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Laboratory Bulletin

DATE:	8 December 2025
TO:	All Zones
FROM:	Molecular Genetics Laboratory, North Sector, Genetics and Genomics, APL
RE:	**REVISED - Update to the Cystic Fibrosis and/or *CFTR*-related Disorders Genetic Test**

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Key Message

- This bulletin replaces the Lab Bulletin "Update to the Cystic Fibrosis and/or *CFTR*-related Disorders Genetic Test" from Sept 2, 2025.
- Molecular genetic testing for cystic fibrosis (CF) and *CFTR*-related disorders has been updated to include 139 pathogenic variants in the *CFTR* gene as the first tier of testing. Criteria for full gene analysis and the polyT tract reporting policy have also been updated. These changes are effective immediately.

How this will impact you

- *CFTR* testing will be performed using a next generation sequencing (NGS) platform which allows further analysis of the *CFTR* gene for specific clinical indications. The test name, ordering criteria, turnaround time and sample types are unchanged.

<u>*CFTR* Genetic Testing Algorithm</u>

- *First tier: CFTR variant panel*
  - A negative *CFTR* panel result significantly *reduces but does not eliminate* the chance that an individual carries one or more *CFTR* variants.
- *Second tier: CFTR full gene analysis*
  - If two cystic fibrosis causing variants were not detected in a symptomatic individual, testing will proceed to second tier testing according to the following criteria.
  - One CF causing variant is detected and patient is:
    - a male with infertility
    - an individual with symptoms of CF or *CFTR*-related disorder where sweat chloride testing
      has not been performed or is normal (e.g. recurrent pancreatitis, bronchiectasis)
    - a fetus with echogenic bowel or parents of fetus with echogenic bowel
  - One or zero CF causing variants are detected and patient is:
    - an individual with abnormal or borderline sweat chloride
    - an Infant with meconium ileus
  - Zero CF causing variants are detected and patient is:
    - the partner of an individual with CF (carries two CF-causing variants, excludes 5T)

The molecular report will indicate what level of analysis was performed.

Retesting of patients is not indicated. For symptomatic patients, ordering providers can contact the laboratory Genetic Counsellors to ensure full *CFTR* analysis was previously performed.

Carrier and familial variant testing:

- Carrier testing is limited to the *CFTR* variant panel.
- Familial variant testing is performed using the *CFTR* variant panel and all variant(s) detected, excluding 5T in the absence of R117H, are reported. If your patient has a family history of CF, provide the name of the relative and a copy of the molecular genetic report. Depending on the variant(s) in the family, additional analysis may be indicated.

PolyT and TG tract lengths:

- The presence of the 5T variant will be reported for all confirmation of diagnosis cases. When 5T is detected, the length of the polyTG tract will also be reported. The polyT and TG tract lengths are not reported in the context of newborn screening, carrier testing or familial variant testing.
- When R117H is identified, the polyT tract length will be reported regardless of the indication for testing.

Newborn Screening

- CF is one of the disorders on the newborn screening panel (https://www.ahs.ca/info/Page9024.aspx). Newborn screening for CF begins with measurement of immunoreactive trypsinogen (IRT) in dried blood spots; when an increased IRT is identified genetic testing using the *CFTR* variant panel is performed. Infants with one panel variant and/or a markedly elevated IRT (≥99.9%ile) will now have full gene analysis. A probable newborn screen for CF indicates that the infant has 2 pathogenic or likely pathogenic *CFTR* variants. An inconclusive newborn screen for CF indicates that the infant has 2 *CFTR* variants, where one or both are variants of uncertain significance (VUS). This will significantly decrease the number of inconclusive CF newborn screens reported. Clinical follow up of infants with probable or inconclusive CF newborn screen results are unchanged. Blood or buccal samples will be required for diagnostic confirmation of infants with probable or inconclusive CF newborn screen results.

Action Required

- Refer to the test directory (Alberta Precision Laboratories | Lab Services), information sheet (Cystic Fibrosis Testing: Information for Ordering Providers)) and variant list (CFTR 139 Variant List Table) for details.

Effective Immediately

Questions/Concerns

- G&G North (Edmonton) MGL Genetic Counsellors at 780-407-1015

Approved by

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