

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE**

A. 510(k) Number:

k123986

B. Purpose for Submission:

New device

C. Measurand:

Insulin-like growth factor binding protein-1 (IGFBP-1)

D. Type of Test:

Qualitative immunoassay test

E. Applicant:

Alere Scarborough, Inc.

F. Proprietary and Established Names:

Actim PROM

G. Regulatory Information:

1. Regulation section:

21 CFR 862.1550; Urinary pH (non-quantitative) Test System

2. Classification:

Class I, Meets 21 CFR 862.9 (c)(9) Limitations of exemptions (For near patient testing (point of care))

3. Product code:

OAM

4. Panel:

Chemistry (75)

H. Intended Use:

1. Intended use(s):

See Indication(s) for Use below.

2. Indication(s) for 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 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.

3. Special conditions for use statement(s):

This device is intended for use in point-of-care and clinical laboratory settings.

4. Special instrument requirements:

No instrument required

I. Device Description:

Actim PROM is available in kits of 1, 10, or 20 individually packed tests. Each Actim PROM test pack contains:

- Individually packaged sterile polyester swabs for specimen collection;
- One (1) polyethylene tube of Specimen Extraction Solution (0.5 ml). The Specimen Extraction Solution is phosphate buffer (pH 6.0) containing bovine serum albumin (BSA), protease inhibitor and preservative;
- One (1) dipstick (6 mm x 120 mm) in a sealed aluminum foil pouch with desiccant. The dipstick contains monoclonal antibodies to IGFBP-1.

Each kit also includes instructions for use.

J. Substantial Equivalence Information:

1. Predicate device name(s):

Actim PROM

2. Predicate 510(k) number(s):

k061886

3. Comparison with predicate:

Similarities and Differences		
Item	Candidate Device Actim PROM (k123986)	Predicate Device Actim PROM (k061886)
Intended Use	To help diagnose the rupture of fetal membranes (ROM) in pregnant women	Same
Intended user	Point-of-Care or clinical laboratory	Same
Gestational Age	≥ 29 weeks gestation	> 34 weeks gestation
Principle	Immunoassay	Same
Type of Test	Qualitative	Same
Detection Method	Visual	Same
Detection Limit	25 µg/L	Same
Test Format	Dipstick	Same
Analyte	Insulin-like growth factor binding protein (IGFBP-1)	Same
Specimen collection and extraction	From vagina in 10-15 seconds with polyester swab, <u>with or without</u> speculum examination; 10 second extraction into buffer solution	From vagina or cervix in 10-15 seconds with polyester swab with speculum examination; 10 second extraction into buffer solution
Read time	1-5 minutes	Same
External quality control materials	Negative, low positive, and high positive controls	Same

K. Standard/Guidance Document Referenced (if applicable):

No standards are referenced.

L. Test Principle:

The Actim PROM test is based on immunochromatography and utilizes two mouse monoclonal antibodies to human insulin-like growth factor binding protein-1 (IGFBP-1). One of the two antibodies is bound to blue latex particles (the detecting label). The other antibody is immobilized as a test line on the membrane (capture 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 capture 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.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

The reproducibility was evaluated at three POC test sites with three different operators per site (total of nine operators). Test panels were prepared containing samples of 0, 5, 12.5, 20, 25, 30, 50 and 100 µg/L of IGFBP-1 in Specimen Extraction Solution. The test panel compositions were masked to the operators. Each operator tested one test panel per day on five different days. Test results were interpreted as positive, negative, or invalid; no invalid tests were observed. The results are shown below. Based on these results (as well as the detection limit study in Section d, below) all results are positive at the Sponsor’s claimed detection level of 25 ug/L.

Conc. (µg/L)	Site 1		Site 2		Site 3		Combined	
	Neg	Pos	Neg	Pos	Neg	Pos	Neg	Pos
0	15	0	15	0	15	0	45	0
5	15	0	14	1	11	4	40	5
12.5	5	10	0	15	0	15	5	40
20	0	15	0	15	0	15	0	45
25	0	15	0	15	0	15	0	45
30	0	15	0	15	0	15	0	45
50	0	15	0	15	0	15	0	45
100	0	15	0	15	0	15	0	45

b. *Linearity/assay reportable range:*

Data supporting linearity testing to validate the measuring range of 25 – 500,000 µg/L was submitted in k061886.

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*

Traceability: This device is traceable to a primary IGFBP-1 purified from soluble extracts of human term placenta/decidua.

Stability: Shelf life stability studies were performed to expand previous shelf life stability claims (k061886). Protocols and acceptance criteria were reviewed and deemed acceptable to support the expanded shelf life of 24 months at 36-77 °F for test kit.

d. *Detection limit:*

A study to establish the detection limit was conducted incorporating masked and randomized samples, two operators, and two lighting conditions. Test panels of 0, 2, 5, 12.5, 25, 50 and 100 µg/L of IGFBP-1 were prepared by diluting internal controls (prepared from purified pooled amniotic fluid) with Specimen Extraction Solution. Test panels were blind coded, and one test panel was used for each of the two

operators in the study. Three different lots of Actim PROM tests were used for testing. Both operators read the test panels under different lighting conditions, laboratory lamp and daylight. Ten replicates per sample per test panel were tested on each lot of Actim PROM for a total of 60 replicates per sample. The percent agreement was calculated for each lot, lighting condition, and operator. The results are summarized below.

Percent Positive Reading by Lot

Lot #	0 µg/L	2 µg/L	5 µg/L	12.5 µg/L	25 µg/L	50 µg/L	100 µg/L
lot 1	0% (0/20)	0% (0/20)	20% (4/20)	100% (20/20)	100% (20/20)	100% (20/20)	100% (20/20)
lot 2	0% (0/20)	0% (0/20)	0% (0/20)	100% (20/20)	100% (20/20)	100% (20/20)	100% (20/20)
lot 3	0% (0/20)	0% (0/20)	50% (10/20)	100% (20/20)	100% (20/20)	100% (20/20)	100% (20/20)

Percent Positive Reading by Lighting Condition

Lighting Condition	0 µg/L	2 µg/L	5 µg/L	12.5 µg/L	25 µg/L	50 µg/L	100 µg/L
Laboratory Lamp	0% (0/40)	0% (0/40)	35% (14/40)	100% (40/40)	100% (40/40)	100% (40/40)	100% (40/40)
Daylight	0% (0/20)	0% (0/20)	0% (0/20)	100% (20/20)	100% (20/20)	100% (20/20)	100% (20/20)

Percent Positive Reading by Operator

Operator	0 µg/L	2 µg/L	5 µg/L	12.5 µg/L	25 µg/L	50 µg/L	100 µg/L
1	0% (0/30)	0% (0/30)	13% (4/30)	100% (30/30)	100% (30/30)	100% (30/30)	100% (30/30)
2	0% (0/30)	0% (0/30)	33% (10/30)	100% (30/30)	100% (30/30)	100% (30/30)	100% (30/30)

e. Analytical specificity:

Interference studies were performed by preparing swab samples containing each potential interferent. Each sample was then extracted into one of three test tubes of Specimen Extraction Solution containing negative, high negative and positive levels of IGFBP-1, respectively. Three replicates of each IGFBP-1 concentration level per product were tested and the results were read by two operators. The following drugs, shower and bath products, odor control products, and vaginal pathogens were tested with the Actim PROM test and were found not to affect test performance.

Interfering Substance	Concentration Tested
Pevaryl (active ingredient: econazol.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	50%
Feminine Deodorant Film	50%
Candida albicans	11.2 x 10 ⁸ CFU/ml
Gardnerella vaginalis	8.6 x 10 ⁸ CFU/ml
Neisseria gonorrhoea	10.6 x 10 ⁸ CFU/ml
Chlamydia trachomatis	*
HSV-1	*
HSV-2	*

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

In addition, samples with pH levels ranging from 3.5-8.5 were tested with the Actim PROM test and were found not to affect test performance. Semen, pregnancy urine, and whole blood with concentrations corresponding to typical pregnancy levels of IGFBP-1 were also tested with the Actim PROM test and were found not to affect test performance.

The sponsor included the following limitation in their labeling regarding blood interference:

“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.”

f. Assay cut-off:

Refer to section M.1.d. above.

2. Comparison studies:

a. Method comparison with predicate device:

See k061886 for method comparison information.

b. Matrix comparison:

Not applicable.

3. Clinical studies:

a. Clinical Sensitivity:

The sponsor conducted a multi-center, prospective study to evaluate the clinical sensitivity and specificity of the Actim PROM test in pregnant women ≥ 29 weeks

gestational age and to evaluate the clinical performance of the test with specimens collected with or without the use of a speculum. Conventional clinical criteria, including visual detection of amniotic fluid leaking from the cervical os, nitrazine test, visual pooling of fluid in the posterior fornix, and microscopic evidence of ferning, collected by performing a diagnostic speculum examination for ROM were utilized as the gold standard.

Device performance was compared to clinical diagnostic criteria for ROM on 222 vaginal swab subject samples collected without a speculum and 220 vaginal swab subject samples collected with a speculum (two sample tests were considered invalid, no control line appeared and insufficient sample remained to repeat the testing). Of the 222 subjects, 97 were between 29 and 34 weeks gestational age and the remainder were >34 weeks gestational age. The overall and stratified (by gestational age and sample collection with/without speculum) results are summarized below.

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.

Actim PROM Test Performance vs. Clinical Diagnosis
Stratified Results (≥ 29 Weeks 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.

b. Clinical specificity:

See section M.3.a. above.

c. Other clinical supportive data (when a. and b. are not applicable):

Not applicable

4. Clinical cut-off:

Not applicable

5. Expected values/Reference range:

The expected values for IGFBP-1 were determined in literature studies. The concentration of IGFBP-1 in amniotic fluid is between 10,500 and 350,000 µg/L (Rutanen, et al., Clinica Chimica Acta 214 (1993) 73-78).

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.