LifeLabs®

INSIDE Diagnostics ONTARIO

AUGUST 2021

THE DIAGNOSTIC NEWSLETTER
FOR **HEALTHCARE PROVIDERS**

PANORAMA™ NON-INVASIVE PRENATAL TESTING (NIPT): PRENATAL SCREENING YOU AND YOUR PATIENTS CAN RELY ON

Offered by LifeLabs since 2013, Non-Invasive Prenatal Tests (NIPT) like Panorama™ provide future parents with reassurance, and peace of mind by screening for common chromosome conditions, with greater accuracy.

Panorama™ is supported by LifeLabs' bilingual genetic customer care experts, Canadian board certified genetic counsellors, and Canadian accredited laboratory geneticists. If the NIPT results indicate an increase in the risk of a chromosome condition in pregnancy, the genetic counsellors will proactively contact the ordering healthcare provider.

HOW PANORAMA™ NON-INVASIVE TESTING WORKS

Traditional maternal serum screening for chromosome differences is based on analyzing certain hormones and proteins present in the mother's blood from pregnancy, with a sensitivity of ~90% and a false positive rate of ~5%. With NIPTs like Panorama™, screening for chromosome anomalies is available by analyzing cell free DNA, which is made up from maternal and placental sources, from a simple maternal blood sample as early as 9 weeks gestation, and determines which pregnancies are at higher risk with a >99% sensitivity and <1% false positive rate.

The non-invasive nature of NIPTs means no risk of miscarriage (unlike invasive diagnostic tests, such as CVS or amniocentesis). The high accuracy of Panorama™ has allowed it to be used as an MOH-covered follow-up screen to positive results from traditional maternal serum screens in Ontario, enabling a significant reduction in invasive testing performed.

HOW LIKELY IS IT THAT YOUR PATIENT'S BABY HAS A CHROMOSOME CONDITION?

Chromosome conditions (or aneuploidies) are not typically inherited, and increase in frequency with the mother's age. As women get older, there is a higher chance that their child will have a chromosome difference, but aneuploidies can occur at any age. Not all chromosomal conditions are linked to maternal age. Some happen completely by chance, even in younger women without a family history.

Aneuploidies such as Trisomy 21 (Down syndrome), Trisomy 18 (Edward syndrome) and Trisomy 13 (Patau syndrome) impact the growth and development of the fetus and increase the chance of miscarriage. Many parents find learning about the possibility of genetic differences helps by either providing them with information to make informed, but difficult decisions about pregnancy, or by preparing them in planning for the care of their baby when they are born.

THE PANORAMA™ DIFFERENCE

Unlike other NIPTs, Panorama™ screens for genetic conditions as early as 9 weeks.

Another differentiator is the methodology used: Panorama™ is the only NIPT that is entirely SNP (single nucleotide polymorphisms) based. Panorama™ uses more than 13,000 SNPs to analyze the difference between the mother and baby's DNA, meaning more reliable results for the pregnancy and enabling more conditions tested (like triploidy).

By request, Panorama™ also tells your patient the sex of their baby. If they are pregnant with twins, it can tell them if the twins are monozygotic (identical) or dizygotic (fraternal), which cannot always be easily differentiated on ultrasound. A 2021 study by Benn and Rebarber, "Non-invasive prenatal testing in the management of twin Pregnancies", further emphasizes the value of SNP-based NIPT in twin pregnancies.

WHEN WILL MY PATIENT RECEIVE THEIR RESULTS?

Results are available within 7-10 calendar days from when the lab receives your patients' sample, making it one of the fastest prenatal screens available.

COMPARING PANEL OPTIONS

Panorama™ NIPT screens a fetus for chromosome abnormalities that include whole extra or missing chromosomes for chromosomes 13, 18, 21, X and Y. Panorama™ can also screen for fetal sex, microdeletions (small missing sections of a specified chromosome) and zygosity in twin pregnancies.

HOW TO ORDER

Requisition & Patient Consent Forms: English | French

Ministry-Funded Requisition for Panorama™ (Ontario Only)

Panorama™ Requisition with Opt-in Cord-Blood Bundle Rebate

To learn more visit LifeLabsGenetics.com/Panorama.

Panel Name	For average risk women in Ontario	For high risk women in Ontario	Testing includes
Basic Prenatal Panel	$550	No cost	Includes Trisomy 21, 18, 13, Monosomy X, sex chromosome trisomies, triploidy, complete molar pregnancy and fetal sex (optional)
Extended Panel	$745	+$195	Basic Prental Panel, plus 22q.11.2 deletion syndrome [DiGeorge Syndrome]
Full Prenatal Panel	$795	+$245	Basic Prental Panel, plus 5 microdeletions (22q.11.2 deletion syndrome [DiGeorge syndrome], 1p36 deletion syndrome, Angelman syndrome, Cri-du-chat syndrome, Prader-Willi syndrome)

NEW AND IMPROVED ALLERGY TEST REQUISITION NOW AVAILABLE

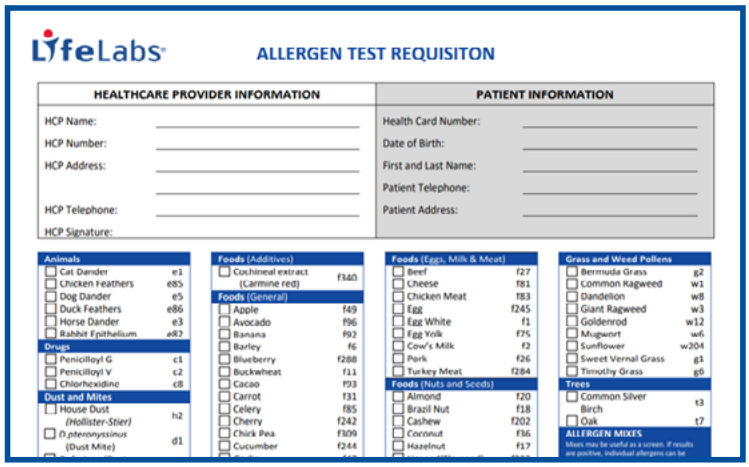
A. NEW AND IMPROVED ALLERGY TEST REQUISITION

LifeLabs has a new and improved Allergy Test Requisition. It can be found on the website at: www.lifelabs.com/healthcare-providers/requisitions/?myProvince=on

New and improved features:

- More user-friendly
- Larger font
- Less clutter
- Updated test menu

Screen shot of the new and improved Allergy Test Requisition (partial view):


LifeLabs ALLERGEN TEST REQUISITON

HEALTHCARE PROVIDER INFORMATION

HCP Name:
HCP Number:
HCP Address:
HCP Telephone:
HCP Signature:

PATIENT INFORMATION

Health Card Number:
Date of Birth:
First and Last Name:
Patient Telephone:
Patient Address:

Animals: Cat Dander e1, Chicken Feathers e85, Dog Dander e5, Duck Feathers e86, Horse Dander e3, Rabbit Epithelium e82
Drugs: Penicilloyl G c1, Penicilloyl V c2, Chlorhexidine c8
Dust and Mites: House Dust (Hollister-Stier) h2, D.pteronyssinus (Dust Mite) d1
Foods (Additives): Cochineal extract (Carmine red) f340
Foods (General): Apple f49, Avocado f96, Banana f92, Barley f6, Blueberry f288, Buckwheat f11, Cacao f93, Carrot f31, Celery f85, Cherry f242, Chick Pea f309, Cucumber f244
Foods (Eggs, Milk & Meat): Beef f27, Cheese f81, Chicken Meat f83, Egg f245, Egg White f1, Egg Yolk f75, Cow's Milk f2, Pork f26, Turkey Meat f284
Foods (Nuts and Seeds): Almond f20, Brazil Nut f18, Cashew f202, Coconut f36, Hazelnut f17
Grass and Weed Pollens: Bermuda Grass g2, Common Ragweed w1, Dandelion w8, Giant Ragweed w3, Goldenrod w12, Mugwort w6, Sunflower w204, Sweet Vernal Grass g1, Timothy Grass g6
Trees: Common Silver Birch t3, Oak t7
ALLERGEN MIXES

ALLERGEN TEST MENU

The majority of the allergen test menu is unchanged. Additional improvements and clarifications include the following:

Enhancements:

1. Milk is now listed as Cow's milk;
2. Linseed is now listed with its common name "Linseed (Flaxseed)";
3. Dust mites are now listed by species name;
4. Peanut, hazelnut, egg and cow's milk components have been moved to a newly developed Allergy Components requisition (see details below);

New additions:

5. Cochineal extract (carmine red), a red dye used in food and cosmetics, has been added to the Foods (Additives) section;
6. Chlorhexidine, an antiseptic agent, has been added to the Drugs section;

Removed:

7. Ampicilloyl and amoxicilloyl have been removed due to the product no longer being available from the manufacturer at this time;
8. Food mixes fx1 (nuts), fx2 (shellfish) and fx5 (mixture) have been removed to align with clinical recommendations (BC Society of Allergy and Immunology) in an effort to discourage unnecessary dietary restrictions, particularly in children. As an alternate, consider ordering individual specific IgE to allergens included in these mixes, which are already listed on the requisition. These include: peanut, hazelnut, brazil nut, almond and coconut; fish, shrimp, mussel, tuna and salmon; egg white, milk, wheat and soya bean.

Food mixes are still available to order by using the 'Miscellaneous Unlisted Allergens' section of the requisition.

B. NEW ALLERGY COMPONENTS REQUISITION WITH EXPANDED TEST MENU FOR ALLERGY SPECIALISTS

A second and separate Allergy Components Requisition has been developed featuring commonly ordered allergy components as well as an expanded test menu for allergy components (it can be downloaded here: www.lifelabs.com/healthcare-providers/requisitions/?myProvince=on.) This is designed for Allergists, who specialize in the clinical utility of these various tests. The expanded test menu

includes allergy components for: cashew and walnut; soy, apple, alpha-gal and wheat; birch, weed-, tree- and grass-pollens; dust mites; dog, cat and horse. Peanut, hazelnut, egg and cow's milk components are now listed in this new requisition.

LEARN MORE ABOUT ALLERGY TESTING

Allergen testing measures immunoglobulin IgE targeted to specific antigens, as listed on the requisition. For example, a test for Common Wasp (yellow jacket), measures a patient's IgE targeted to known antigenic proteins from Yellow Jacket Wasp as a result of exposure. These IgE are commonly referred to as allergen specific IgE.

Results from allergen specific IgE are quantitative and are currently reported in a range of 0.35 to 100 kU/L. The lower limit of the reporting range will be expanded to 0.10 kU/L in the near future.

CLINICAL SIGNIFICANCE OF ALLERGY TESTING

Allergen specific IgE test results can guide health care professionals in their clinical investigation of IgE mediated allergy in patients. Allergen specific IgE testing is useful both in the initial investigation of allergy, as well as monitoring patients with a diagnosis.

Allergen specific IgE testing should not be used in isolation for the diagnosis of allergy. Both positive and negative test results should always be interpreted within the context of the patient's allergy history. A negative allergen specific IgE test result does not necessarily exclude allergy to the tested allergen. Similarly, a positive allergen specific IgE test result does not necessarily rule in allergy to the tested allergen. Also, allergen specific IgE levels do not necessarily correlate with symptom severity.

ALLERGY TESTING RESOURCE COMING SOON AT LIFELABS.COM

A Physician Ordering Guide will soon be available on a dedicated LifeLabs Allergens webpage to further assist health care professionals interested in ordering Allergens. See www.LifeLabs.com for updates and notifications.

TIPS FOR ORDERING

- Please see the Allergy Test Requisition www.lifelabs.com/healthcare-providers/requisitions/?myProvince=on for a variety of commonly ordered allergens. Allergen specific IgE are listed in categories.
- For allergens not included on the requisition, please list the name, as well as specific details for allergens with more than one species or type, such as drugs, mold and yeast, in the 'Miscellaneous Unlisted Allergens' section of the requisition to ensure the correct allergen is tested. For a full selection of orderable allergens, see the product catalogue in the LifeLabs Test Directory tests.lifelabs.com/Laboratory_Test_Information/Search.aspx, search for Allergen (Unlisted on requisition), and then select the "Forms" tab.

For Inquires, please contact LifeLabs Customer Care Centre 1-877-849-3637. We welcome your feedback!

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DISCONTINUATION OF URINE UROBILINOGEN/BILIRUBIN TEST

IN JUNE 2021, LIFELABS DISCONTINUED URINE UROBILINOGEN/BILIRUBIN TESTING.

This decision was made based on:

- Poor analytical performance of this test, primarily due to a high proportion of false negative results due to instability of bilirubin and urobilinogen to temperature and light, and less frequently, false positive results due to urine colour[1-2].
- Very low number of requests for this test at LifeLabs (eight or less specimens per month).
- Availability of serum liver function tests with superior sensitivity, and better analyte stability.

Please note that if you order Urine Urobilinogen/Bilirubin after this date, the specimen will not be processed. Please request serum liver function test(s) instead, as clinically appropriate (including ALT, AST, GGT and/or Total Bilirubin).

For further information, please contact the LifeLabs clinical biochemist below, or LifeLabs Customer Care Centre at 1-877-849-3637.

We welcome your feedback!

REFERENCES:

1. Foley KF, Wasserman J: Are unexpected positive dipstick urine bilirubin results clinically significant? A retrospective review. *Laboratory Medicine* 2014; 45: 59.
2. Binder L, Smith D, Kupka T and al.: Failure of prediction of liver function test abnormalities with the urine urobilinogen and urine bilirubin assays. *Archives of Pathology and Laboratory Medicine* 1989; 113: 73.

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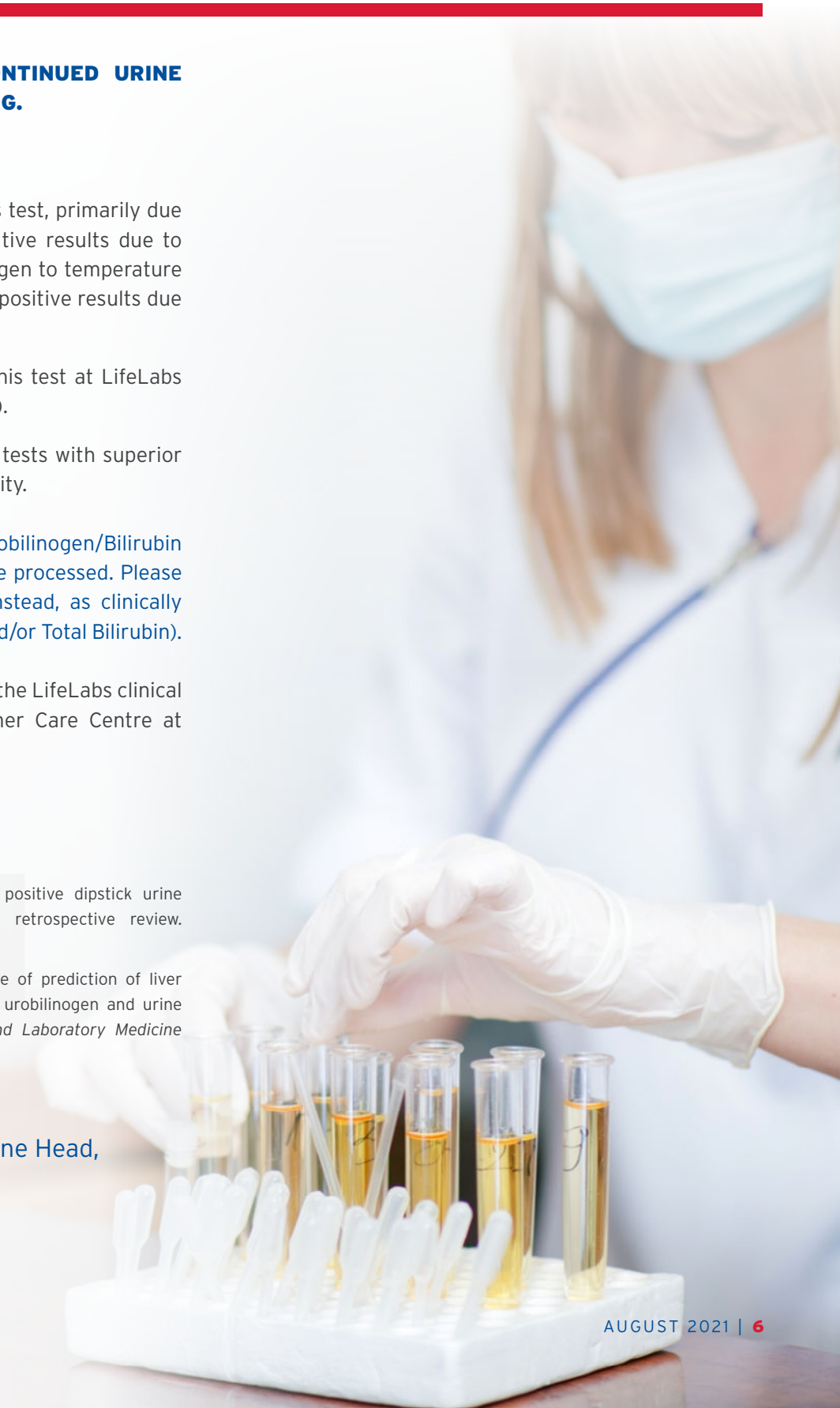

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CASE STUDIES: AND THE ANSWER IS....?
URINE BROAD SPECTRUM TOXICOLOGY SCREEN INTERPRETATION

CASE DESCRIPTION:

The Broad Spectrum Toxicology (BST) report for a 38 year old female is shown below. The test detected cocaine metabolite in patient's urine sample. When asked about this report, the patient claims that she just returned from her trip to Madrid on Oct 19th, 2020. While in Madrid, she drank some tea and experienced headache, nausea, confusion, increased heart rate and flushing following ingestion. She is convinced that the tea contained cocaine. She brought some of the tea bags home with her, and wants the physician to send it to the lab for testing. This patient's medical history is otherwise unremarkable. She is not prescribed any medication and claims she does not use illicit drugs.

Example of LifeLabs Urine BST report:

BROAD SPECTRUM TOXICOLOGY SCREEN

OPIOIDS	NOT DETECTED
AMPHETAMINES	NOT DETECTED
BENZODIAZEPINES	NOT DETECTED
ANTI DEPRESSANTS	NOT DETECTED
ANTI-PSYCHOTICS	NOT DETECTED
CANNABINOIDS	NOT DETECTED
OTHER	DETECTED **

Benzoylecgonine

COMMENT:

Benzoylecgonine is the main metabolite of cocaine.

NOTE:

Testing performed by liquid chromatography tandem mass spectrometry - LC-MS/MS.

WHAT SHOULD THE PHYSICIAN'S RESPONSE BE?

A. Two weeks have passed since she returned from Madrid. Cocaine should not be detectable after two weeks.

B. This won't work. The Broad Spectrum Toxicology Test is not validated for tea.

C. This won't work. The Broad Spectrum Toxicology Test detects cocaine metabolite.

D. Let's call LifeLabs and ask them to test the tea.

ANSWER:

All of the above are valid answers!

A. The window of detection for cocaine is approximately 2 - 4 days[1]. The patient claims she returned from Madrid on Oct 19th, 2020 and the urine specimen was collected two weeks later on Nov 2nd, 2020. Given the short window of detection for benzoylecgonine, it is highly unlikely that the source of cocaine was from this patient's recent Madrid trip.

B. Our BST test is a lab-developed LC-MS/MS test. As a lab-developed test, we subject it through rigorous validations to ensure performance characteristics are fit for use. One of these validations includes testing performance characteristics in different specimens. Our BST test is only validated for urine specimens. We cannot reliably provide a result from liquid produced from a tea bag nor can we process tea leaves through our BST test.

C. Cocaine is metabolized to benzoylecgonine through deesterification in the liver[2]. Benzoylecgonine is the major metabolite of cocaine that is detectable in urine. Our BST test specifically detects benzoylecgonine. Even if the tea contained cocaine, the BST test will not detect the parent drug, leading to a false negative result.

D. If you have any questions about your patient's lab report, please feel free to call our Customer Care Centre at 1-877-849-3637 and they will connect you with our Medical/Scientific staff who will be able to provide assistance with result interpretation.

REFERENCES:

1. Medications for Opioid Use Disorder: For Healthcare and Addiction Professionals, Policymakers, Patients, and Families [Internet]. Rockville (MD): Substance Abuse and Mental Health Services Administration (US); 2018. (Treatment Improvement Protocol (TIP) Series, No. 63.) [Table, Urine Drug Testing Window of Detection]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK535272/table/t.33/
2. Shimomura, E.T. (2019). 'Cocaine, Crack Cocaine and Ethanol: A Deadly Mix.' In A. Degupta (ed.), *Critical Issues in Alcohol and Drugs of Abuse Testing* (2nd ed., pgs 215-224). Academic Press.

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