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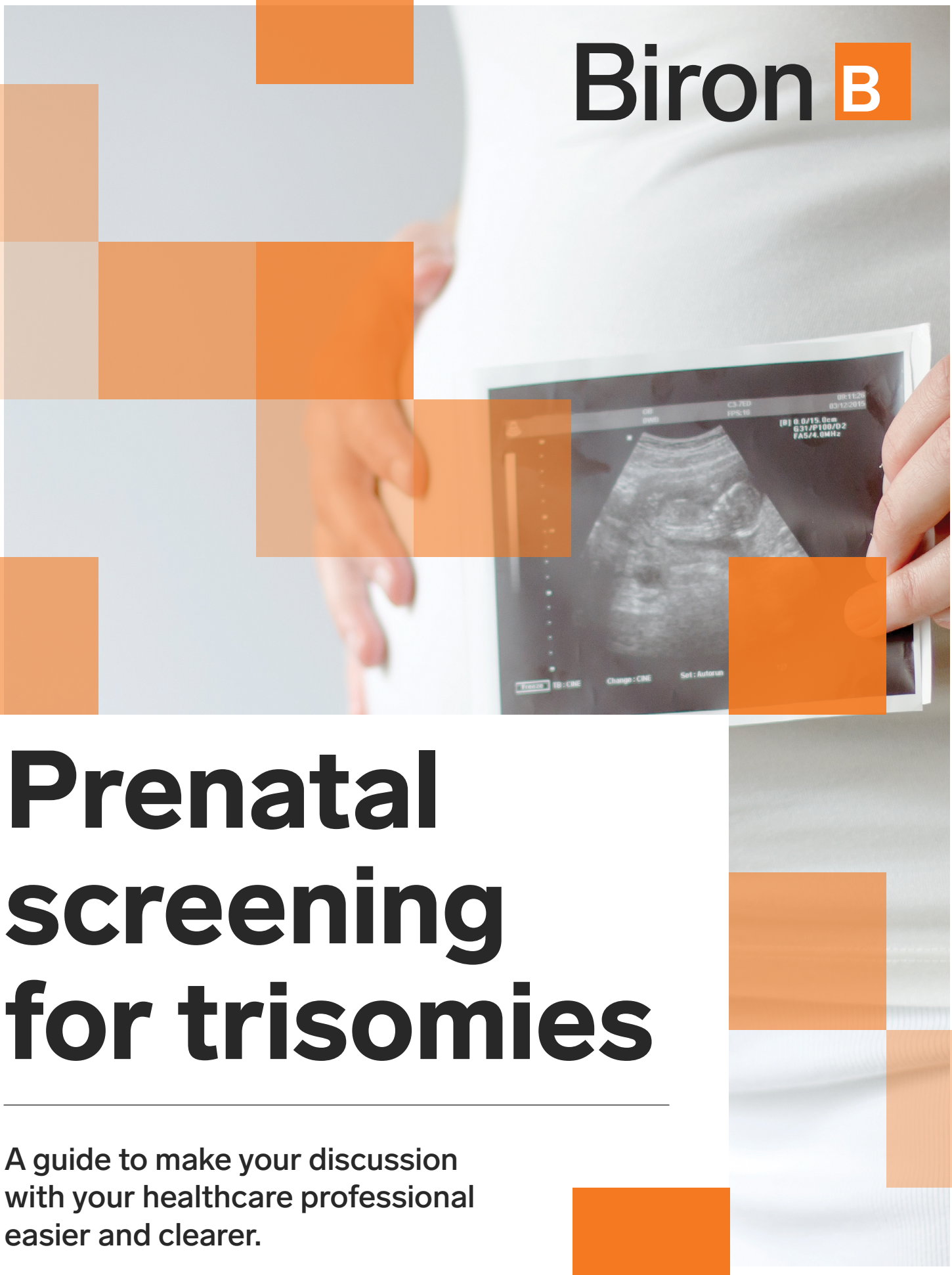

Prenatal screening for trisomies

A guide to make your discussion with your healthcare professional easier and clearer.

Biron

For the mom-to-be

Understanding screening for chromosomal abnormalities in fetal DNA: the Verifi™ test

This discussion guide was designed to help you as you consider prenatal chromosomal abnormalities screening. It is intended to facilitate your discussion with your healthcare professional so you can make an informed choice for you and your baby.

Who is the fetal DNA chromosomal abnormality screening test for?

Regardless of age, any pregnant woman runs the risk of giving birth to a child with one or more chromosomal abnormalities (such as trisomy 21 /Down syndrome). There are several screening options available for you to assess the risk during pregnancy:

- **"Traditional" screening tests, which include various biochemical tests and nuchal translucency ultrasound.**
- **Non-invasive prenatal testing (NIPT) using fetal DNA, such as the Verifi test, which may be accompanied by a nuchal translucency ultrasound.**

These tests are performed at your discretion. It is important for you to fully understand the benefits and implications of each option so you can choose the one that best fits your needs.

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What is the Verifi™ test?

The **Verifi** NIPT test is advanced technology which analyzes fetal DNA in the mother's blood. This test is offered to pregnant women who want a precise assessment of the risk of genetic abnormalities, including trisomy 21, 18 or 13.

Compared to traditional screening tests, NIPT offers several advantages:

→ **a higher detection rate: the test is more sensitive and more reliable;**

→ **a lower false positive rate, reducing the number of unnecessary invasive procedures, such as amniocentesis.**

Here are some questions to ask your healthcare professional:

1. Can the test reveal the sex of my baby?
2. What does the test measure?
3. How do you interpret your results?
4. What is the next step if the test indicates a high risk of abnormalities?

If you would like to take the Verifi test, please bring this Guide and the Requisition Form below to your appointment with your healthcare professional.

Blood sampling at Biron

Once your healthcare professional has completed and signed the enclosed Verifi NIPT Requisition Form, please make an appointment by checking availability online at **biron.com** or by calling **1 800 463-7674**.

Make an appointment

biron.com/NIPT

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For your healthcare professional

Screening for chromosomal abnormalities in fetal DNA: the Verifi™ test

What is Verifi NIPT ?

The **Verifi** test is a genomic non-invasive prenatal screening test designed to detect common chromosomal aneuploidies from the tenth week of gestation, using a simple blood sample. Based on sequencing technology, this test provides accurate information for pregnant women, regardless of their age or the pregnancy's risk factors.

The Verifi test can detect trisomy disorders:

- 21 (Down syndrome)
- 18 (Edwards syndrome)
- 13 (Patau syndrome)

Go to this link for more information: Biron's Neat Little Guide on Trisomy Disorders

Identifying the sex of the fetus and sex chromosome aneuploidy

This test can also reveal the sex of the fetus and the presence of sex chromosome aneuploidy. The sex of the fetus can be communicated if there is no sex chromosome aneuploidy. If a pregnant woman chooses to find out the sex of the fetus, any of these aneuploidies may be detected:

- Monosomy X (Turner syndrome)
- XXX (Triple X syndrome)
- XXY (Klinefelter syndrome)
- XYY (Jacob syndrome)

What does the test measure?

The test does not directly analyze fetal DNA but **maternal placental DNA**.

Even though its performance is superior to traditional integrated biochemical screening, this test is also used only for screening. **If an aneuploidy is detected, it is recommended that an invasive diagnostic test be performed, such as amniocentesis or chorionic villus sampling**.

Test performance

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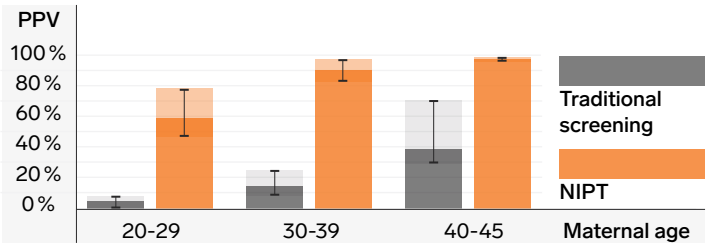
Positive predictive value

Positive predictive value (PPV) refers to the proportion of positive results which are actually positive. PPV depends on fixed variables—the test's sensitivity and specificity—and the prevalence of the trisomy disorders detected. **With the Verifi test, since the prevalence of trisomy disorders rises with maternal age**, PPV also rises. As a result, the PPV for a given trisomy disorder varies from one woman to another.

Because the NIPT has greater specificity than traditional tests, its PPV is also higher[1].

Compared positive predictive values for trisomy 21



1. Bianchi DW, Parker RL, Wentworth J, et al. DNA sequencing versus standard prenatal aneuploidy screening. N Engl J Med. 2014;370(9):799-808.

For **1,000 pregnancies**, there will be **40 times more** unnecessary invasive procedures with traditional screening than with the Verifi test:

Verifi	Traditional screening
Detection rate: 99%+	Detection rate: 95%
False positives: 0.12%	False positives: 4%

Verifi's failure rate

This test has one of the lowest failure rates on the NIPT market (0.6%[2]). This is an important statistic: when a test fails, there is a direct impact on the pregnant woman's care.

The test may fail because the fetal fraction in the mother's blood is too low.

A higher frequency of aneuploidies has been observed in women who had a failed test. As a result, it is recommended that additional investigations be carried out when it is not possible to obtain a result[3].

2. Internal data. Illumina, Inc 2022.
3. Norton ME, Jacobsson B, Swamy GK, et al. Cell-free DNA analysis for noninvasive examination of trisomy. N Engl J Med. 2015: 372(17): 1589-97.

Overview of results summary

Chromosomes	Results	PPV (%)
Chromosome 21	**Positive** (aneuploidy detected)	85.7 %
Chromosome 18	**Negative** (no aneuploidy detected)	
Chromosome 13	**Negative** (no aneuploidy detected)	
Chromosomes sexuels	Predicted sex of fetus: femal	

The fetal fraction is provided in the report.

What do the results mean?

Positive: aneuploidy detected

Screening indicates a high risk of a trisomy disorder, with an associated positive predictive value (PPV).

To confirm the condition, a diagnostic test such as amniocentesis or chorionic villus sampling is required.

Negative: no aneuploidy detected

Screening indicates low risk of a trisomy disorder. However, this results is not a 100% guarantee that there is no chromosomal condition.

How to prescribe the Verifi test?

→ Complete and sign the Verifi test Requisition Form. The form can be used as a prescription.

→ If your patient wishes to know the sex of the fetus, check the **"sex foetal and sexual chromosome aneuploidies"** option on the Verifi test Requisition Form. Your patient will not be able to add this option later without your authorization.

In this document, words with the masculine gender refer to both men and women.

Verifi™ Prenatal Test

Biron

Non-Invasive Prenatal Genomic Test Request Form (fetal DNA)

Important: The gestational age must be at least 10 weeks 0 days at the time of blood collection.

Patient Informations

Last Name: _____ First Name: _____

DOB: YYYY / MM / DD Sexe: _____ N° Health insurance: _____ Phone: _____

Health Care Provider Informations

Full Name: _____ License N°: _____

Clinic: _____ Phone: _____ Fax: _____

Adress: _____

(Civic N°, Street's Name) (City) (Province) (Postal Code)

Email: _____ Signature: _____

Additional reporting to: _____ Email: _____

Clinical Informations

Gestational Age: Weeks: _____ Days: _____ As estimated on: YYYY / MM / DD

Type of Pregnancy: ☐ Singleton ☐ Twin Maternal weight: _____ ○ kg ○ lbs

Dating Method - MUST CHOOSE ONE

- ☐ Last Menstrual Period
- ☐ Date of Implantation (IVF)
- ☐ Crown Rump Length (CRL)
- ☐ Other: _____ (Specify)

Verifi Prenatal Test - CHECK ONE OF THE CHOSEN OPTIONS (chromosomes 21, 18, 13)

Singleton Pregnancy

☐ **Option Available**

Sex foetal and sexual chromosome aneuploidies (MX, XXX, XXY et XYY)

Twin Pregnancy

☐ **Option Available**

Presence of Y chromosome

Patient Consent

- ☐ I certify that I have read and understood the information on the reverse side of this form and have had the opportunity to ask questions and discuss the capabilities, limitations and potential risks of the test(s) with my health care provider or a designated representative of my health care provider.
- ☐ I consent to this test and will discuss the results and appropriate medical management with my health care provider.
- ☐ I consent to the remaining portion of my sample being used by Illumina for laboratory validation studies, process development, quality control, and/or other research purposes.
- ☐ I consent to the use and disclosure of my personal information for the purposes set out and in accordance with this form.

Non-invasive prenatal testing (NIPT) based on cell-free DNA analysis from maternal blood is a screening test. Screening tests are not diagnostic or definitive. Because there is a small possibility that a screening result might be incorrect, it is important to talk to your health care provider to determine if further testing is needed.

The Verifi Prenatal Test is validated for singleton and twin pregnancies. Verifi Prenatal Test is validated for singleton pregnancies with gestational age of at least 10 weeks 0 days.

Patient Signature: _____ Date: YYYY / MM / DD

Book an appointment

biron.com/pregnancy | 1 800 463-7674

Patient Informed Consent

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Introduction: This form describes the benefits, risks, and limitations of this screening test. You should seek pre test counselling by an experienced health care provider prior to undergoing this test. Read this form carefully – and ask any questions you may have to your health care provider— before making your decision about testing.

Purpose: The purpose of the Verifi Test is to screen your pregnancy for certain chromosomal abnormalities, also known as" aneuploidies." the test gives information about whether there may be extra copies (trisomy) of chromosomes 21, 18, and 13, and the option to know if there is an extra copy of a sex chromosome (X or Y), and/or a missing copy of sex chromosome (MX). Fetal sex may also be reported.

For chromosomes 21, 18, and 13, the Verifi Test is validated in singleton and twin pregnancies. In twin pregnancies, sex chromosome testing can only screen for the presence or absence of the Y chromosome, and not for extra or missing sex chromosomes. Verifi can be performed as early as 10 weeks 0 days gestational age.

Consult your health care provider if you would like more information about this screening test, including risks, limitations, performance data, error rates, descriptions of the conditions being screened, and what these results may mean to your pregnancy.

How This Test Works: This test screens for specific chromosomal abnormalities by looking at the DNA (genetic material) in your blood. The sample of blood includes a combination of both your DNA and the DNA from the pregnancy. A technology called massively parallel sequencing is used to count the amount of DNA from each test chromosome and/or from specific regions of chromosomes. The laboratory then uses an analysis method to determine if each of the conditions you have elected to test for is likely to be present or absent.

Sex Of Pregnancy: Depending upon the option you and your health care provider elect, the test results may include the sex of the pregnancy. If you do not wish to know the sex, please tell your health care provider not to disclose this information to you. Depending upon the test ordered, you may not be able to prevent learning the sex of your pregnancy.

In rare instances, incorrect sex results can occur.

Limitations Of The Test: These are screening tests that look only for specific chromosomal abnormalities. This means that other chromosomal abnormalities may be present and could affect your pregnancy. A "No Aneuploidy Detected" result does not guarantee a healthy pregnancy or baby and does not eliminate the possibility that your pregnancy may have birth defects, genetic conditions, or other conditions, such as open neural tube defects or autism.

There is a small possibility that the test results might not reflect the chromosomes of the fetus, but may reflect chromosomal changes of the placenta (confined placental mosaicism, CPM) or of you (maternal chromosomal abnormalities). While these tests are not designed to assess your health, in some cases, information about your health may be revealed directly or indirectly (e.g., when combined with other information). Examples include maternal XXX, sex chromosome status or benign or malignant maternal neoplasms. In a twin pregnancy, the status of each individual fetus cannot be determined.

These tests, like many tests, have limitations, including false negative and false positive results. This means that the chromosomal abnormality being tested for may be present even if you receive a negative result (this is called a 'false negative'), or that you may receive a positive result for the chromosomal abnormality being tested for, even though the abnormality is not actually present (this is called a 'false positive').

In the case of a twin pregnancy, the presence or absence of Y chromosome material can be reported. The occurrence of sex chromosome aneuploidies cannot be evaluated in twin pregnancies. In the case of a vanishing twin, the test result may reflect the DNA of the vanishing twin, leading to a higher probability of false positive or false negative results.

No irreversible clinical decisions should be made based on these screening results alone. If definitive diagnosis is desired, chorionic villus sampling or amniocentesis would be necessary. In some cases, other testing may also be necessary. Some rare chromosomal aneuploidies may only occur in mosaic form. Clinical consequences depend on the chromosome involved and can not be predicted prenatally.

Consult your health care provider for more information about your results and what they may mean for your pregnancy, what options you will have for further testing, and whether additional testing is recommended for you based on your clinical history.

Test Procedure: A tube of your blood will be drawn and sent to Verinata Health, Inc., a wholly owned subsidiary of Illumina, Inc. (a Biron Medical Laboratory Inc. "Bironpartner), which will then analyze your blood.

Physical Risks: Side effects of having blood drawn are uncommon, but may include dizziness, fainting, soreness, bleeding, bruising, and, rarely, infection.

Discrimination Risks: Genetic information could be used as a basis of discrimination. To address concerns regarding possible health insurance and employment discrimination, some countries, U.S. states and the U.S. government have enacted laws to prohibit genetic discrimination in those circumstances. The laws may not protect against genetic discrimination in other circumstances, such as when applying for life insurance or long-term disability insurance.

Talk to your health care provider or genetic counselor if you have concerns about genetic discrimination prior to testing.

Pregnancy Outcome Information: Collecting information on your pregnancy after testing is part of a laboratory's standard practice for quality purposes and is required in several states. As such, our partner Illumina or its designee may contact Biron Laboratory to obtain this information.

Secondary Findings: In the course of performing the analysis for the indicated tests, information regarding other chromosomal alterations, also known as "secondary findings" may become evident. Our policy is to NOT REPORT on any secondary findings that may be noted in the course of analyzing the test data.

Privacy: Test results are kept confidential. Your test results will only be released in connection with the testing service, to your health care provider, his or her designee, other health care providers involved in your medical care, or to another health care provider as directed by you (or a person legally authorized to act on your behalf) in writing, or otherwise as required or authorized by applicable law.

Cross-Border Data Transfer: If you are from outside the United States, your specimen and associated health information will be sent to the United States in order for the testing to be completed. As part of the testing, additional health information about you will be created and maintained. Your country may consider the legal privacy protections in the United States to be inadequate.

Use Of Information And Leftover Specimens: Pursuant to best practices and clinical laboratory standards, leftover de-identified specimens (unless prohibited by law), as well as de-identified genetic and other information learned from your testing, may be used by Illumina or others on its behalf for purposes of quality control, laboratory operations, laboratory test development, and laboratory improvement. All such uses will be in compliance with applicable laws. Leftover specimens will be destroyed either within sixty (60) days of the date on which the Sample was taken or following completion of the Test Services, whichever occurs later.

Research: We may use your leftover specimen and your health information, including genetic information, in a de-identified form (unless otherwise allowed by applicable law) for research purposes. Such uses may result in the development of commercial products and services. You will not receive notice of any specific uses and you will not receive any compensation for these uses. All such uses will be in compliance with applicable law. This does not apply to leftover specimens collected from New York State.

Test Results: Your test results will be sent to the health care provider. Test results will be sent directly to the healthcare provider who prescribed the test.

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To book an appointment

biron.com/grossesse | 1 800 463-7674

About Biron Health Group

We support you every step of your healthcare journey, making available a variety of services and tests to help your doctor make the right diagnosis.

Our healthcare specialists are there for you, offering lab tests (blood draws and sample collections) and screening/medical imaging exams (MRI, ultrasound, and infiltration). Our team also looks after other aspects of your health: sleep care and disorders (such as sleep apnea), workplace health, and genetics.

Founded in 1952, our family-owned company proudly serves Canadians through its 120 service centres and clinics in Quebec and New Brunswick.

Biron: for everything important, over a full lifetime.