AmniSure® ROM (Rupture of [fetal] Membranes) Test

INSTRUCTIONS FOR *IN VITRO* DIAGNOSTIC USE

INTENDED USE

The AmniSure ROM Test is a rapid, qualitative immunochromatographic test for the *in vitro* detection of amniotic fluid in vaginal discharge of pregnant women. The test is for use by healthcare professionals to aid in the detection of rupture of fetal membranes in pregnant women.[1]

SUMMARY AND EXPLANATION OF THE TEST

Premature rupture of fetal membranes (PROM) occurs in about 10% of pregnancies and poses one of the most important therapeutic dilemmas in current obstetric practice.[1] Management of patients with PROM and PPROM (pre-term PROM, occurring before 37 weeks gestation) is expensive and remains an important perinatal dilemma as the clinician attempts to balance the risk of prolonging gestation against the risks of infection.[1]

Risks of PROM at term are related to serious neonatal consequences such as pre-term delivery, fetal distress, prolapsed cord, abruptio placentae and infection.[1] PPROM accounts for 20% to 40% of PROM cases, and is associated with 20% to 50% of premature births, infectious morbidity in the mother and fetus, pulmonary hypoplasia of the fetus, prolapse of the umbilical cord, development of fetal deformities, and postnatal endometritis.[1] All these consequences significantly increase fetal and maternal morbidity and mortality.

The AmniSure ROM Test kit is a self-contained system that provides rapid, accurate diagnosis of PROM crucial to ensure appropriate obstetric measures are taken in the event of a rupture. Additionally, accurate PROM diagnosis helps to avoid unwarranted intervention such as induction of labor or hospitalisation.

PRINCIPLE OF THE TEST

The AmniSure ROM Test uses the principles of immunochromatography to detect human PAMG-1 protein present in amniotic fluid. The test employs highly sensitive monoclonal antibodies that detect even a minimal amount of PAMG-1, which is present in cervicovaginal discharge after rupture of fetal membranes. PAMG-1 was selected as a marker of fetal membranes rupture due to its high level in amniotic fluid, low level in blood, and extremely low background level in cervicovaginal discharge when fetal membranes are intact. To minimize the frequency of false results, several monoclonal antibodies were selected to set the sensitivity threshold of the AmniSure ROM Test at the optimal low level of 5 ng/ml. The maximum background concentration of PAMG-1 in cervicovaginal discharge is slightly lower than the sensitivity cut-off of the AmniSure ROM Test, minimizing false positive/negative results and allowing for ~99% accuracy.[1] A sample of cervicovaginal discharge (collected by vaginal swab) is placed into a vial with solvent for extraction. PAMG-1 is then detected in the vial by inserting a test strip (lateral flow device) into it. The result is read visually by the presence of one or two lines in the test region of the strip.

REAGENTS AND COMPONENTS

The AmniSure ROM Test kit includes the following components: 1) Instructions for use 2) AmniSure ROM Test strip in foil pouch with desiccant 3) Sterile polyester vaginal swabs 4) Plastic vial with solvent solution containing: 0.9% NaCl, 0.01% Triton X-100, 0.05% NaN_3.

PRECAUTIONS AND WARNINGS

- Safety precautions should be observed when collecting, handling, and disposing of test samples
- Do not use damaged components of the test
- Used test kits are biohazardous
- Do not use after the expiration date, which is printed on the labeling
- Do not reuse the test kit components
- Do not bend or fold the test strip or the aluminum foil pouch with the test strip in it

STORAGE AND STABILITY

- Store the kit in a dry place at 4 to 25°C (40 to 77°F). DO NOT FREEZE.
- When stored in the foil pouch at the recommended temperature, the test is stable until the expiration date on the box
- The AmniSure ROM Test should be used within 6 hours after removing the test strip from the foil pouch

QUALITY CONTROL

The AmniSure ROM Test contains an internal control mechanism that ensures the analytic portion of the test is functional. The appearance of one or two lines in the test results region of the test strip verifies the integrity of the test procedure and components.

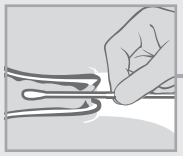
Note: If separating the kit components prior to use, please record the AmniSure ROM Test kit lot numbers and/or specific strip, swab, and solvent lot numbers used for each test.

EXPECTED VALUES

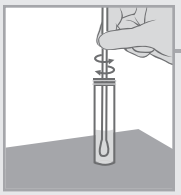
Leakage of amniotic fluid is indicative of rupture of fetal membranes in all women. Studies of PAMG-1 have established it as a marker of amniotic fluid.[2] Clinically significant leakage of amniotic fluid increases PAMG-1 concentration in cervicovaginal discharge by a factor of thousands. The sensitivity threshold of the AmniSure ROM Test is set to eliminate the dependence of the test results on possible variations of expected values (levels of PAMG-1) in any given population.

TEST PROCEDURE

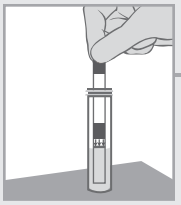
NOTE: Read and follow exactly the directions for use; failure to do so may result in inaccurate results.
The AmniSure ROM Test should not be used earlier than 6 hours after the removal of any disinfectant solutions or medicines from the vagina.
Placenta previa and performing digital exams prior to sample collection can lead to inaccurate test results.



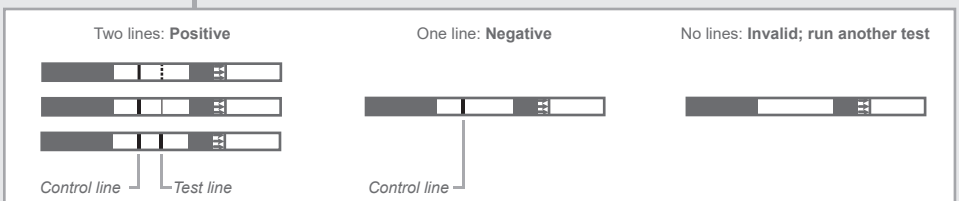
1. Take the solvent vial by its cap and shake well to make sure all liquid in the vial has dropped on the bottom. Open the solvent vial and put it in a vertical position.
2. To collect a sample from the surface of the vagina, use the sterile polyester swab provided. Remove the sterile swab from its package following instructions on the package. The polyester tip should not touch anything prior to insertion into the vagina. Hold the swab by the middle of the shaft and, while the patient is lying on her back, carefully insert the polyester tip of the swab into the vagina until the fingers contact the skin (no more than 5-7 cm deep). Withdraw the swab from the vagina after **1 minute**.



3. Place the polyester tip of the swab into the provided solution vial and rinse the swab by rotating for **1 minute**.
4. Remove and dispose of the swab.
5. Test the patient sample within 30 minutes after collection. If the patient sample is not tested within 30 minutes and sample storage is necessary, tightly close the sample vial and place in a refrigerator for no more than 6 hours before testing.



6. Tear open the foil pouch at the tear notches and remove the AmniSure ROM Test strip.
7. Insert the white end of the test strip (marked with arrows) into the solution vial. Strong leakage of amniotic fluid will make the results visible early (within seconds), while a very small leak may take the full **5 minutes**.
8. **Remove the test strip if two lines are clearly visible in the vial or after 5 minutes sharp.** Read the results by placing the test strip on a clean, dry, flat surface. A positive result is indicated by two lines in the test region, while a negatvie result is indicated by a single line in the test region.



The intensity of the lines may vary; the test result is valid even if the lines are faint or uneven. Do not interpret the test result based on the intensity of the lines. Do not read or interpret the results after 10 minutes have passed since inserting the test strip into the vial.

LIMITATIONS OF THE TEST

- **Results should be used in conjunction with other clinical information**
- The test is intended for detecting leaking amniotic fluid at a given point in time
- In rare cases, when a sample is taken 12 hours or later after a rupture has occurred and the leakage of amniotic fluid has stopped, the test may not detect ROM due to several factors, including (but not limited to) resealing of the rupture, denaturing antigen, etc. Periodic retesting in such cases may be advisable.
- The AmniSure ROM Test results are qualitative. No quantitative interpretation should be made based on the test results.
- In cases of only trace amounts of blood on the swab, the test functions properly. When there is a signifcant presence of blood on the swab, the test can malfunction and is not recommended.
- Failure to detect membrane rupture does not assure the absence of membrane rupture
- Women may labor spontaneously despite a negative test result
- The performance of the AmniSure ROM Test has not been established in the presence of the following contaminants: meconium, anti-fungal creams or suppositories, K-Y® Jelly, Monistat® Yeast Infection Treatment, Baby Powder (Starch and Talc), Replens® Feminine Moisturizer, or Baby Oil

PERFORMANCE CHARACTERISTICS

The following performance metrics of the AmniSure ROM Test were established by an independent clinical trial of 203 patients in the US that served as the basis for original FDA clearance:[1] Sensitivity: 98.9%. Specificity: 100%. PPV (Positive Predictive Value): 100%. NPV (Negative Predictive Value): 99.1%.

In recent studies, the AmniSure ROM Test has been shown to be superior to the *combination* of clinical assessment, nitrazine test, and fern test to diagnose ROM.[1] Additionally, according to four recent studies, the AmniSure ROM Test has been shown to be superior to IGFBP-1-based assays.[3-6] According to recent guidelines on the management of spontaneous preterm labor, the test based on the detection of PAMG-1 (i.e. the AmniSure ROM Test) was deemed the more accurate bedside test compared with others.[7]

INTERFERENCE STUDIES

Vaginal infections, urine, semen, or insignicant blood admixtures do not interfere with the results of the AmniSure ROM Test.

BIBLIOGRAPHY

1. *Cousins LM et al. AmniSure Placental Alpha Microglobulin-1 Rapid Immunoassay versus Standard Diagnostic Methods for Detection of Rupture of Membranes. Am J Perinatol. 2005; (22):317-320.* **2.** *Petrunin, D. Immnunochemical identification of organ specific human placental alpha-globulin and its concentration in amniotic fliud. Akush Ginekol (Mosk) 1977; (1):64-5.* **3.** *Chen, F, Dudenhausen, J. Comparison of Two Rapid Strip Tests Based on IGFBP-1 and PAMG-1 for the Detection of Amniotic Fluid. Am J Perinatol 2008; (25):243-246.* **4.** *Gaucherand P., Doret M., et al. Detection of Placental Alpha Microglobulin-1 versus Insulin-Like Growth Factor-Binding Protein-1 in Amniotic Fluid at Term: A Comparative Study. Am J Perinatol 2011; (6):489-94.* **5.** *Tagore S, Kwek K. Comparative analysis of insulin-like growth factor binding protein-1 (IGFBP-1), placental alpha microglobulin-1 (PAMG-1) and nitrazine test to diagnose premature rupture of membranes in pregnancy. Am J Perinatol 2008; (25):243-6.* **6.** *Albayrak M, Ozdemir I, Koc O, Ankarali H, & Oren O. Comparison of the diagnostic efficacy of the two rapid bedside immunoassays and combined clinical conventional diagnosis in prelabour rupture of membranes. Eur J Obstet Gynecol Reprod Biol. 2011 Oct; 158(2):179-82.* **7.** *Di Renzo GC, Cabero Roura L, Facchinetti F & the EAPM-Study Group on "Preterm Birth". Guidelines for the management of spontaneous preterm labor: indentification of spontaneous preterm labor, diagnosis of preterm premature rupture of membranes, and preventive tools for preterm birth. The Journal of Maternal-Fetal & Neonatal Medicine 2011; 24(5):659-667.*

TRADEMARKS

K-Y® Jelly (Owned by Reckitt Benckiser, Slough, England)

Monistat® Yeast Infection Treatment (Owned by Insight Pharmaceuticals, White Plains, New York)

Replens® Feminine Moisturizer (Owned by Church and Dwight Co., Inc., Ewing, New Jersey)

GLOSSARY OF SYMBOLS

CE	European Conformity		Do not re-use
IVD	In-Vitro Diagnostic Medical Device		Do not use if package is damaged
EC REP	European Authorized Representative	Σ n	Contains reagents sufficient for <N> reactions
MAT	Material Number		Consult Instructions for Use
REF	Catalog Number		Temperature Limitation
LOT	Batch Code		Use-By Date
GTIN	Global Trade Identification Number		Manufacturer
Warning: Do not fold or bend the foil pouch and/or the test strip.	Warning: Do not fold or bend the foil pouch and/or the test strip.		

CE IVD

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REF FMRT-1-10-ML-RT
FMRT-1-25-ML-RT

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DOCUMENT REVISION HISTORY

Revision	Release Date	Change
01	Mar. 2015	Initial Release
02	Apr. 2016	Updated timing on testing and reading
03	Jan. 2017	Updated to accommodate French translations
04	Feb. 2017	Added Dutch, Norwegian, Swedish and Danish Translations
05	Dec. 2019	Added Portuguese (Brazil), Finnish, Indonesian, Korean (South Korea), Polish Translations
06	Mar. 2020	Removed Hungarian Translation
07	Jan. 2025	Reorganized instructions to have clarity and better definition of instructions; removed translations