | | | |

Full applications for CTIP projects will receive scores for each theme outlined in the evaluation rubric above (Table 3), as well as an overall score for the project. The final overall score will be used to rank projects for funding consideration. Scores will be assigned as outlined in Table 4.

***Table 4:*** *Scoring*

| Score | Description |
|---|---|
| 4.7 – 5.0 | Excellent with no weaknesses identified |
| 4.2 – 4.6 | Excellent with minor weaknesses identified |
| 3.6 – 4.1 | Very good with minor weaknesses identified |
| 3.0 – 3.5 | Very good with moderate weaknesses identified |
| 2.4 – 2.9 | Good with moderate weaknesses identified |
| 1.7 – 2.3 | Fair with moderate weaknesses identified |
| 1.0 – 1.6 | Poor with moderate to major weaknesses identified |
| Below 1.0 | Poor with major weaknesses identified |

## 10. APPENDIX II: ELIGIBLE EXPENSES

Eligible expenses are actual expenses necessary for the completion of the approved Deliverables, subject to the terms and conditions of the Agreement and the guidelines in this Schedule, and subject to review and approval by OICR. Unspent funds must be returned to OICR upon request by OICR. It is expected that the Recipient will withhold payment of expenses should it become known that any OICR, institutional, provincial, and/or federal regulations and/or policies have been breached.

Funding for the Projects/Sub-Projects is provided by the Government of Ontario through the Ministry of Colleges and Universities. **Awarded funds will be solely disbursed to and administered by eligible institutions in Ontario. Further, with the exception of budget items classified as external research services, eligible expenses *may only be incurred in the province of Ontario*.** Allocation of funds to institutions outside of Ontario is allowable only when the studies outlined cannot be performed in whole at eligible Ontario institutions. Justification for such an allowance must be provided to and approved by OICR in advance of the investigator utilizing OICR funds for such a purpose.

Expenditures are actual outlays that can be documented through invoices or receipts. Expenses must support and be essential to carry out the activities described in the approved proposal for funding. Evidence of payment must be maintained for audit purposes.

In-kind expenses may include the contribution of goods, services, labour, fixed assets, or other such items that would otherwise have been provided and paid for in order to carry out the Projects/Sub-Projects. In-kind expenses are not reimbursable.

Eligible expenses are described in the categories below. Expenses of the Projects/Sub-Projects, which are not described in the categories below, require written approval by OICR. Pre-award budget questions should be submitted to the OICR Scientific Secretariat at ScientificSecretariat@oicr.on.ca. Post-award budget questions should be addressed to OICR Research Operations at ResearchOps@oicr.on.ca.

Table 5 outlines eligible expense categories and specifies which are eligible for overhead.

***Table 5**: Eligible expenses*

| Expense category | Eligible for overhead? |
|---|---|
| Salaries and benefits | Yes |
| Laboratory consumables (wet or dry lab) | Yes |
| External research services | No |
| Internal charge-back for laboratory services | No |
| Equipment, information technology (IT) support services and software | No |
| Dissemination of research results | No |

| Expense category | Eligible for overhead? |
|---|---|
| Educational outreach activities | No |
| Hospitality | No |
| Training and professional development | No |
| Travel | No |
| Commercialization activities | No |
| Audit costs | No |
| General office and administrative costs | No |
| Clinical/health intervention trial costs | No |
| ***NOTE:*** *All expenses incurred at OICR are NOT eligible for overhead* | |
| ***NOTE:*** *Overhead is NOT provided for personnel awards, including the OICR Investigator Award Program* | |

## Direct research expenses

**Stipends, salaries and benefits:** Eligible expenses include the stipends or salaries and benefits for those staff responsible for supporting the conduct of the funded proposal, including research assistants and associates, technicians, statisticians, informaticians, support staff, postdoctoral fellows, students, project and program managers, study coordinators, and other highly qualified personnel. Applicable stipend levels for students are those used by the institution in which the research will be carried out. While benefits for postdoctoral fellows, research assistants, technicians, and support staff are eligible, stipends and student training awards are not to include allowances for CPP, Employment Insurance, health taxes, or any extra fringe benefits.

The eligible cost of salaries and benefits should be calculated using the employee's actual base salary amount, plus actual payroll benefits (vacation, medical, dental, etc.). The amount to be charged should reflect the proportion of the employee's normal total hours for payroll purposes spent working directly on the Projects/Sub-Projects. The host institution is required to maintain time sheets or other appropriate records for all personnel working directly on the Projects/Sub-Projects.

Staff and trainee hiring should align with the Equity, Diversity, and Inclusion (EDI) principles of the host institution and, when requested, meet the criteria outlined in the Request for Applications (RFA).

Provision of salary increases should reflect applicable host institution guidelines.

Discretionary severance and separation packages are not eligible expenses.

Funds cannot be used to cover the salaries of applicants, including Principal Investigators and Co-Investigators. The exception being the *OICR Investigator Awards Program*, where the salary

of the Principal Investigator is an eligible expense. The OICR Investigator Awards Program does not provide overhead.

Salaries and benefits are eligible for overhead.

**Laboratory consumables:** Expenditures are permitted on the actual cost of research materials, laboratory materials and supplies necessary for the Projects/Sub-Projects. Procurement should be in accordance with the policies of the host institution and occur in a commercially reasonable manner in order to achieve value for money.

Costs related to animal expenses are only eligible as a laboratory consumable in cases where the institution does not operate an internal facility that provides animal purchasing and husbandry, and the lab maintains the animals themselves. Costs related to animals housed and cared for in institutional or other facilities should be classified as an external research service or internal charge-back, as appropriate (see below).

Laboratory consumables are eligible for overhead.

**External research services:** Contracted services related to the Projects/Sub-Projects provided and invoiced by other research groups, platforms or companies are eligible. To be eligible, fees for use of services or equipment must be consistent with fees charged to all institutional users in accordance with a published schedule. The service provider will issue an itemized purchase order/invoice that will include the full cost of the services rendered (e.g., labour, consumables, sample handling, etc.). The services must be free from any intellectual property (IP) restrictions or restrictions on use of data. Service providers do not need to be located in Ontario, but whenever possible, Ontario-based service providers, with the capability to provide the required capacity, quality, timeliness, and value of the service, should be selected.

External research services are not eligible for overhead.

**Internal charge-back:** Funds for laboratory and/or technical services provided within an institution.

Internal charge-back amounts are not eligible for overhead.

**Equipment, information technology (IT) support services, data retention, and software:** Eligible expenses include research equipment and components, IT support services, data retention, software, and licenses required for the Projects/Sub-Projects (beyond what is typically provided by the host institution), as listed in the Application, and agreed upon with OICR. Data retention charges are capped at five per cent of the direct, annual award value and are eligible over the term of the award only. Requests in excess of five per cent may be considered with appropriate justification. The plan for data retention over the term, and beyond (as required by the specific RFA) must be detailed within the application. Costs for equipment maintenance and service contracts, training of staff operating equipment/software, travel costs to visit manufacturers to select major equipment purchases, transportation costs for purchased equipment, and extended warranty for equipment are eligible. Since the approved budget may reflect changes from the Application, these should be confirmed with the Senior Director, Research Operations. Procurement must be in accordance with the policies of the host institution and should occur in a commercially reasonable manner to achieve value for money. Note that equipment costs exceeding $25,000 per item require appropriate justification and prior approval from the OICR President and Scientific Director and/or Deputy Director.

Equipment purchased with OICR funding will belong to the host institution. The host institution is responsible for the proper functioning and maintenance of research equipment purchased using OICR funds. Final disposition of research equipment will be the responsibility of the host institution. However, no OICR-purchased equipment should be sold within five (5) years of its acquisition without written approval from the OICR President and Scientific Director and/or Deputy Director.

Should the equipment no longer be required during the funding period, OICR reserves the right to relocate it at OICR's expense.

Equipment, IT support services, data retention, and software are not eligible for overhead.

**Dissemination of research results:** Expenses associated with the dissemination of research results and/or knowledge translation strategies, including publication costs directly related to the funded proposal, as well as costs to ensure open access of research results (up to a maximum of $10,000 per year, or five per cent of the overall budget (excluding overhead) per year, whichever is less), are eligible.

Dissemination of research results costs are not eligible for overhead.

**Educational outreach activities:** Expenses associated with educational outreach activities/workshops for the general public, students, stakeholders, and peer groups are eligible.

Educational outreach activities costs are not eligible for overhead.

**Hospitality:** When directly related to the funded Projects/Sub-Projects, hospitality costs (non-alcoholic beverages and meals) for the purpose of essential communications between the awardee and other individuals involved in the Projects/Sub-Projects, are eligible. The purchase of alcohol and entertainment is not eligible.

Hospitality costs are not eligible for overhead.

**Training and professional development:** Expenses for scientific staff training and/or professional development (e.g., novel techniques, specialized courses and membership fees in professional associations or scientific societies) related to the execution of the Projects/Sub-Projects are eligible. Training and professional development must be carried out in accordance with the host institution's policies.

Training and professional development costs are not eligible for overhead.

**Travel costs:** Expenses for Project/Sub-Project-related travel (including accommodation) are eligible and are capped at five per cent of direct research expenses per year. Travel must always be by the most practical and economical method. When air or rail are the most practical and economical methods, only the cost of an economy class seat will be reimbursed by OICR funds, and the Recipient must maintain appropriate records of travel expenses and their purpose.

Travel costs are not limited to travel within Ontario.

Travel costs are not eligible for overhead.

**Commercialization activities:** Expenses related to IP protection are eligible. Costs for securing external expertise for the preparation of a commercialization plan or for patent filings are capped at $10,000 per Project/Sub-Project ($5,000 if it is part of a contract with another academic institution, a business development office, a private consultant, or equivalent).

Commercialization activities are not eligible for overhead.

**Audit costs:** The Ontario Government can audit OICR and any of its funded programs at any time during the award, with a forty-eight (48) hour advance notice and at the expense of the Government of Ontario. OICR may audit the research programs annually and/or at the end of the term.

Recipients of financial contributions may be requested to submit an independent auditor's certificate with their year-end financial report.

Audit costs are not eligible for overhead.

**General office and administrative costs:** Expenses directly related to office expenses and communications necessary for the successful completion of the Projects/Sub-Projects are eligible and capped at three per cent of direct research expenses per year.

General office and administrative costs are not eligible for overhead.

**Clinical/health intervention trials:** Trial costs fall under two categories:

1. ***Fixed costs*:** Costs that are necessary to implement the trial regardless of patient recruitment status, which may include, but are not limited to:
   a. *Trial start-up costs* (e.g., protocol development, investigator meetings, Research Ethics Board costs, site initiation costs, etc.);
   b. *Central trial management and site monitoring*; and
   c. *Data management and statistical support*.
2. ***Per-case funding costs*:** Costs that are dependent on patient accrual, which include, but are not limited to:
   a. *Study coordinator salary and benefits*;
   b. *Screening costs*;
   c. *Patient visit costs*: physical exams, blood test, imaging assessments, etc.;
   d. *Clinical sample collection and processing*; and
   e. *Correlative laboratory analyses* (e.g., immune correlates, gene panels, etc.)

   Per-case funding costs should not exceed standard Ontario Health Insurance Plan/Canadian Medical Association rates if rates have been published. Details of each type of assessment will be required in the budget justification for per-case funding costs.

Clinical/health intervention trial costs **are not eligible** for overhead.
Clinical/health intervention trial costs **are not an eligible CTIP expense**.

### Cost recovery

Although cost recovery is a form of revenue, and not an expense, it may be reported as part of the budget to demonstrate that recoveries are part of the plan to cover all true expenses to ensure that the project or program does not exceed the OICR-approved budget.

Cost recovery is not eligible for overhead.

## Overhead/indirect costs

Overhead (also known as indirect costs) will be automatically calculated in CaAwardNet, OICR's financial tracking tool. Overhead is not eligible for OICR-based expenses. OICR will provide up to thirty per cent with respect to eligible direct research expenses of the approved proposal to cover institutional overhead. The total amount of the OICR award that can be allocated for overhead will be listed in the Agreement.

When changes to funded research activities result in a reallocation of funds between projects/sites or expense categories, the resulting calculations of overhead will require adjustments.

Overhead costs are:

- The facility or infrastructure costs required to perform research, and typically include costs associated with maintaining, renovating, and operating physical facilities (e.g., heating, lighting, maintenance, insurance), project administration costs (e.g., accounting), expenses associated with regulatory requirements and accreditation, and technology transfer offices and support facilities (e.g., libraries and computing facilities); and
- Calculated based on overhead-eligible expense categories as detailed above.

The allowable budget listed in the Request for Applications (RFA), or program guidelines (as applicable) is inclusive of overhead costs. **Overhead must be accounted for in the allowable budget.**

***NOTE: Overhead is NOT provided for projects funded through the OICR Investigator Award Program, consistent with other salary award programs. Overhead is NOT provided for expenses that will occur at OICR.***

The host institution will not be eligible for reimbursement of overhead costs for the Projects/Sub-Projects from any other Government of Ontario funds.

If an overhead amount of less than 30 percent is requested, this must be detailed in the host institution Letter of Support as part of the proposal submission process.

## Placeholder budget

When eligible as per the RFA/Guidelines, a placeholder budget for future research activities (up to a maximum of 15 per cent of the total budget including overhead costs) will be allowed at the time of submission.

Placeholder budgets are **not eligible for CTIP projects**.

## Non-eligible expenses

The items below are not eligible for OICR funding:

- Salaries and benefits of the PIs, Co-PIs, etc. (with the exception of the Investigator Awards Program which will pay the salary and benefits for the awardee);
- Insurance for equipment;
- Benefits for trainees (i.e., undergraduate and graduate students). Note that benefits for postdoctoral fellows are an allowable cost and should be in accordance with the host institution's policy; and

- Funding for any project where there is significant scientific overlap (e.g., the research objective and design are identical or very closely related) with a project currently funded through other sources.

### Deviation from proposed activities and/or budget

A significant deviation (as assessed by the PI(s) in consultation with the Heads* of Adaptive Oncology, Clinical Translation or Therapeutic Innovation) in a project's anticipated deliverables/milestones and/or end date can be the result of significant delays (i.e., more than six months) in recruitment of qualified personnel, regulatory approvals, recruitment of patients, availability of supplies/drugs, or inter-institutional transfer of funds/activities due to enhanced collaborative activities. In such instances, the PI must provide an explanation for the change/delay, and formally request budget amendments/transfers or extensions, providing justification for all changes. Such changes will require a budget and agreement amendment. Any resulting budget amendment should be reported to OICR. Minor variances/shifts can be reported through quarterly reports and may not require changes to contractual obligations.

**In instances where the Head is also a recipient of OICR funding, the deviation should also be discussed with the Senior Director, Research Operations.*

### Reallocation of budget

Reallocation of more than 15 per cent of the total budget will require express written permission of OICR's Deputy Director and relevant Head.

Any resulting changes will require an amendment to the agreement and a corresponding budget amendment.

### Carryover funds and no-cost extensions (NCE)

Budget monitoring must be carried out to ensure that funds allocated for a given fiscal year are utilized, as OICR does not have the ability to allow carryover of funds into the subsequent fiscal year. Host institutions are also strongly encouraged to utilize the funds for the fiscal year for which they are intended.

An NCE may be granted in exceptional cases with prior approval from OICR's Deputy Director or Senior Director, Research Operations. Application for an NCE must be made in writing and supported by appropriate justification.

## 11. APPENDIX III: "ONTARIO FIRST" POLICY

In order to promote the commercialization and public availability of inventions made in Ontario by Ontario industry and, to ensure that Ontario businesses obtain sufficient opportunity to commercialize provincially-supported inventions, the host institution agrees that the following options to commercialize the arising intellectual property (IP) will be considered:

- An existing organization in Ontario with receptor capacity;
- An expansion of an existing company in Ontario;
- The formation of a new company in Ontario;
- Joint ventures or strategic alliances with a company in Ontario;
- Co-manufacturing involving a company in Ontario;
- Cross-licensing or co-development with a company in Ontario; establishment of a new subsidiary in Ontario (R&D, manufacturing, sales, marketing, distribution); and
- Development and/or production in Ontario by a foreign company.

If reasonable efforts to grant licenses to potential licensees to commercialize and manufacture the arising IP substantially in Ontario are unsuccessful, then the host institution agrees that OICR's commercialization agent or assignee will be responsible for documenting the rationale and circumstances that led to any proposed decision or step to pursue commercialization/exploitation by a non-Ontario company, including an account of the benefits to Ontario for review by an IP Commercialization Committee prior to finalizing the decision or step. The documentation will be forwarded to OICR.

## 12. APPENDIX IV: TESTING CASCADE

*The images in Appendix IV (Figures 5, 6 and 7) are the property of the Ontario Institute for Cancer Research.*

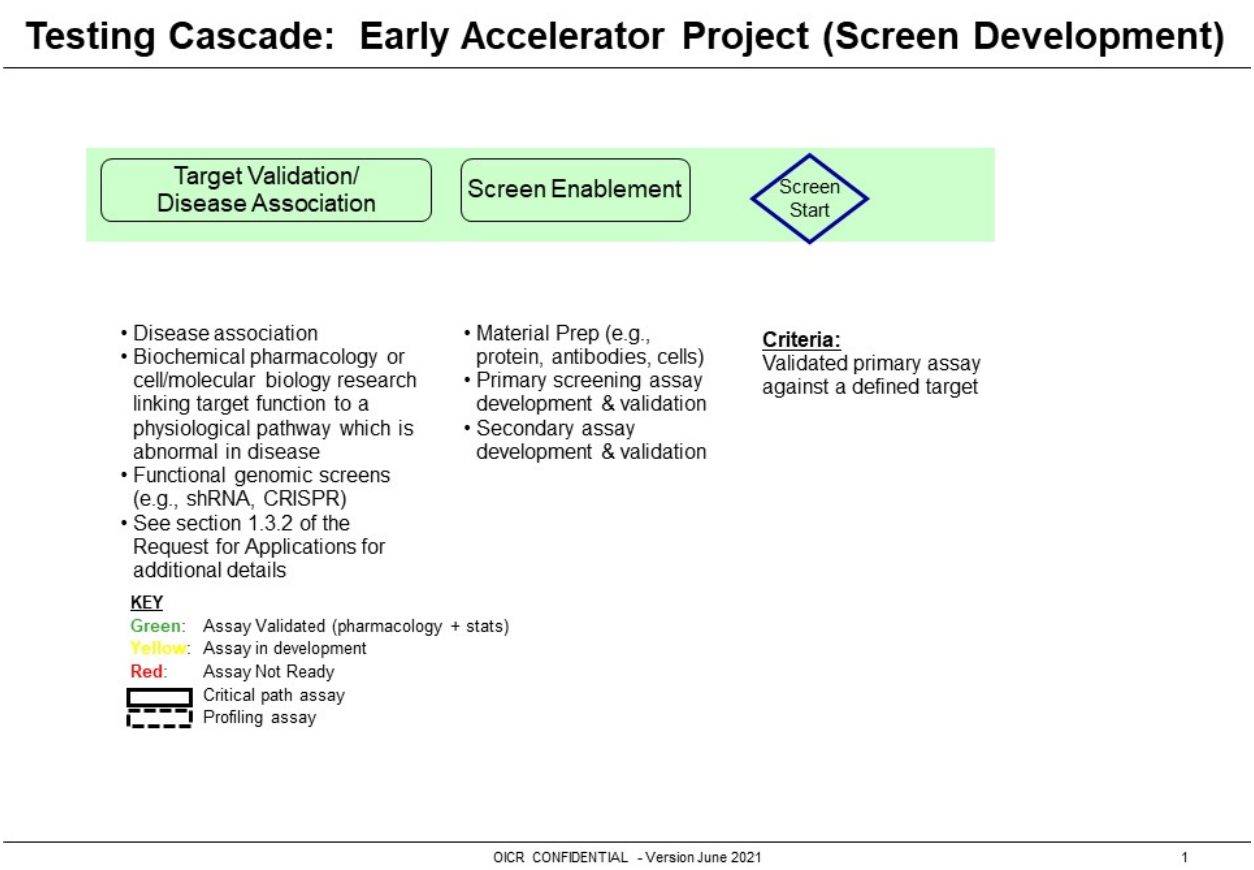


***Figure 5:*** *Testing cascade for Early Accelerator projects*

- The testing cascade should identify which assays are completely validated (in green boxes), in progress (yellow boxes), or required (red boxes);
- Critical path assays should be in solid boxes, profiling assays in dotted boxes; and
- Statistical validation data (both inter- and intra-assay) should be listed and documented in a supporting document.

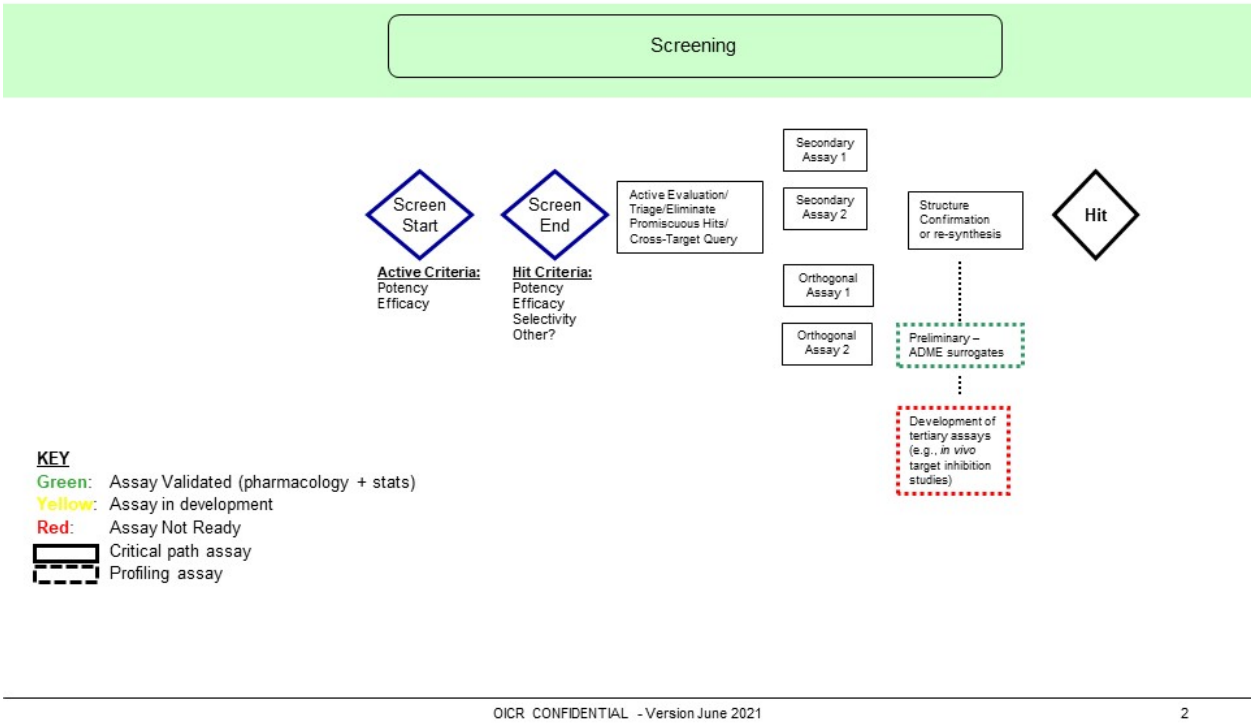


***Figure 6:*** *Testing cascade for Late Accelerator projects*

- The testing cascade should identify which assays are completely validated (in green boxes), in progress (yellow boxes), or required (red boxes);
- Critical path assays should be in solid boxes, profiling assays in dotted boxes; and
- Statistical validation data (both inter- and intra-assay) should be listed and documented in a supporting document.

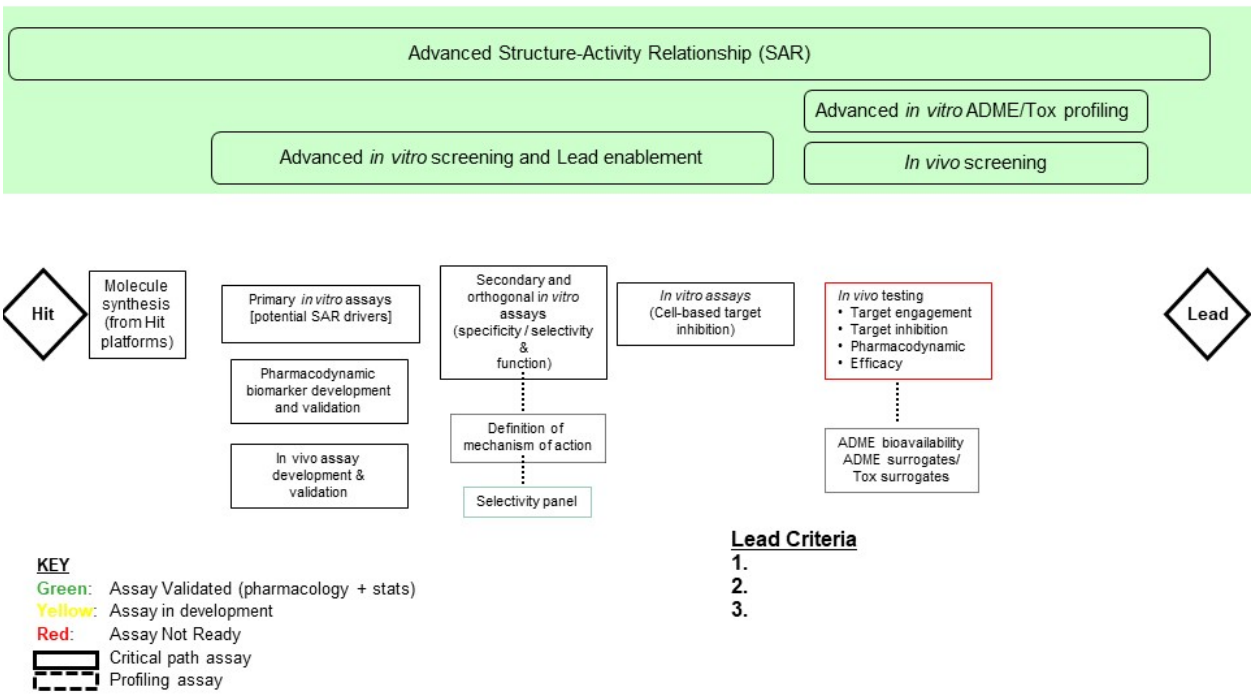


***Figure 7:*** *Testing cascade for Lead Generation projects*

- The testing cascade should identify which assays are completely validated (in green boxes), in progress (yellow boxes), or required (red boxes);
- Critical path assays should be in solid boxes, profiling assays in dotted boxes;
- Statistical validation data (both inter- and intra-assay) should be listed and documented in a supporting document.

## 13. APPENDIX V: DATA SHARING, OPEN ACCESS AND RETENTION

Applicants agree to adhere to the Global Alliance for Genomics and Health's Framework for Responsible Sharing of Genomic and Health-Related Data. The Framework interprets the right of all people to share in the benefits of scientific progress and its applications as being the duty of data producers and users to engage in responsible scientific inquiry and to access and share genomic and health-related data across the translation continuum, from basic research through practical applications. It recognizes the rights of data producers and users to be recognized for their contributions to research, balanced by the rights of those who donate their data. In addition to being founded on the right of all citizens in all countries to the benefits of the advancements of science, and on the right of attribution of scientists, it also reinforces the right of scientific freedom.

OICR promotes the GA4GH framework related to the deposition of publication-related data in openly accessible databases. OICR funding recipients are required to deposit bioinformatics, atomic, molecular coordinate data and source code for software into the appropriate public database, as already required by most journals, immediately upon publication of research results (e.g., deposition of nucleic acid sequences into GenBank, and source code into a publicly accessible FTP or web server).

OICR strongly supports unrestricted access to research outputs and aligns with the Tri-Agency Open Access policy on Publications. Funding agreements for successful applicants will include the expectation for adherence to Open Access principles. Applicants must provide a data sharing and accessibility plan, specifying how data generated by the OICR-funded research will be shared and how the research community can access the data.

Recipients of OICR funding are required to retain original data sets arising from OICR-funded research for a minimum of five (5) years after the end of the research project as defined by the research agreement or Notice of Award. This applies to all data, whether published or not. Applicants must provide a data retention plan, specifying how data generated will be stored during the course of the project and for the five-year period after its conclusion. If needed, applicants can request funds to support this data retention requirement, however, charges are capped at five (5) percent of the direct, annual award value and are eligible over the term of the award only. For clarity, data retention costs must be accounted for within the allowable budget and are not in addition to the budget requested to conduct the project.