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TERMS OF REFERENCE FOR PRENATAL CELL-FREE DNA SCREENING CCMG AD HOC WORKING GROUP

Date ToR approved by Board: January 21, 2025

Brief Background for Formation of Working Group:

Prenatal Cell-Free DNA Screening (also known as Non-Invasive Prenatal Test (NIPT) or Non-Invasive Prenatal Screening (NIPS)) is a screening test to provide a risk estimate for fetal aneuploidy. The use, eligibility criteria and funding of prenatal cell-free DNA screening varies across Canada. Recently, concerns regarding atypical results have been raised, regarding both the patient understanding of the technology and proper practice (2023 CCMG Annual Meeting).

Mandate

The purpose of this CCMG Ad hoc Working Group is to develop and publish a document providing a clinical perspective, aligning the country with a clear message that will allow for clear evidence-based advocacy for standard practices regardless of location in Canada. This includes eligibility for testing, conditions for testing, and follow-up investigations for different scenarios, including atypical results. Our role is to determine best practice for clinical work-up. This document is intended to work in conjunction with a separate document from the Laboratory Practice Committee. They are planning to update the Recommendations for the Indications, Analysis and Reporting of Prenatal Specimens guidance with Best Practices for Prenatal Cell-Free DNA Screening through input from this working group. The Lab Practice Committee document will include standardized wording for atypical findings in clinical reports.

There is recognition that accessibility varies across Canada. It is hoped that by recommending practice standards this will support advocacy within provincial screening programs that are not providing that practice standard. A standardized approach to reporting of findings is a key component spanning all clinical practices (clinic and laboratory).

Timeline

March 2024, met to brainstorm and develop parameters for the Terms of Reference. April 2024, met to finalize the draft of the Terms of Reference (TOR). July 2024, submitted TOR to the BOD for approval. The official formation of the Working Group will be following the approval of the TOR by Jan 2025. An expression of interest call will be made to the general CCMG membership to be a working group member. Over Mar and April 2025, the group membership will be finalized and then meetings will start monthly or every other month based on the

decision of the group. The draft outline for the document will be submitted to the CCMG board by Oct 2025. The draft document will be sent to the Board by May 2026 with internal CCMG committee review over summer 2026 and membership review in fall of 2026. External review will be done in late fall 2026 and finalized document will be submitted back to Board by January 2027.

Membership:

Membership will consist of representation of individuals from across Canada who work in prenatal genetics. The members will consistent of at least 1 individual from Clinical Practice, 1 from Education Ethics and Public Policy (E2P2) and 1 from Laboratory Practice committees representing:

- CCMG laboratory geneticists (CCMG molecular, cytogenetics or combined certified).
- CCMG clinical geneticists
- genetic counsellor/(s)
- 1 person who has expertise in Bioethics
- Medical writer

Additional members will be sought to round out geographic representation from the general membership expression of interest. The members who express interest will be selected through deliberation with the co-chairs.

For the development of this document, no industry partners will be primary writers. However, CCMG/CAGC members who work in industry may review this document as part of the committee/general membership review.

Patient representation will rely on obtaining the patient perspective through literature review since a single patient cannot fully represent the patient perspective. There will be opportunity for patient feedback early on as part of the draft outline and then later the draft document when it is reviewed externally. The Canadian Down Syndrome Society, Support Organization for Trisomy 18, 13 and Related Disorders, the Turner Syndrome Society, the Klinefelter Syndrome Association of Canada, Pregnancy and Infant Loss Network and Canadian Organization for Rare Disorders will be included.

Consultation with existing provincial programs that deliver aneuploidy screening will occur at multiple timepoints in the development of the document.

Confidentiality

Matters discussed at meetings and teleconferences are confidential and may not be disclosed to others. Exclusion to this includes information that was previously published or in the public domain, or it is information was already known to the member and was not acquired by the member directly or indirectly from the committee.

Conflict of Interest

Members should disclose any known or perceived conflicts of interest. When the main goal of the working group is development of educational materials, guidelines or recommendations on a specific topic, participation in similar activities (during the time frame of the Working Group activities) on the same topic led by external organizations might be perceived as a conflict of interest. If such situations arise, the member of working group should discuss this with the chair(s) and BoD representative, which if required could seek the advice of the BoD on that matter.

Appointment and term of chair

Following the brainstorm session, individuals were invited to express their interest to be the chair. Following the approval of the TOR, the plan will likely be for two potential co-chairs to be selected from the membership of the Ad Hoc Working group for the duration of the existence of the Working Group.

Conduct of Meetings

- The chair or co-chairs will convene regular zoom meetings of the Ad Hoc Working Group, with approximately one meeting held each month or more frequent if required.
- Quorum for decisions will be at least 50% of Working Group members
- Draft minutes of all meetings will be prepared and circulated to the Working group members for comment, ideally within 10 working days of the meeting.
- All meeting minutes will be made available to CCMG Board of Directors via the Board of Directors Representative.

Reporting

The co-chairs will report to the CCMG Board of Directors via the Board representative for monthly updates.

After completion of the manuscript, it will be submitted to CCMG Board of Directors to seek the feedback from the following CCMG committees: Clinical Practice, E2P2, and Laboratory Practice. It will then go to the CCMG general membership. External feedback will be requested from the Canadian Association of Genetic Counsellors (CAGC) and the document circulated to

the Society of Obstetricians and Gynaecologists of Canada (SOGC), if a mechanism to do so exists, and College of Family Physicians of Canada (CFPC). Patient feedback will also be solicited through family support groups.

Endorsement from CAGC will be requested.

The final manuscript must be submitted to BoD for approval.