Phase 2 – Consortium Launch Proposals

Request for Applications – Frequently Asked Questions

RFA scope and eligible studies

1. Is this RFA open to proposals that are pan-Canadian (not specifically linked to one consortium) or only through each consortium? How would funding work for cross-consortia initiatives?

   Submissions will have to be through one consortium, but can include collaborations across consortia—in fact, these are strongly encouraged.

2. Are the proposals for this RFA intended to be separate/distinct from the *GenerationAll* and *KnowMyGenes* programs? Will there be separate funding for *GenerationAll*?

   There will not be separate funding for GenerationAll and KnowMyGenes; these programs should be incorporated into consortia's proposals. GenerationAll is a Network protocol for prospective accrual of patients and return of results to medical teams, and all consortia are highly encouraged to adopt it.

3. For this RFA, are non-case generating pilot tool development projects (e.g. trial-matching software, LLM-assisted data curation pipelines) considered in scope? If so, can they be included as brief appendices, given the tight page limit required for case-generating work, or should we expect a future RFA specifically for these pilots?

   The examples mentioned in this question are not in scope for this RFA; however, we recognize that these are important areas of study, and they will be addressed through other means (working groups and/or other RFAs) in coming months.

   Prospective case-generating projects are meant to be a major output of this RFA. While the RFA is also open to other non-case generating projects, these should be mainly related to health economics, health technology assessments, and health equity and increasing access to precision oncology for underserved populations.

   Consortia may include a 1-page appendix per project to provide additional information if needed. The RFA documents will be updated to reflect this change. However, you should ensure that the main application includes a clear rationalization of how all projects relate to each other and work together.

4. Will there be more RFAs to come, and should we expect these to only come annually?

   Yes, there will be other RFAs to come. They will not necessarily be only annually.

5. Are all consortia of similar size/scale and returning similar case numbers? If not, why is it that each consortium is given the same maximum budget?

   We are giving equal opportunities to all consortia. The budget does not only cover case costs, but also other, non-case-generating projects. Additionally, case costs differ across regions. Some consortia may have more funding available from other sources as match, and thus have more ability to expand. This is a pan-Canadian initiative funded federally.

6. Do you expect an iterative process after the May 8 ESAC review, but before finalization?

   Yes. We expect that there will be some back-and-forth, with final decisions coming around early June.

Budget & match funds

7. How should we prepare our zero-based budget?

   A zero-based budget approach is required for these proposals, meaning that the budget must start from zero and expenses must be identified and justified with granularity. For example, for prospective (e.g. GenerationAll) cases, you must itemize the costs of sample retrieving, sample processing, sequencing, data analysis, reporting, etc. Budget lines for consortia, secretariat, and other pilot projects must reflect actual costs for these line items to complete the deliverables of the RFA.

8. Will matching funds be required and can it be in-kind or only cash?

   Matching funds are required, as outlined in the RFA documents. The same rules apply as in Phase 1, meaning that matching funds must be cash. In-kind contributions are not eligible.

   Matching fund ratios will depend on individual RFAs. For this consortium launch RFA, we are requesting a 1:0.5, Health Canada : match funds, ratio to help with the initial Phase 2 ramp-up and facilitate the rapid use of Health Canada funds in Year 1.

9. Is the match based on the whole institution rather than per-cohort?

   Match amounts are per-proposal. We are not prescriptive on match per-line or per-cohort/project. For example, one deliverable could be supported by 100% Health Canada funds and another one by 100% match—the final ratio is what matters.

10. Is the $5,000 per case expected to be spent entirely on WGTS sequencing? Can teams use part of the $5,000 on other types of case profiling?

    The $5,000/case figure is an estimate, and consortia are expected to determine projected costs for their own context. Part of the $5,000 can be used for other types of profiling, and additional costs can be requested as necessary (see also next question). Please ensure that costs for different steps and types of profiling are clearly indicated in the zero-based budget.

11. If a cohort wants to perform non-genomic assays on their cases and the $5,000 doesn't cover all costs, could the consortium cover part of the expenses with the Consortium HC budget?

    These expenses should not come from the consortium budget, but they can be requested as budget for additional deliverables.

12. If a cohort wants to conduct longitudinal profiling of multiple samples (e.g., pre-, on-, and post-treatment), could they request more than 5K if justified with a zero-cost budget?

    Yes.

13. Is there a larger budget for cases obtained in rural areas?

    Additional funds may be requested for cases that address questions of health equity and improved access. As per the RFA (page 6): "Additional funds may be required to support activities involving underserved populations, longitudinal studies, multiomics studies, and KnowMyGenes studies. Zero-based estimates of the incremental costs associated with these components, along with the proposed source(s) of funding—particularly the availability of regional matching funds—must be documented."

14. Would funds to travel to rural/remote locations to engage with underserved communities be eligible for TFRI/Health Canada funds?

    Yes. These costs must be clearly outlined and justified in the proposal (see also question 13).

15. Do we have to budget for the costs associated with *KnowMyGenes* study enrollment? If so, how much does it cost per sample?

    Costs associated with KnowMyGenes projects are eligible to include in the proposals. Anticipated per-case costs should be determined by the consortia and/or relevant projects.

16. Is the secretariat budget separate from the consortium budget?

    The secretariat budget should be included as part of the consortium budget, but clearly outlined and justified separately from consortium/centre infrastructure support.

17. Can general administrative expenses be included in the consortium budget?

    Yes. As with all other expenses, these costs must be clearly justified and itemized.

Clinical studies

18. Is there funding to support clinicians with precision oncology? For example, to write the onerous paperwork to get access to drugs off-label and liaise with patients if we fail to get access.

    Proposals for prospective clinical studies can include funding requests for these types of activities, as appropriate. The Network and relevant working groups will continue to develop supports for e.g. clinician education related to GenerationAll and WGTS-informed precision oncology. Opportunities may arise to help facilitate drug access through, for example, national collaborations and new clinical trials.

19. To rapidly deliver precision oncology to patients, will projects making use of already established sequencing infrastructure at clinical sites be eligible? For example, clinical studies using targeted panels or plasma/tumour whole-exome sequencing?

    Cases delivered through Phase 2 must still meet standards outlined in the MOHCCN Gold Cohort Policy; i.e. whole-genome and transcriptome sequencing (WGTS). The

examples provided address additional profiling that may be proposed as part of prospective studies (e.g. comparing WGTS to targeted panels and/or exomes; profiling circulating tumour/cell-free DNA (ct/cfDNA) in addition to tumour), as outlined in examples provided in the RFA.

20. Plan for Phase 2 seem to be built on a foundation of prospective cohorts, likely of participants already enrolled in Phase 1. Are prospective clinical trials anchored in WGTS with return of results to patients (which could also build in health economic analyses) in scope?

    Yes, these types of trials and studies are in scope. Participants should be new for Phase 2 (i.e. patients who participated in Phase 1 are not eligible as new cases for Phase 2).

21. Using WGS data to develop tumour-informed liquid biopsies would enormously enhance clinical impact. Once assays are generated, then serial blood samples can be analyzed to determine recurrence, treatment response, resistance, etc.—is that feasible within Phase 2/this RFA?

    Yes, this type of project is in scope. Please refer to Appendix 1 of the RFA for further examples.

22. Can you clarify the distinction between the requirement to return results to patients in time to influence care versus the mandate that excludes healthcare delivery. Some of the research questions such as residual disease detection and disease management that arise, may not be suitable to safely return results that are not part of standard of care. Will this type of research be excluded?

    There is an expectation that return of results will be prioritized and addressed where feasible and safe and in a research setting. This mainly applies to WGTS data, although it can be applied to other data types where relevant and feasible.

    Return of results is not mandated for all data types and all projects; however, justification should be provided where this is not possible. Please refer to Appendix 1 of the RFA for examples of projects that may not include return of results.

Equity, diversity, inclusion & access

23. How will we capture socio-demographic information to ensure that we are capturing diverse populations, including underserved communities? If our own Consortium has EDIA initiatives from Phase I, can we continue with that in Phase 2 or will we have to collect the MOHCCN-branded socio-demographic survey for patients we sequence through MOHCCN?

    The Canadian Spectrum Working Group has developed a socio-demographic data model to collect this kind of information consistently across the Network. The self-reported questionnaire was recently endorsed by Network Council and will be distributed shortly. Implementation plans are to come. We anticipate that the model will become mandatory (similarly to the Clinical Data Model) once relevant pieces are in place.

Molecular profiling & data sharing

24. Is there a limit to the number of cases that can be proposed per consortium in Year 1?

    No. We estimate that ~2,000 cases will be profiled in Year 1, which can be used as a guide. As per the RFA: "When proposing case numbers, it is generally recommended to scale case numbers per consortium according to the consortium case delivery in Phase 1. For example, if a consortium delivered 20% of all cases in Phase 1, it is suggested to develop a proposal for ~400 cases in Year 1. Justifications, including late joining of the Network by some consortia, should be provided if the proposed number differs significantly." (page 6)

    However, if cases can be delivered for less than the estimated $5,000 per case, and depending on consortium priorities and other projects in the proposal, then more cases may be accommodated within the budget..

25. Are we allowed to do longitudinal samples (i.e. testing more than one tumour sample per patient with WGTS) using Health Canada/TFF funds?

    Yes, longitudinal samples are eligible in Phase 2. However, only new participants are eligible; for example, a recurrent sample from a patient whose primary tumour was

profiled in Phase 1 is not eligible. Any projects aiming to profile longitudinal samples should be clearly outlined in the proposal as doing so.

26. Are there specific data deliverable requirements for Phase 2? Are these the same as Phase 1 (i.e. as outlined in the Gold Cohort Policy—for example, sequencing coverage minimums)?

    The data deliverables outlined in the MOHCCN Gold Cohort Policy still apply. Additional data deliverables (e.g. socio-demographic and economic/health technology assessment data) may be added as they are developed and endorsed for Network use.

27. Can we create two tiers of patient deliverables? One with the germline + WGTS and another that is germline only?

    For Year 1, KnowMyGenes pilot projects should be proposed as part of GenerationAll projects. This means that a tier with germline WGS only is not eligible for this RFA. This may change in future years.

28. Will consortia be expected to continue uploading Phase 2 data to CanDIG?

    Yes. Any budget associated with the maintenance of regional CanDIG nodes should be included in the RFA.

29. Are cell-free DNA/circulating tumour assays considered 'multiomics'?

    Yes. Please refer to Appendix 1 in the RFA document for additional examples.

30. In Phase 1, there was a requirement to use Illumina reagents and purchase a certain amount. Does a similar requirement apply in Phase 2? If so, are there any minimum purchasing expectations for consortia?

    This remains under discussion with relevant working groups, with more information to come. Operationalization will differ from Phase 1, and centres will have more independence to order directly from providers.

31. Are Ultima and other non-Illumina platforms acceptable for WGTS sequencing?

    The expectation is that Illumina technologies will be used for WGTS cases at this stage as a continuation of Phase 1. Groups wishing to use another sequencing platform should propose a pilot project that includes a comparison with Illumina

sequencing to demonstrate feasibility and interoperability with existing and future Gold Cohort data.

32. There was a mention in the webinar about different centres using different workflows and sequencing methods. What does this mean in terms of harmonization and interoperability between data from different cohorts?

    As in Phase 1, the Network (through its working groups and governance structure) will continue to set minimum standards and guidelines for genomic profiling—this allows consortia and institutions to implement workflows and pipelines that function for them while generating consistent, interoperable data.