Ruptured Membranes Assessment Module

ROM plus®
Rupture of Membranes Test

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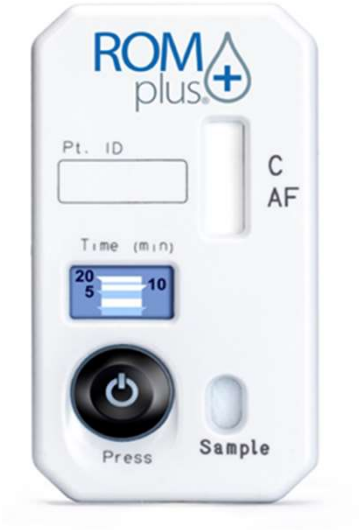
ROM plus

ROM plus is a point of care test that can aid in the detection of ROM in pregnant women reporting signs, symptoms, or complaints suggestive of ROM.



Diagnosing Rupture of Membranes

Sterile Speculum Exam (SSE)

1. Pooling
2. Nitrazine
3. Ferning

*Diagnosis requires at least 2 of 3 to be confirmed positive

Sensitivity: 51-98%

Specificity: 16-88%

Caughey, et al. Rev. Obstet. Gynecol. 2008, 1:11-22

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ROM Plus Rupture of Membranes

- Rapid, qualitative immunoassay test for rupture of fetal membranes
- No gestational age limitations
- Detects amniotic fluid proteins in cervicovaginal secretions of pregnant women
    - Insulin-like Growth Factor Binding Protein-1 (IGFBP-1)
    - Alpha-Fetoprotein (AFP)
- Uses unique monoclonal and polyclonal antibody approach

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Why IGFBP-1 & AFP?

- IGFBP-1 has been recognized in the literature as an excellent marker for amniotic fluid
  - Present in high levels during all 3 trimesters
  - 100-1,000X higher concentrations in AF than other bodily fluids
- AFP peaks during the 2nd trimester and then declines
  - Increases ROM Plus' accuracy in preterm patients
  - 100-1,000X higher concentrations in AF than other bodily fluids

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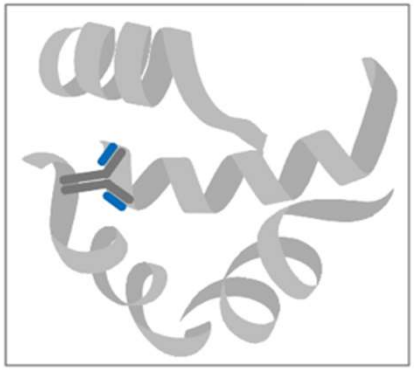
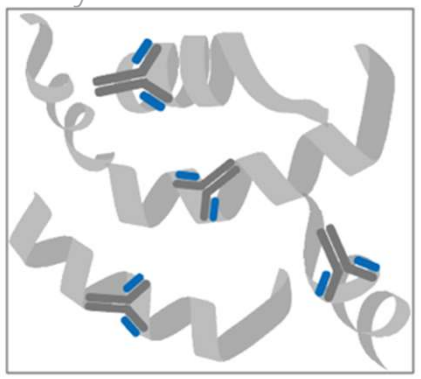
How ROM Plus works

- Uses the principles of immunochromatograpahy to proteins present in amniotic fluid of pregnant women.
- Detects two proteins-AFP and IGFBP-1
- Uses both monoclonal and polyclonal antibodies to detect proteins
  - May reduce potential effects of protein degradation
  - Decreases potential false negatives
  - Reducing chance of discharging a patient who is ruptured

Monoclonal Antibody



Polyclonal Antibodies



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Patient Criteria for ROM plus Testing

- No gestational age limit.

ROM plus

- Tested to work with up to 10% concentration of whole blood
- Ease of Use
  - 15 second vaginal swab
  - 15 second mix buffer solution
  - Spill resistant vial

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ROM Plus Performance Metrics

	PATIENTS	SENSITIVITY	SPECIFICITY
THOMASINO, 2013[1]	285	99.5%	90.7%
IGBINOSA, 2017[2]	111	96.4%	98.8%
SENANAYAKE, 2013[3]	95	98.9%	N/A
ROGERS, 2016[4]	75	100%	94.8%
ESPLIN, 2019[11]	324	91.7%	97%
ROM Plus IFU	264	99%	75%

1. Thomasino T, Levi C, Draper M, Neubert AG. Diagnosing rupture of membranes using combination monoclonal/polyclonal immunologic protein detection. J Reprod Med. 2013;58(5–6):187–194.
2. Igbinosa, Irogue & A. Moore, Ferney & Johnson, Cheri & Block, Jon. (2017). Comparison of rapid immunoassays for rupture of fetal membranes. BMC Pregnancy and Childbirth. 17. . 10.1186/s12884-017-1311-y.
3. Senanayake HM. Actim™ PROM, ROM plus®, and ROM+plus®: Rupture of membrane kits tested on amniotic fluid from women at C-section: a comparative study. Sri Lanka Journal of Obstetrics and Gynaecology. 2013; 116-121.
4. Rogers LC, Scott L, Block JE. Accurate point-of-care detection of ruptured fetal membranes: improved diagnostic performance characteristics with a monoclonal/polyclonal immunoassay. Clin Med Insights Reprod Health. 2016;10:15–8.
11. Esplin, et. al. Prospective evaluation of the efficacy of immunoassays in the diagnosis of rupture of the membranes. J Matern Fetal Neonatal Med. 2019 Jan 13:1-7. doi: 10.1080/14767058.2018.1555809. [Epub ahead of print]

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ROM Plus Test Components

Control Vials

Cassette

Buffer

Sterile Swab

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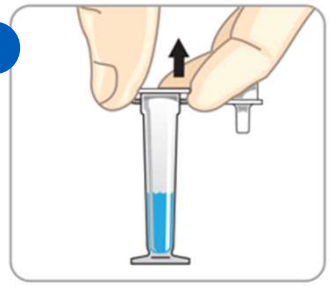
Test Procedure

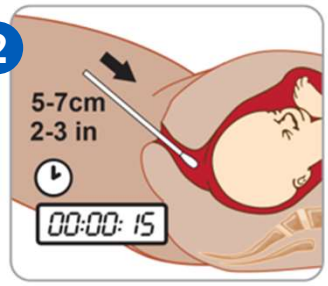
See Package Insert for Full Instructions, Warnings, Precautions & Contraindications

1



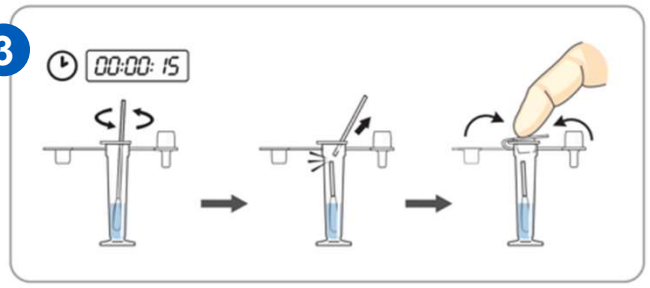
Remove ROM Plus contents from packaging. Holding buffer vial upright, remove shipping cap and set vial aside.

2



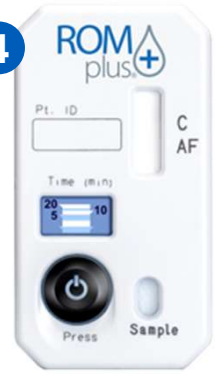
Remove sterile swab to collect sample. Swab tip should not touch anything prior to its insertion. Insert swab tip into vagina 2-3 inches (5-7 cm) deep. Withdraw swab after a minimum of 15 seconds.

3



Place swab tip into vial and mix in buffer solution for at least 15 seconds. Break off swab tip at the scored mark and leave swab tip in the vial. Replace dropper cap on vial and dispose swab stick.

4



Tear open foil pouch and remove ROM Plus® cassette.

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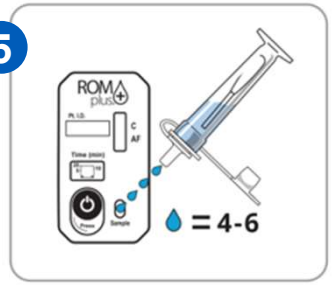
Test Procedure Cont.

See Package Insert for Full Instructions, Warnings, Precautions & Contraindications

5

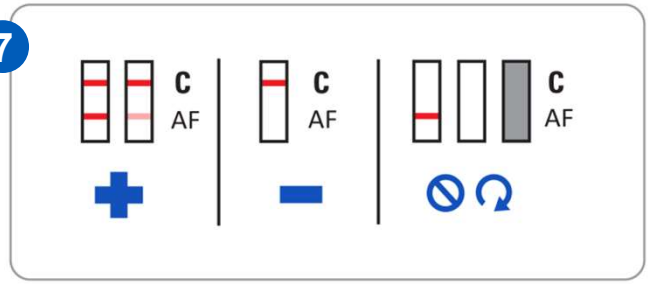


Add 4-6 drops to the sample well in cassette.

6

Set external timer to 20 minutes. Wait 5-20 minutes for test results to manifest in test window (C/AF). A positive test result may be visible within 1-3 minutes or may take the full 20 minutes. Darkness of the stripes may vary, however test is valid even if stripes are faint. Do not interpret test results based on darkness of stripes.

7



Read test result. If only a control line (C) is visible, the test result is negative. If both the control line (C) and test result line (AF) are visible, the test result is positive. If no lines are visible, or just the test line (AF) is visible, the test result is invalid. A light visible line located in the test (AF) region should be considered a positive. In addition, very high concentrations of proteins may result in a light test (AF) line. It is recommended to read the strip by 20 minutes.

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Quality Control (QC)

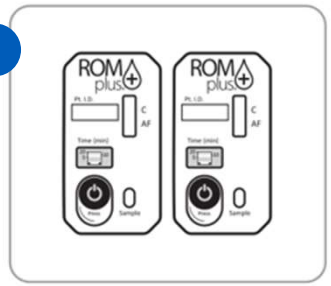
- Reagents
  - Negative-Saline (self-contained glass ampoule of buffer)
  - Positive-lyophilized human amniotic fluid (self-contained glass ampoule of buffer)

- Frequency
  - New shipment/lot
  - Clinical symptoms do not match results
  - Suspicion that product performance is compromised or when kits have not been stored according to manufacturer instructions

Quality Control Procedure

See Package Insert for Full Instructions, Warnings, Precautions & Contraindications

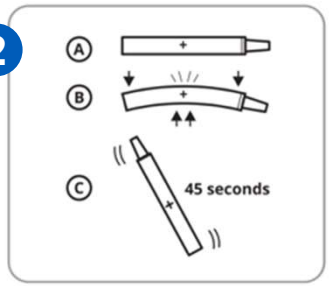
1



Prepare Test Cassettes

Prepare two ROM Plus test cassettes, one for the Positive Control and one for the Negative Control. Since this is a quality control test and no human sample is required, the polyester vaginal swab and standard dropper vial should not be used.

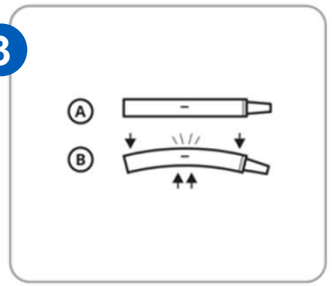
2



Prepare Positive Control

Tear open the Positive Control Vial foil pouch and remove the vial. Place the vial in the safety sleeve, gently squeeze and bend to break the Positive control glass vial inside. Mix the buffer with the lyophilized positive sample for at least 45 seconds. Be careful not to let the sample drip out of the vial.

3



Prepare Negative Control

Gently bend or squeeze the Negative Control Vial, breaking the glass ampoule inside. Be careful not to let the sample drip out of the vial.

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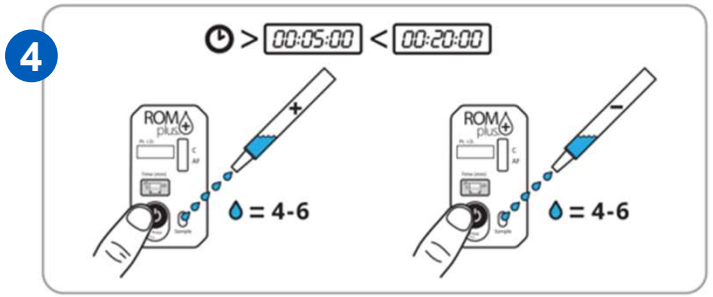
Quality Control Procedure Cont.

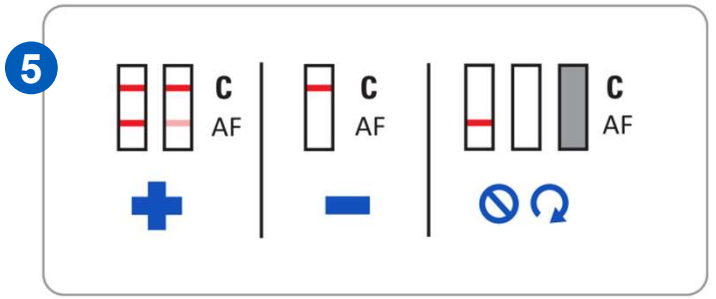
See Package Insert for Full Instructions, Warnings, Precautions & Contraindications



Run Tests

- Add 4-6, or more, drops of the Positive Control solution to one ROM Plus test cassette.
- Add 4-6, or more, drops of the Negative Control solution to the other ROM Plus test cassette.

Start the external timers. Wait 5-20 minutes for test results to manifest in test window (C/AF).



Read Test Results

Read the test results from 5 to 20 minutes. Only a control line (C) should be visible for the negative control. Both the control line (C) and test line (AF) should be visible for the positive control. The test is positive even if the stripes are faint.

The external positive control is four times the threshold cutoff concentration prior to dilution of the patient sample with extraction buffer, and will appear at approximately 5 minutes; however, the full 20 minutes should be used before interpreting final results. Do not interpret test results based on the darkness of the stripes. It is recommended to read the strip by 20 minutes.

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ROM Plus Summary

- Reliable sensitivity delivered conveniently and cost effectively
- Detects “2 Proteins 2 Ways”
  - AFP & IGFBP-1
  - Monoclonal and Polyclonal antibodies
- **No gestational age limitations**
- Tested with blood
  - No loss of activity in samples containing up to 10% blood concentration
- Configured for either Lab or L&D interpretation

- 15 second vaginal swab, 15 second mix in the buffer solution
- Specimen stable for 6 hours after collection
- Test cassette & spill resistant vial
- External QC stays at room temperature with no reconstitution or special storage needed

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Precautions

- Store the kit in a dry place at 4° to 37°C (40° to 99°F). Do not freeze.
- When stored in the foil pouch at the recommended temperature, the test is stable until the “Expiration” date on the pouch.
- Use ROM Plus within six (6) hours after opening foil pouch.
- Use ROM Plus within six (6) hours of collecting the vaginal swab sample and placing it into the buffer vial
- Do not use expired kits
- Do not reuse swabs

Test Limitations

- ROM diagnoses should not be based on any single test.
- ROM Plus is for in vitro diagnostic use only.
- ROM Plus is for healthcare professional use only.
- Allow pouch containing ROM Plus to reach room temperature prior to utilizing the test.
- All instructions should be followed carefully for accurate results.
- Each ROM Plus test kit is single use and disposable and should not be reused.
- ROM Plus results are qualitative. No quantitative interpretations should be made.
- ROM Plus test kits will function properly with trace amounts of blood in the sample. Significant amounts of blood discharge may cause the test to malfunction and is not recommended.
- Safety precautions should be observed when collecting, handling, and disposing of test samples. Used test kits are biohazardous.
- Elevated fetal serum, urine, cord blood, and amniotic fluid as well as maternal serum levels of AFP have been reported in the literature in various developmental disorders such as neural-tube defects, hypothyroidism, autoimmune states, congenital heart defects, cystic fibrosis, etc. ROM Plus has not been evaluated for potential interference in these conditions.

- **Warning: The test may report positive results in patients with intact membranes (see specificity in the performance section) and therefore decisions to induce labor should not be based solely on the ROM Plus test results.**

Any patient result that is inconsistent with patient's clinical condition should be repeated.

Potential Causes of False Negatives

- Insufficient protein from the patient (high and/or minimal fluid leak)
- Too much protein from patient which typically appears in patients with grossly rupture membranes (High Dose Hook effect)
- Over-active vaginal proteases in the vaginal flora that break down the protein
- User error-did not follow IFU

Potential Causes of False Positives

- Proper IFU procedure not followed
- Microtransudation of protein across the membranes as the membranes are stressed near term-causing a leakage of protein without a gross membrane rupture
- Small, high leak
- Potential for resealing of the membranes

Remember to Check the Following:

- Procedural timing was strictly followed.
- The provided sterile swab touched nothing prior to insertion.
- Sample collected within 6 hours
- There are no significant blood admixture.
- The test kit was stored according to manufacturer instructions between 4-37^{o}C or 40-99^{o}F.

Frequently Asked Questions

- **Is a faint line a positive result?**

  Yes, even faint and broken lines are a positive result.

- **What is the maximum time between the sample collection and application of drops to cassette?**

  Up to 6 hours when swab is in buffer solution.

- **What is the maximum time between opening the test cassette and using it?**

  You can leave a test cassette open for up to 6 hours.

- **Does blood contamination affect the test result?**

ROM Plus test kits have been tested up to 10% blood concentration. In other words, it will function properly with trace amounts of blood in the sample, however, significant amounts of bloody discharge may cause the test to malfunction. ROM Plus is not recommended for use in these situations and it should be determined what is causing the bleeding.

- **Will semen, urine or disinfectants interfere with test?**

Tylenol, aspirin, Lever Soap, Noxema cream, Pert Shampoo, human semen, urine and blood were tested as possible interference's and were shown to be negative. For additional information please see the ROM Plus IFU

- **Is there a time limit for reading the test?**

Yes. The ROM Plus test is an immunoassay test and as with all immunoassay tests the results will diminish over time. Do not read the test results after 30 minutes have passed.

Frequently Asked Questions

- **Does blood contamination affect the test result?**

ROM Plus test kits have been tested up to 10% blood concentration. In other words, it will function properly with trace amounts of blood in the sample, however, significant amounts of bloody discharge may cause the test to malfunction. ROM Plus is not recommended for use in these situations and it should be determined what is causing the bleeding.

- **What is sensitivity/specificity?**

Sensitivity is the percentage probability that a positive test will occur in a patient who is really experiencing rupture of membranes, or the proportion of actual positives which are correctly identified as such. In a multi-site hospital study involving 285 patients, ROM Plus resulted in an overall sensitivity of 99% (see IFU for details). Specificity is the percentage probability that a negative test will occur in a patient who is not experiencing rupture of membranes, or the proportion of actual negatives which are correctly identified as such. Specificity also refers to the ability of the test to detect the correct result in the presence of interfering components that may be present in a sample matrix (i.e., blood, urine, semen, etc.). ROM Plus resulted in an overall specificity of 85%.

- **Are there gestational age limitations for using ROM Plus?**

ROM Plus does not have any gestational age limits.