Actim® PROM

Detect membrane ruptures reliably

For *In Vitro* Diagnostic Use

TEST KIT INSTRUCTIONS FOR USE

CooperSurgical

ACTIM PROM CONTENTS & DESCRIPTIONS

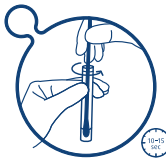
The components of each Actim® PROM Test are:

1. One tube of Specimen Extraction Solution (0.5 mL). This phosphate-buffered solution contains bovine serum albumin (BSA), protease inhibitors and preservatives.
2. One dipstick in a sealed aluminum foil pouch with desiccant.
3. One sterile polyester swab for specimen collection.

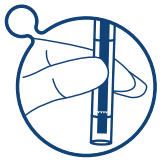
ACTIM PROM TEST PROTOCOL – QUICK REFERENCE*

*Please see Sections 7 and 8 for expanded step-by-step instructions

Hold the swab in vagina for 10-15 seconds.



Place the swab in the Specimen Extraction Solution and swirl around vigorously for 10-15 seconds.



Dip the yellow area of the dipstick into the Specimen Extraction Solution and hold it there until the liquid front reaches the result area.

Remove the dipstick from the Specimen Extraction Solution as soon as the liquid front reaches the result area.

POSITIVE RESULT:
- Positive result can be read as soon as it becomes visible.
- Two blue lines = Membranes are ruptured.

NEGATIVE RESULT:
- Negative result should be confirmed at 5 minutes.
- One blue line = Membranes are intact.

SECTION 1: INTENDED USE

The Actim PROM test is a visually interpreted, qualitative immunoassay rapid test for the detection of amniotic fluid in cervicovaginal secretions during pregnancy. The Actim PROM test detects IGFBP-1, a major protein in amniotic fluid and a marker of the presence of amniotic fluid in a vaginal sample. The test is intended for prescription use in the point of care and clinical laboratory settings to help diagnose the rupture of fetal membranes (ROM) in pregnant women ≥ 29 weeks gestation who present with signs, symptoms or complaints suggestive of ROM.

SECTION 2: SUMMARY AND EXPLANATION OF THE ACTIM PROM TEST

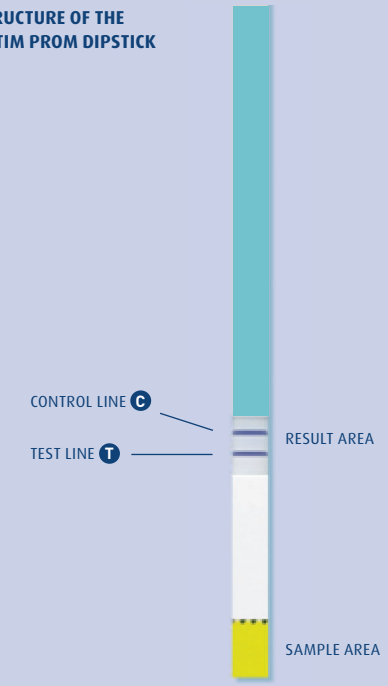
Premature rupture of fetal membranes (PROM) is associated with increased risk of intra-uterine infection and thus increases the risk of both maternal and perinatal morbidity and mortality. This makes well-timed and accurate diagnosis of the condition important.

When PROM occurs at term (≥ 37 weeks gestational age), labor typically ensues spontaneously or is induced within 12 to 24 hours. If membrane rupture occurs before 37 weeks, it is referred to as preterm PROM.[1] Literature supports that PROM affects 3 % to 4.5 % of all pregnancies[1] and that less than (<) 1 % of pregnancies are complicated by PROM before viability.[2]

Management hinges on knowledge of gestational age and evaluation of the relative risks of preterm birth that could occur with expectant management. The Actim PROM test is intended to assist the treating clinician in making an informed decision about how to manage the patient.

The concentration of IGFBP-1 (insulin-like growth factor binding protein-1) in amniotic fluid is 100–1,000 times higher than that in maternal serum. IGFBP-1 is not usually present in the vagina or cervix, but after rupture of fetal membranes, amniotic fluid with a high concentration of IGFBP-1 mixes with vaginal fluids.[3] In the Actim PROM test, a specimen of vaginal fluid is taken with a sterile polyester swab and the specimen is extracted into the Specimen Extraction Solution. The presence of IGFBP-1 in the extracted sample is detected using a dipstick.

STRUCTURE OF THE ACTIM PROM DIPSTICK



The main challenge in diagnosing PROM is to distinguish small amounts of amniotic fluid from other body fluids which may be present in the vagina or cervix. The detection limit of the Actim PROM test (25 µg/L IGFBP-1 in the extracted sample, corresponding to 400 µg/L IGFBP-1 in the original sample) is above the highest known IGFBP-1 level (300 µg/L IGFBP-1) in maternal blood.[3,7] The test is also sensitive enough to detect less than one micro liter of amniotic fluid.[5-7]

SECTION 3: PRINCIPLE OF THE ACTIM PROM TEST

The test is based on immunochromatography. It utilizes two mice monoclonal antibodies to human IGFBP-1. One of the two antibodies is bound to blue latex particles (detecting antibody). The other antibody is immobilized as a test line on the membrane (catching antibody). The test strip (dipstick) is composed of the sample/conjugate pad, the membrane with test and control lines, and the absorbent pad assembled between plastic films. The upper film contains a test window. When the sample area of the dipstick is placed in an extracted sample, the dipstick absorbs liquid, which starts to flow up the dipstick. If the sample contains IGFBP-1 it binds to the antibody labeled with latex particles. The particles are carried by the liquid flow and, if IGFBP-1 is bound to them, they bind to the catching antibody. A blue line (test line) will appear in the result area if the concentration of IGFBP-1 in the sample exceeds the detection limit of the test. A second blue line, the procedural control line, confirms correct operator performance of the test.

SECTION 4: MATERIALS PROVIDED WITHIN THE KIT

- Actim PROM test packs containing:
  - One sterile polyester swab for specimen collection
  - One tube (0.5 mL) of Specimen Extraction Solution
  - One dipstick in a sealed aluminum foil pouch with desiccant
  - Instructions for use.
- Materials Required but not Provided
  - Timer or a watch
  - Quality Control materials

SECTION 5: PRECAUTIONS AND WARNINGS

- The Actim PROM test is intended for professional *in vitro* diagnostic use only.
- The test requires approximately 150 µL of extracted sample to ensure proper performance.
- Carefully follow the instructions for use of the Actim PROM test to ensure correct results.
- Do not use the test after the expiration date, which is printed on the labels of the kit components.
- Use only the swab provided with the Actim PROM kit.
- Do not reuse the test kit components.
- Do not take the dipstick out of the aluminum foil pouch until just before use.
- Do not bend or fold the dipstick or the aluminum foil pouch with the dipstick in it.
- Do not use the dipstick if its aluminum foil pouch or the seals of the pouch are not intact.
- Use care when placing the dipstick in the sample tube. The upper part of the dipstick must stay dry. Do not use a dipstick that has become wet before use as moisture damages the dipstick.
- Do not use the dipstick if you notice a blue coloring in the result area before testing.
- Improper sample collection may lead to false result.
- When dipping, be careful to hold the dipstick in position (with the sample area in the sample extract) until the sample liquid front reaches the result area.
- A positive Actim PROM test result, although intended to detect the presence of amniotic fluid in the sample, does not locate the site of the rupture.

- All biological specimens and materials must be treated as potentially hazardous and disposed of in accordance with Federal, State and Local requirements.
- The IGFBP-1 antigen in the Positive Controls has been shown to be negative for HBsAg, HIV type 1 and 2 antibodies, HCV and syphilis. Nevertheless, such tests are unable to prove the complete absence of viruses, and **therefore the controls should be treated as potentially infectious**.

SECTION 6: STORAGE AND STABILITY

Store the test kit at 2 °–25 °C (36 °–77 °F). Stored unopened at the recommended temperature, each component can be used until the expiration date marked on the component. The test kit and the test packs can be stored for 2 months up to 30 °C (86 °F), as long as the expiration date is not exceeded.

Open the aluminum foil pouch and remove the dipstick from the pouch just prior to use.

SECTION 7: SPECIMEN COLLECTION AND EXTRACTION

The test specimen is vaginal fluid that is extracted into the Specimen Extraction Solution provided. A sample is collected from the vagina using a sterile polyester swab (provided in the kit). The sample should be collected prior to performing digital examination and/or transvaginal ultrasound. Take care not to touch anything with the swab before taking the sample. Separate the labia and carefully insert the tip of the swab into the vagina toward the posterior fornix until resistance is met. Alternatively the sample can be taken from the posterior fornix during a sterile speculum examination. The swab should be left in the vagina for approximately 10–15 seconds to allow it to absorb the vaginal fluid specimen.

- Open the Specimen Extraction Solution tube and put it in a vertical position.
- Extract the specimen from the swab immediately by swirling the swab vigorously in the extraction solution for approximately 10 seconds.
- Press the swab against the wall of the Specimen Extraction Solution tube while removing the swab so that most of the liquid stays in the tube. Discard the swab.
- Specimens should ideally be tested immediately after extraction. If testing is not performed immediately, extracted samples may be stored at room temperature for 4 hours. If a specimen cannot be tested within this time, it should be frozen at or below -20 °C. After thawing, the specimen should be mixed and tested as described below.

SECTION 8: TEST PROCEDURE

1. If stored refrigerated, allow the aluminum foil pouch to reach room temperature before use. Open the foil pouch containing the dipstick. Do not touch the yellow sample area at the lower part of the dipstick. Identifying marks may be written on the upper turquoise part of the dipstick. The dipstick must be used as soon as possible after its removal from the foil pouch.
2. Place the yellow sample area (the lower end of the dipstick) into the extracted sample and hold it there **until you see the liquid front enter the result area**. Remove the dipstick from the solution and place it on a non-absorbent flat surface. Start the timer.
3. The result can be interpreted as **positive** as soon as two blue lines become visible in the result area. **Negative** results should be read at 5 minutes. **Do not interpret results after 5 minutes.**

SECTION 9: INTERPRETING THE RESULTS

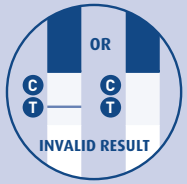
POSITIVE TEST RESULT:
MEMRANES HAVE RUPTURED

- **Two blue lines appear.**
- One line should be in the test line area T and the other in the control line area C.

Note: The intensity of the line in the test line area T may vary. **Any test line appearing at or before the 5 minute read time can be considered a positive result, assuming a control line is also present.** Disregard any lines seen after 5 minutes.

NEGATIVE TEST RESULT:
MEMRANES ARE INTACT

- **One blue line appears in the control line area C.**
- Negative result should be confirmed at 5 minutes.



INVALID TEST RESULT:

- **Control line fails to appear.** Note: repeat using another dipstick. If the test result cannot be interpreted clearly (e.g. if the lines are blotched or uneven) it is recommended that the test be repeated. If the problem persists, discontinue using the test kit and contact Technical Support (page 11).

SECTION 10: QUALITY CONTROL

Internal procedural controls are included in the test. Appearance of the control line is an internal positive control and demonstrates that sufficient capillary flow has occurred and the functional integrity of the dipstick was maintained.

Actim PROM Control tests are available for order (REF number: 30800ETUS). The kit contains one (1) low positive, one (1) high positive and one (1) negative controls to be used as external controls. Laboratories should follow the guidelines or requirements of Federal, State and/or Local regulations or accrediting organizations in the use of controls.

SECTION 11: LIMITATIONS OF THE TEST

- As with all diagnostic tests, **results must be interpreted in conjunction with all other clinical and laboratory findings.**
- If rupture of fetal membranes has occurred and the leakage of amniotic fluid has ceased more than 12 hours before the specimen is taken, IGFBP-1 may have been degraded and the test may give a false negative result.
- The test results are qualitative. No quantitative interpretation should be made based on the test results.
- Women may enter labor spontaneously despite a negative test result.
- A negative result is an indication of the present condition and cannot be used to predict future events.
- The test has been designed to minimize interference from bleeding, but in cases of heavy bleeding the blood locally may have a higher concentration of IGFBP-1 protein. In these cases, a positive result should be interpreted with caution.

SECTION 12: EXPECTED VALUES

Insulin-like Growth Factor Binding Protein-1 (IGFBP-1) is one of the major proteins in amniotic fluid. Its concentration in amniotic fluid is 100–1,000 times higher than in maternal serum. It is not present in measurable amounts in semen or urine.[3] The concentration of IGFBP-1 in amniotic fluid increases rapidly during the first weeks of pregnancy and reaches its peak by the 16th week. The level remains high throughout the pregnancy.[4] The IGFBP-1 concentration in amniotic fluid is in between 10,500 and 350,000 µg/L. [3]

The lowest consistently detectable amount of IGFBP-1 in the extracted sample is approximately 25 µg/L, which corresponds to a concentration of 400 µg/L in the original sample.[7] This limit of detection takes into account both the specimen collection and extraction procedures and also minimizes the possible interference of blood in the sample.[5-7]

SECTION 13: PERFORMANCE CHARACTERISTICS

Clinical Performance

The clinical performance of the Actim PROM test was established in a multi-center, prospective clinical study conducted at six US clinical sites over an 18 month period. A total of 222 pregnant women presenting with signs/symptoms suggestive of ROM were evaluated using the Actim PROM test and compared to results obtained from conventional clinical criteria. Subjects were considered clinically positive for PROM if amniotic fluid was seen leaking from the cervical os upon diagnostic speculum examination, or if two of the three following clinical signs were positive: visual pooling of fluid in the posterior fornix, positive nitrazine test or microscopic evidence of ferning. Actim PROM test performance was established relative to clinical diagnosis as determined by the conventional clinical criteria identified above.

FIG 1.

ACTIM PROM TEST PERFORMANCE VS. CLINICAL DIAGNOSIS – OVERALL RESULTS - ≥ 29 Weeks Gestational Age

	N	SENSITIVITY (95 % Confidence Intervals)	SPECIFICITY (95 % Confidence Intervals)
≥ 29 weeks (Without Speculum)	222	90.1 % (100/111) (95 % CI: 83.1-94.4 %)	91.0 % (101/111) (95 % CI: 84.2-95.0 %)
≥ 29 weeks (With Speculum)	220*	95.5 % (105/110) (95 % CI: 89.8-98.0 %)	86.4 % (95/110) (95 % CI: 78.7-91.6 %)

*2 invalid test results (control lines were not visible) were not included in the analysis for sample collected with speculum.

FIG 2.

ACTIM PROM TEST PERFORMANCE VS. CLINICAL DIAGNOSIS - ≥ 29 to 34 Weeks Gestational Age

	N	SENSITIVITY (95 % Confidence Intervals)	SPECIFICITY (95 % Confidence Intervals)
≥ 29 to 34 weeks (Without Speculum)	97	95.7 % (44/46) (95 % CI: 85.5-98.8 %)	96.1 % (49/51) (95 % CI: 86.8-98.9 %)
≥ 29 to 34 weeks (With Speculum)	96*	95.7 % (44/46) (95 % CI: 85.8-98.8 %)	90.0 % (45/50) (95 % CI: 78.6-95.7 %)

*1 invalid test result (control line was not visible) was not included in the analysis for sample collected with speculum.

Actim PROM test performance by sample type and gestational age versus clinical diagnosis, including 95 % Confidence Intervals (CI) [Fig. 1-2].

Performance of the Actim PROM test was further analyzed based on a patient's gestational age at the time of sample collection [Fig 2].

Repeatability

A panel of specimens consisting of samples of different IGFBP-1 concentration levels was evaluated for intra-assay precision. The samples were tested with 10 replicates during the same day using three different lots of the Actim PROM test. Repeatable results were obtained.

Reproducibility

A study of the Actim PROM test was conducted at three separate sites using panels of blind coded specimens containing negative (0 µg/L of IGFBP-1), high negative (5 µg/L of IGFBP-1), moderate negative (12.5 µg/L of IGFBP-1), low positive (20 µg/L of IGFBP-1), moderate positive (25 µg/L of IGFBP-1), and high positive (30, 50, and 100 µg/L of IGFBP-1) specimens. Test operators (n=9) tested each level multiple times over a period of five days. A total of 360 tests were performed (120 per site) with a total of 45 tests per sample type. The overall reproducibility of the Actim PROM test is 97 % (350/360) with no significant differences within runs (replicates tested by one operator), between runs (five different days), between sites (three sites) or between operators (nine operators).

Analytical Sensitivity

The analytical sensitivity (detection limit) of the Actim PROM test was identified by evaluating different concentrations of IGFBP-1 in extracted samples on three different lots of the Actim PROM test. Two different operators each interpreted ten devices run at each concentration under various lighting conditions for a total of 60 determinations per level. The Actim PROM test limit of detection (100 % positive) is approximately 25 µg/L of IGFBP-1 in extracted sample by two operators under various lighting conditions. The measuring range of the Actim PROM test is approximately 25–500,000 µg/L in extracted sample.

Analytical Specificity

Analytical specificity (cross-reactivity) was tested with human IGFBP proteins at concentrations ranging from 10–5,000 µg/L of each protein in extracted sample. No cross-reactivity was seen using human IGFBP-2, -3, -4, -5 and -6 proteins. The Actim PROM test is specific to human IGFBP-1.

Interfering Substances

The following drugs, shower and bath products, odor control products, and vaginal pathogens were tested with Actim PROM test and were found not to affect Actim PROM test performance [Fig. 3].

Semen and pregnancy urine were tested with the Actim PROM test. No interference of these substances was observed with the performance of the Actim PROM test. Whole blood with concentrations corresponding to typical pregnancy levels of IGFBP-1 was tested and did not affect Actim PROM test performance. Samples with different pH levels (pH levels from 3.5–8.5) were tested with the Actim PROM test and were found not to affect Actim PROM test performance.

FIG 3.

INTERFERING SUBSTANCE	CONCENTRATION TESTED
Pevaryl (active ingredient: econatzol.nitras)	30 mg/mL
Gyno-Trosyd (tioconazol)	20 mg/mL
Flagyl (metronidazole)	100 mg/mL
Canesten (clotrimazol)	40 mg/mL
Personal Lubricant	50 %
Baby Oil	50 %
Baby Powder	50 %
Feminine Deodorant Suppositories	50 %
Vaginal Gel	25 % (RepHresh)
Feminine Deodorant Film	0.1 % (VCF)
Candida albicans	11.2×10^8 CFU/mL
Gardnerella vaginalis	8.6×10^8 CFU/mL
Neisseria gonorrhea	10.6×10^8 CFU/mL
Chlamydia trachomatis	*
HSV-1	*
HSV-2	*

* Supplied as high concentrations from the University of Turku, Finland

EXPLANATION OF SYMBOLS

Use by
YYYY-MM-DD

Temperature
limitation

Manufacturer

Contains sufficient
for <n> tests

LOT

Batch code

IVD

In Vitro Diagnostic
Medical Device

STERILE EO

Sterilized using ethylene oxide

Consult instructions
for use

Do not reuse

REF

Catalogue number

TECHNICAL SUPPORT:
United States Technical Support: 1-800-243-2974 or contact your local distributor.

BIBLIOGRAPHY

1. Silver, Thomas Lee and Helayne. Etiology and Epidemiology of Preterm Premature Rupture of the Membranes. 2001. Clinics in Perinatology. Vol. 28, Issue 4.

2. Mara J. Dinsmoor, Rebecca Bachman, Elaine I. Haney, Marci Goldstein, and William MacKendrick. Outcomes after expectant management of extremely preterm premature rupture of the membranes. 2004. Am J Obstet Gynec. Vol. 190. 183–187.

3. Rutanen E-M, Pekonen F, Kärkkäinen T. Measurement of insulin-like growth factor binding protein-1 in cervical/vaginal secretions: comparison with the ROM-check membrane immunoassay in the diagnosis of ruptured fetal membranes. Clinica Chimica Acta (1993) 214: 73–81.

4. Wathen N, Egembah S, Campbell D, Farkas A, Chard T. Levels of insulin-like growth factor-binding protein-1 increase rapidly in amniotic fluid from 11 to 16 weeks of pregnancy. J.Endocrinol (1993) 137:R1–R4.

5. Erdemoglu E, Mungan T. Significance of detecting insulin-like growth factor binding protein-1 in cervicovaginal secretions: comparison with nitrazine test and amniotic fluid volume assessment. Acta Obstet Gynecol Scand (2004) 83: 622–626.

6. Kubota T, Takeuchi H. Evaluation of insulin-like growth factor binding protein-1 as a diagnostic tool for rupture of the membranes. J. Obstet. Gynaecol. Res. (1998) 24: 411–417.

7. Rutanen E-M, Kärkkäinen T, Lehtovirta J, Uotila J, Hinkula M, Hartikainen A-L. Evaluation of a rapid strip test for insulin-like growth factor binding protein-1 in the diagnosis of ruptured fetal membranes. Clinica Chimica Acta (1996) 253: 91–101.

Actim® PROM

Detect membrane ruptures reliably

For *In Vitro* Diagnostic Use

REF **30831ETUS** Actim PROM Kit, 10 tests

REF **30800ETUS** Actim PROM Controls

Actim

- a subsidiary of Medix Biochemica

Actim Oy

Klovinpellontie 3, FI-02180 Espoo, Finland

Tel. +358 9 547 680, Fax +358 9 505 3441

www.medixbiochemica.com

Distributed by:

CooperSurgical

95 Corporate Drive • Trumbull, CT 06611 USA

Phone 800-243-2974 • Fax 800-262-0105

www.coopersurgical.com

A30831ETUS-IFU Rev. A 2019-04-26