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Rapid Fetal Fibronectin (fFN)- Troy

Document Type: Procedure

I. PURPOSE AND OBJECTIVE:

To instruct technologists in the operation of the Rapid Fetal Fibronectin assay (fFN).

II. CLINICAL SIGNIFICANCE:

A. The Rapid fFN test is to be used as an aid in assessing the risk of preterm delivery in less than or equal to 7 to 14 days from the time of cervicovaginal sample collection in pregnant women with signs and symptoms of early preterm labor, intact amniotic membranes and minimal cervical dilation (< 3 cm), sampled between 24 weeks, 0 days and 34 weeks, 6 days gestation.

B. The Rapid fFN test is further indicated for use in conjunction with other clinical information as an aid in assessing the risk of preterm delivery in less than or equal to 34 weeks, 6 days when a cervicovaginal sample is obtained during a routine prenatal visit between 22 weeks, 0 days and 30 weeks, 6 days of gestation in women with a singleton pregnancy.

III. SPECIMEN COLLECTION AND HANDLING:

A. Specimen Collection

1. Obtain the specimen using the Hologic Specimen Collection Kit.
   The specimen should be obtained from the posterior fornix of the vagina during a speculum examination. The polyester-tipped swab provided in the Specimen Collection Kit should be inserted into the vagina and lightly rotated across the posterior fornix for approximately 10 seconds to absorb the cervicovaginal secretions.
2. Once the specimen is obtained, carefully remove the swab from the vagina and immerse the swab tip in the tube of buffer provided with the Specimen Collection Kit.

3. Break the shaft (at the score) even with the top of the tube. Align the shaft with the hole inside the tube cap and push down tightly over the shaft, sealing the tube.
4. Write the patient's name and any other identifying information required on the tube label.

B. Specimen Storage and Transport:

1. Specimens that are not tested within eight (8) hours of collection must be stored refrigerated at 2 to 8°C and assayed within three (3) days of collection, or frozen and assayed within three (3) months to avoid degradation of fetal fibronectin. Store appropriately and avoid extreme temperatures.
2. Once the test has been ordered, quickly transport the specimen to the laboratory. Exposure of the specimen to heat for even a short period of time can be detrimental. It is best to keep the specimen cool whenever possible.
3. After testing, store specimen tube in the daily specimen rack.

C. Unacceptable Specimens

1. Specimens collected in or by any sample device other than the Hologic Specimen Collection Kit.
2. Specimens with insufficient volume for testing.
3. Specimens received unlabeled.
4. Specimens which were not frozen and received > 3 days after the sampling date.
5. Frozen specimens older than 3 months from the sampling date.
6. Specimens received at temperatures > 25°C.
7. Specimens subjected to more than one freeze-thaw cycle.
8. Specimens received after 8 hours from time of collection that have not been refrigerated or frozen.
9. Bloody specimens.

IV. REAGENTS:

A. Rapid fFN for the TLi_{IQ} System, Catalog No: 01200

1. **Rapid fFN Cassettes:** 26 cassettes containing all necessary reagents (murine monoclonal anti-fFN antibody conjugated to blue microspheres, goat polyclonal anti-human fibronectin antibody, and goat polyclonal anti-mouse IgG antibody) dried onto membranes. Each cassette contains a desiccant and is sealed in a foil pouch.
    a. The shelf life of the Rapid fFN Cassette is 18 months from the date of manufacture. Unopened cassettes may be used until the expiration date printed on the foil pouch and the box containing the pouched cassettes.
    b. Once the foil pouch is opened, the Rapid fFN Cassette should be used immediately.

c. The Rapid fFN Cassette should be stored at room temperature (15 to 30°C / 59 to 86°F).

B. Rapid fFN Control Kit, Catalog No: 01166

1. Rapid fFN Positive Control: 1.2 mL (0.090-0.100 µg/mL fFN)
2. Rapid fFN Negative Control: 1.2 mL (<0.020 µg/mL fFN)
    a. The shelf life of the Rapid fFN Control Kit is one year from the date of manufacture. Unopened controls may be used until the expiration date printed on the bottle.
    b. **Once opened, they should be used within 6 months.** However, controls should not be used if they are cloudy or discolored.
    c. The Rapid fFN Control Kit should be stored refrigerated (2 to 8°C).

V. EQUIPMENT:

A. TLi_{IQ} System, Catalog No: 01202 - TLi_{IQ} Analyzer and Printer The TLi_{IQ} Analyzer and Printer should be operated at room temperature (18 to 30°C /64 to 86°F).

B. TLi_{IQ} QCette, Catalog No: 01175 The TLi_{IQ} QCette should be stored at room temperature (15 to 30°C / 59 to 86°F).

VI. SUPPLIES:

A. Pipettor

B. 200 ml pipette tips

VII. CALIBRATION:

A. Setting Calibration for a Rapid fFN Cassette Lot – **Performed with each new lot of cassettes.**

1. Select Option 2 (SET CALIBRATION) from the Main Menu of the analyzer.
2. Enter the Employee ID number and press ENTER.
3. Enter the cassette lot number. All letters and numbers must be entered. Enter the number that corresponds to the correct letter and use the up and down arrows to scroll to the correct letter. Press ENTER when completed.
4. Enter the Calibration Code provided on each box of cassettes. The calibration code consists of two letters followed by two numbers. If the code is not entered correctly or does not match the cassette lot number that has been entered, the analyzer will request that the code be re-entered. This calibration code will be used for all cassettes of that lot number.
5. When calibration is complete, the result will be displayed on the analyzer screen and the printed label as SYSTEM CALIBRATED.
6. Press ESC to return to the Main Menu.

VIII. IQCP QUALITY CONTROL PLAN:

The Quality Control Plan defines all aspects of the test system monitored based on potential errors identified during the risk assessment. The components of the quality control plan must meet regulatory and College of American Pathologists (CAP) accreditation requirements and be in compliance with the manufacturer instructions an recommendations, at minimum. The quality control plan must control the quality of the test process and ensure accurate and reliable test results.

A. Quality Controls (number, types and frequency) and acceptability criteria:

1. Internal controls check for:
    a. A threshold level of signal at the procedural control position.
    b. Proper sample flow across the Rapid fFN cassette.
    c. The absence of conjugate aggregation.
    d. Proper function of the analyzer hardware.
    e. Internal controls are performed with each test.
    f. These QC results will print with the patient test results.
2. External Controls:
    a. Liquid controls will be performed once at least every 30 days.
    b. When a new lot number or shipment is received.
    c. Liquid controls should be performed by newly trained operators.
    d. Liquid control results are recorded on the fFN maintenance log.
3. QC-ette
    a. The TLi_{IQ} QCette is a quality control device to verify that the TLiIQ analyzer performs within specification.
    b. TLi_{IQ} QCette will be tested every 24 hours or prior to testing patients if it has not been tested in the past 24 hours.
    c. Results print and are recorded on a worksheet with the performing Tech's ID.

B. Documentation of Complaints and Testing Errors (preanalytic, analytic and post analytic):

1. Documentation of testing errors or specimen rejections will be recorded on the testing log.
2. Complaints or serious safety errors can also be documented via the Quality and Safety Report (QSR) system.

C. Monitoring of the testing environment and reagents:

1. Rapid fFN cassettes and the TLi_{IQ} QCette device are stored at room temperature (15-30°C).
2. Rapid fFN liquid QC is stored refrigerated (2-8°C).
3. Temperatures for refrigerators and room temperature are monitored by the TempTrak system.

D. Specimen Quality:

1. Specimens not collected with the approved collection kit will be rejected.
2. Visual inspection for large amounts of mucus, blood or other foreign material will be performed by the operator prior to running each test. Bloody specimens are not acceptable for testing.
3. If sample quality does not meet the standards as determined by the device during testing, results will print as FAIL or INVALID and the sample must be tested with another cassette and 200µL of sample.
4. If there is not enough sample for re-testing the test must be canceled as Quantity Not Sufficient (QNS).

E. Instrument Calibration, Maintenance, and Function Checks:

1. Instrument calibration is performed with each new Rapid fFN cassette lot.
2. Daily maintenance includes recording the cassette lot number and running the .
3. Function checks are automatically performed with each patient as internal QC.

F. Training and Competency of Testing Personnel:

1. Training is completed with a training checklist when a new tech is trained on the Rapid fFN procedure.
2. Competency assessment occurs in accordance with system Competency Assessment Policy.

G. Provisions for Multiple Identical Devices, Variations in Use of the Test System:

1. The Rapid fFN test is a cassette-based test that is single use.
2. Each cassette has an internal control.
3. Each lot number is validated with external controls as described above.
4. The back-up system for Beaumont Troy is William Beaumont University Hospital, Royal Oak.

IX. IQCP:Quality Assessment Monitoring

Ongoing quality assessment monitoring ensures that the quality control plan is effective in mitigating the identified risks for the IQCP. If ongoing assessments identify failures in one or more components of the quality control plan, the laboratory must investigate the cause and consider if modifications are needed to the quality control plan to mitigate potential risk. The CAP requires the following for quality assessment monitoring:

A. Monthly Review of Quality Control, Instrument Maintenance and Function Check Data

1. The maintenance log for the TLi_{IQ} analyzer is reviewed and signed monthly by the Lead Medical Technologist.
2. The maintenance log includes a check for running the daily Q-Cette as well as running the liquid controls monthly (at least every 30 days) and with each new lot number.

B. Evaluation of Errors Relating to Pre,Post and Analytic Phases of the Testing Process:

1. The occurrence and a description of errors are recorded and available for review on the monthly function check.
2. Additional errors may be documented in the LIS and made available via the hospital QSR system.
3. These are checked using the Monthly Function Check Log.

C. Review of Complaints from Clinicians Regarding Quality of Testing.

1. Complaints reported using the QSR system monitoring software will include specific response to the complaint and actions taken.
2. Corrective actions will also be tracked and reviewed using the Monthly Function Check Log.

D. Annual Re-approval of the Quality Control Plan by the Laboratory Director or Designee:

1. On an annual basis, the Rapid fN specific IQCP binder will be updated for the medical director or designee to review and make adjustments to the current IQCP plan as needed.
2. Reports are maintained in the Supervisor's office.

X. SPECIAL SAFETY PRECAUTIONS:

A. Do not use glass tubes or glass pipettes, as fetal fibronectin binds to glass. Tubes and

pipettes of polypropylene or polyethylene are acceptable.

B. Test results may not be interpreted visually and must be based on the use of the TLi_{IQ} analyzer.

C. Do not mix materials from different kit lot numbers.

D. Do not use cassettes or controls past their expiration dates.

E. Do not use controls if they are cloudy or discolored.

F. Handle cassettes with care: Do not touch, scratch, or compress membrane materials in the Rapid fFN Cassette.

G. Avoid cross-contamination of reagents. Recap controls tightly with the correct color-coded caps.

H. Source material used to prepare the controls if of human origin. the donors were tested and found to be negative for HIV1, HIV2, HCV antibody and hepatitis B surface antigen (HBsAg) using established methods. No known test method can offer total assurance that HIV1, HIV2, HCV virus and hepatitis B virus or other infectious agents are absent. Handle the controls and all patient specimens as if potentially infectious.

I. Labels (e.g. barcode labels) can be placed on the thumb grip are of the cassette.

J. Do not place labels on an area of the cassette that will be inserted into the TLI_{IQ} analyzer.

XI. PROCEDURE:

A. Daily Analyzer Quality Control:
NOTE: The TLi_{IQ} QCette setup must be performed PRIOR to running the QCette as a daily quality control device. Setup is performed once per TLiIQ QCette received. (See the TLi_{IQ} QCette directional insert for details)

1. Select Option 3 (DAILY QC) from the Main Menu of the analyzer.
2. Enter the Employee ID number and press ENTER.
3. Enter the TLi_{IQ} QCette serial number and press ENTER.
4. Insert the QCette into the analyzer and press ENTER.
5. When analysis is complete, the result will be displayed on the analyzer screen and the printed label as SYSTEM PASS.
6. A FAIL or INVALID result should be repeated.
7. Press ESC to return to the MAIN MENU.

B. Liquid Positive and Negative Controls:

NOTE: The Liquid controls **MUST** be performed with each new lot or shipment of cassettes but, a minimum of once every 30 days- **EVEN IF THE LOT NUMBER REMAINS THE SAME.**

1. Allow the refrigerated Liquid Controls to come to room temperature.
2. Select option 8 (Liquid Controls) from the Main Menu of the analyzer.
3. Enter employee ID number and press ENTER.
4. Enter cassette lot number and press ENTER.

5. Indicate which control will be run. NEGATIVE or POSITIVE and press ENTER.
6. Enter control lot number and press ENTER.
7. Tear open and remove the cassette from the foil pouch, being careful no tho touch the sample well or reaction area. When prompted, insert the cassette into the analyzer.
8. Push in in until it clicks and press ENTER.
9. Gently invert the control vial to mix before testing.
10. Using a calibrated pipette, add 200µL of the liquid control to the sample well and IMMEDIATELY press Enter.
11. The analyzer times the 20-minute incubation of the cassette and starts the analysis.
12. When the analysis is complete, the result will be displayed on the screen and a result label will be printed.
13. Place this label on the Quality Control Log Sheet in the Procedure Manual.
14. Remove the cassette from the analyzer.
15. Press ESC to return to the MAIN MENU.
16. A FAIL or INVALID control result must be repeated before any patient testing.

C. Patient Testing:
NOTE: Patient specimen should be at room temperature prior to testing.

1. Select Option 1 (TEST PATIENT) from the MAIN MENU.
2. Enter employee ID number and press ENTER.
3. Enter cassette lot number and press ENTER.
4. Tear open and remove the cassette from the foil pouch, being careful no tho touch the sample well or reaction area. When prompted, insert the cassette into the analyzer.
5. Push in in until it clicks and press ENTER.
6. Gently invert the sample and express as much liquid from the swab as much as possible.
7. Remove swab from sample and discard.
8. Using a calibrated pipette, add 200µL of the liquid control to the sample well and IMMEDIATELY press Enter.
9. The analyzer times the 20-minute incubation of the cassette and starts the analysis.
10. When the analysis is complete, the result will be displayed on the screen and a result label will be printed.
11. Place the label on the Patient Log Sheet in the Procedure Manual.
12. Remove the cassette from the analyzer.
13. Press ESC to return to the MAIN MENU.
14. A FAIL or INVALID control result must be repeated.

15. Report the patient result in the computer.

XII. CALCULATIONS AND INTERPRETATIONS:

A. The fFN result for the patient sample will be displayed on the TLi_{IQ} Analyzer display screen as POSITIVE, NEGATIVE, or INVALID.

B. The result is positive if the value derived from the patient sample is greater than or equal to the reference calibration value specified by the calibration code.

C. The result is negative if the value derived from the patient sample is less than the reference calibration value specified by the calibration code.

D. The result is invalid if the test does not meet internal quality controls.

E. If the assay does not meet internal acceptance criteria for a valid test, retest with 200 µL of additional sample, if available, on a new Rapid fFN Cassette. If the problem is not corrected, contact Hologic for technical assistance.

XIII. EXPECTED VALUES:

A. FFN is a qualitative test with results reported as POSITIVE or NEGATIVE.

B. The following note appears on the patient chart report with each qualitative result:

1. This test is reported to have a negative predictive value for preterm birth within the next 1-2 weeks of 94-100%. However, the positive predictive value (<40%) is low.
2. A positive result may be caused by any cervical disruption within 24 hours of testing; e.g., cervical examination, ultrasound probe, sexual intercourse.
3. Results are unreliable in the presence of placental abruption, placenta previa, moderate bleeding or contamination of the swab by creams or lubricants.
4. Testing is not useful if membranes have ruptured.

C. If the analyzer reports an INVALID result, then the floor or Dr.'s office must be notified and the test canceled with a comment: "Invalid test result – notified (name and time of call)".

D. If the analyzer is inoperable, all Fetal Fibronectin tests should be sent to the WBH-RO STAT lab. Call ext 80526, notify them that a test will be coming.

E. Specimen must be put onto a packing list in order to send specimen to Royal Oak STAT Lab.

XIV. LIMITATIONS:

A. The Rapid fFN result should not be interpreted as absolute evidence for the presence or absence of a process that will result in delivery in less than or equal to 7 to 14 days from specimen collection in symptomatic women or delivery in less than or equal to 34 weeks, 6 days in asymptomatic women evaluated between 22 weeks, 0 days and 30 weeks, 6 days of gestation.

B. A positive Rapid fFN result may be observed for patients who have experienced cervical disruption caused by, but not limited to, events such as sexual intercourse, digital cervical examination, or vaginal probe ultrasound.

C. The Rapid fFN result should always be used in conjunction with information available from the clinical evaluation of the patient and other diagnostic procedures such as cervical examination, cervical microbiological culture, assessment of uterine activity, and evaluation of other risk factors.

D. Modification of the assay protocol described herein may yield erroneous results.

E. The assay has been optimized with specimens taken from the posterior fornix of the vagina or the ectocervical region of the external cervical os. Samples obtained from other locations should not be used.

F. The safety and effectiveness of using a cutoff other than that provided by the Rapid fFN Cassette Calibration Code has not been established.

G. Manipulation of the cervix may lead to false positive results. Specimens should be obtained prior to digital examination or manipulation of the cervix.

H. Patients with suspected or known placental abruption, placenta previa, or moderate or gross vaginal bleeding should not be tested for fFN.

XV. INTERFERING SUBSTANCES:

A. Assay interference from the following components has not been ruled out: douches, white blood cells, red blood cells, bacteria and bilirubin.

B. The presence of infections has not been ruled out as a confounding factor to risk of preterm delivery.

C. Assay interference from semen has not been ruled out. Specimens should not be collected less than 24 hours after intercourse. However, even when a patient reports having had intercourse in the previous 24 hours, a negative fetal fibronectin test result is valid.

D. Care must be taken not to contaminate the swab or cervicovaginal secretions with lubricants, soaps, disinfectants, or creams (e.g., K-Y® Jelly lubricant, Betadine® disinfectant, Monistat® cream, hexachlorophene). These substances may interfere with absorption of the specimen by the swab or with the antibody-antigen reaction of the Rapid fFN test.

XVI. REFERENCES:

1. TLiIQ System User Manual. Hologic Inc. 2016

Attachments

ffn maintenance.pdf

fFN result form.pdf

IQCP monthly monitor.pdf

Approval Signatures

Step Description	Approver	Date
	Vaishali Pansare: Chief, Pathology	3/6/2023
Policy and Forms Steering Committee (as needed)	Gail Juleff: Project Mgr Policy	2/22/2023
Policy and Forms Steering Committee (as needed)	Kristin Russell: Supv, Laboratory	2/21/2023
	Kristin Russell: Supv, Laboratory	2/21/2023