January 2025

PartoSure® Test
Summary of Safety and Performance

Version 1

IVD

For In Vitro Diagnostic Use

CE 0197

REF TTDT-1-20-IVDR

QIAGEN Sciences LLC,
19300 Germantown Road,
Germantown,
MD 20874, USA

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Summary of Safety and Performance

This Summary of Safety and Performance (SSP) is intended to provide public access to an up-to-date summary of the main aspects of the safety and performance of the device.

The SSP is not intended to replace the Instructions For Use as the main document to ensure the safe use of the device, nor is it intended to provide diagnostic or therapeutic suggestions to intended users.

The following information is intended for professional users.

Document revision: 03
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Manufacturer's reference number for the SSP: HB-3629-SPR

1. Device identification and general information	
1.1 Device trade name(s)	PartoSure® Test
1.2 Manufacturer's name and address	QIAGEN Sciences LLC, 19300 Germantown Road, Germantown, MD 20874, USA
1.3 Manufacturer's single registration number (SRN)	US-MF-000014502
1.4 Basic UDI-DI	4053228RPS0000000000001BT
1.5 European Medical Device Nomenclature	W01020190

(EMDN) description / text	
1.6 Risk Class of the device	Class C (Rule 3j and 4b)
1.7 Year when the first certificate was issued under Regulation (EU) 2017/746 covering the device	The PartoSure Test was certified under the EU Regulation 2017/746 in 2024.
1.8 Authorised representative if applicable; name and the SRN	QIAGEN GmbH, QIAGEN Strasse 1, 40724 Hilden, Germany SRN: DE-MF-000004949
1.9 Notified body and the single identification number (SIN)	TÜV Rheinland LGA Products GmbH Tillystraße 2 90431 Nürnberg Germany SIN: TÜV: 0197
2. Intended use of the device	
2.1 Intended purpose	The PartoSure Test is a rapid, non-instrumented, qualitative immunochromatographic test for the *in vitro* detection of placental alpha microglobulin-1 (PAMG-1) in vaginal secretions of pregnant women using a sterile vaginal swab provided in the kit. The device is designed as an aid to rapidly assess the risk of preterm delivery in ≤7 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 dilatation (≤ 3 cm), sampled between 20 weeks, 0 days and 36 weeks, 6 days gestation. The PartoSure Test is intended for use in a clinical setting by trained healthcare professionals and is not intended for self-testing.

2.2 Indication(s) and target population(s)	The PartoSure test is intended to be used on pregnant women with signs and symptoms of early preterm labor, intact amniotic membranes, and minimal cervical dilatation (≤ 3 cm), sampled between 20 weeks, 0 days and 36 weeks, 6 days gestation.
2.3 Indication whether it is a device for near-patient testing and/or a companion diagnostic	The PartoSure Test is a device for near-patient testing. Not a companion diagnostic test.
2.4 Limitations and/or contra-indications	The PartoSure Test should only be used in patients with signs and symptoms of preterm labor. Care must be taken not to contaminate the swab or cervicovaginal secretions with personal lubricants (e.g., K-Y® lubricating jelly). When the specimen contains > 25% of personal lubricant, it may interfere with absorption of the specimen by the swab or with the antibody-antigen reaction of the PartoSure Test and lead to invalid test results. If it is suspected that the patient has applied a topical disinfectant (e.g., Miconazole nitrate cream) to the vaginal area within 24 hours, delay specimen collection until 24 hours from application of the topical disinfectant have passed as these products, when greater than 32% of the specimen, can lead to false-negative test results. The PartoSure Test is not intended for use in women with moderate or gross vaginal bleeding. The presence of vaginal bleeding may contribute to difficulty in interpreting the PartoSure Test result. Testing a moderately to grossly bloody sample may lead to false-positive results. If upon visual examination you are concerned about the presence of moderate or gross vaginal blood, it is recommended that the sample be collected following the cessation of active vaginal bleeding. If concentrations of *Trichomonas vaginalis* greater than 10^5 cfu/mL are present in a specimen, false-negative test results may occur.
3. Device description	

3.1 Description of the device, including the conditions to use the device	**a) General description of the device, including its intended purpose and intended users** The PartoSure Test is a rapid, non-instrumented, qualitative immunochromatographic test for the *in vitro* detection of placental alpha microglobulin-1 (PAMG-1) in vaginal secretions of pregnant women using a sterile vaginal swab provided in the kit. The device is designed as an aid to rapidly assess the risk of preterm delivery in ≤7 days from the time of cervicovaginal sample collection in pregnant women with signs and symptoms of preterm labor, intact amniotic membranes, and minimal cervical dilatation (≤3 cm), sampled between 20 weeks, 0 days and 36 weeks, 6 days gestation. The PartoSure Test is intended for use in a clinical setting by trained healthcare professionals and is not intended for self-testing. **b) Description of the principle of the assay method or principles of operation of the instrument** The PartoSure Test uses the principles of immunochromatography to identify the presence of human PAMG-1, a protein released from decidual cells into the amniotic cavity throughout pregnancy, is present in cervicovaginal discharge when labor and delivery are imminent. PAMG-1 was selected as a marker of preterm birth due to its unique characteristics, i.e. its high level in the amniotic fluid, low level in blood and extremely low background level in cervicovaginal secretions when the fetal membrane is completely intact. The PartoSure Test employs highly sensitive monoclonal antibodies (M271 and M52) that detect very low levels of PAMG-1 present in cervicovaginal secretions of pregnant women. Background concentration of PAMG-1 is approximately 50-220 picograms (i.e. 0.05-0.22 ng) per 1mL of vaginal discharge of pregnant women without complications. The test sensitivity cut-off is 13-18 times above the maximum background PAMG-1 concentration. Using the sterile swab, a sample is collected from the vagina for 30 seconds. The swab (containing collected sample) is then rotated in the solvent vial for 30 seconds, after which the swab is disposed. The PartoSure Test Strip is then inserted into the solvent vial containing diluted sample. The test result is read visually after 5 minutes.

	The presence of both test and control lines indicates a positive result, the presence of only control line indicates a negative result. Absence of both lines or presence of only test line indicates that the test is invalid and should be repeated. Transport materials are not provided, as the device is intended to be used where the sample is collected. If the test is to be run in a different area within the site from where the sample is collected, the sample is transported in the solvent for which is was eluted. Based on the risk-based classification rules defined in Annex VIII of the IVDR (EU) 2017/746, it has been determined that the PartoSure Test is a Class C (Rule 3j and 4b) IVD medical device.
3.2 In case the device is a kit, description of the components (including regulatory status of components, for example, IVDs, medical devices and any Basic UDI-DIs)	The PartoSure Test kit consists of three parts: a sterile vaginal swab, a transparent plastic vial with solvent solution, and a lateral flow Test Strip. Each Kit contains 20 test kits and each test kit contains 1x swab, 1x solvent and 1x test strip.
3.3 A reference to previous generation(s) or variants if such exists, and a description of the differences	No previous version.
3.4 Description of accessories intended to be used in	Not Applicable.

combination with the device	
3.5 Description of any other devices and products which are intended to be used in combination with the device	Not Applicable.
4. Reference to any harmonized standards and CS applied	
4 Harmonized standards and Common Specifications (CS) applied	EN 13612:2002+AC:2002 EN 62366-1:2015+AC:2015+AC:2016+A1:2020 EN ISO 13485:2016+AC:2018 EN ISO 14971:2019 EN ISO 15223-1:2021 EN ISO 18113-1:2011 EN ISO 18113-2:2011 ISO 20916:2019 EN ISO 23640:2015 EN13975:2003
5. Risks and warnings	
5.1 Residual risks and undesirable effects	• Specimens and samples are potentially infectious and used PartoSure Test kits are biohazardous. Discard sample and assay waste according to local safety procedures. • The PartoSure Test result should not be interpreted as absolute evidence for the presence or absence of a process that will result in delivery ≤7 days from specimen collection. • The PartoSure Test 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, assessment of uterine activity, and evaluation of other risk factors.

	• The information and instructions provided by the manufacturer are easy for the intended user to understand and apply, to correctly interpret the result provided by the device and to avoid misleading information. • Results should be interpreted with caution when a specimen is obtained from a patient with unconfirmed gestational age. • Specimens should be collected prior to collection of culture specimens. Collection of vaginal specimens for microbiologic culture frequently requires aggressive collection techniques that may abrade the cervical or vaginal mucosa and may potentially interfere with sample preparation. • Specimens should not be obtained from patients with suspected or known placental abruption or placenta previa. • The PartoSure Test is for in vitro diagnostic use only and no component of the test kit, other than the swab, should come into contact with the patient. • PartoSure Test performance has been characterized from specimens taken from the vaginal cavity. Samples obtained from other locations should not be used. • PartoSure Test kit components are for single use only. • PartoSure Test results are qualitative and not quantitative. No quantitative interpretation should be made based on the strength of the test or control lines. • 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. • The PartoSure Test should only be used in patients with signs and symptoms of preterm labor. • Care must be taken not to contaminate the swab or cervicovaginal secretions with personal lubricants (e.g., K-Y® lubricating jelly). When the specimen contains >25% of personal lubricant, it may interfere with absorption of the specimen by the swab or with the antibody-antigen reaction of the PartoSure Test and lead to invalid test results.

	• If it is suspected that the patient has applied a topical disinfectant (e.g., Miconazole nitrate cream) to the vaginal area within 24 hours, delay specimen collection until 24 hours from application of the topical disinfectant have passed as these products, when greater than 32% of the specimen, can lead to false-negative test results. • The PartoSure Test is not intended for use in women with moderate or gross vaginal bleeding. The presence of vaginal bleeding may contribute to difficulty in interpreting the PartoSure Test result. Testing a moderately to grossly bloody sample may lead to false-positive results. If upon visual examination you are concerned about the presence of moderate or gross vaginal blood, it is recommended that the sample be collected following the cessation of active vaginal bleeding. • If concentrations of *Trichomonas vaginalis* greater than 10^5 cfu/mL are present in a specimen, false-negative test results may occur.
5.2 Warnings and precautions	• Do not use the PartoSure Test after the expiration date, which is printed on the product packaging. • Do not use the kit if the swab or test strip package integrity is compromised or if the solvent vial has leaked. • Do not bend or fold the test strip or the foil pouch with the test strip in it; doing so may damage the strip and lead to inaccurate results. • Store the PartoSure Test kit in a dry place at 15°C to 25°C (59F to 77°F). The test should not be frozen. • When stored in the foil pouch at the recommended temperature, the test is stable until the expiration date printed on the pouch. • PartoSure solvent contains Sodium azide. Warning! May be harmful if swallowed. Wear protective gloves/ protective clothing/ eye protection/ face protection. Sodium azide may react with plumbing to form potentially explosive metal azides. Avoid contact with skin, eyes, and clothing. In case of contact with any of these reagents, wash area thoroughly with water. If disposing of this reagent, always flush the drain with large volumes of water to prevent azide build-up. • PartoSure Test kit components are for single use only.

5.3 Other relevant aspects of safety, including a summary of any field safety corrective action (FSCA including FSN), if applicable	There have been no FSCAs since QIAGEN acquired the PartoSure Test in 2018.
6. Summary of the performance evaluation and post-market performance follow-up (PMPF)	
6.1 Summary of scientific validity of the device	Below is a brief summary of the scientific validity related to the analyte as well as State of the Art. This is based on a combination of the following sources: a) relevant information on the scientific validity of devices measuring same analytes or markers; which are, in the context of this evaluation, pre-term delivery, in conjunction with other clinical, laboratory, and epidemiological data. b) scientific (peer-reviewed) literature, as obtained from the searches performed as described. c) results from clinical performance studies Preterm labor is defined as regular contractions of the uterus resulting in changes in the cervix that start before 37 weeks of pregnancy. Preterm labor and birth are fairly common in the UK, with 8% of babies born before 37 weeks of pregnancy; however, less than 1% of babies are born between 22 and 28 weeks of pregnancy. The WHO defines sub-categories of Preterm Birth (PTB), based on gestational age: • extremely preterm (less than 28 weeks of pregnancy) • very preterm (28 to less than 32 weeks of pregnancy) • moderate to late preterm (32 to less than 37 weeks of pregnancy). Biomarker tests such as PAMG-1, as utilized in the PartoSure Test, help to diagnose preterm labor and are intended for use alongside other clinical information to assess the risk of PTB in women with symptoms of preterm labor who have intact amniotic membranes. These tests may be used as alternatives

	to qualitative fetal fibronectin testing or clinical assessment alone, where transvaginal ultrasound (TVU) measurement of cervical length (CL) is not available or acceptable. The results of the biomarker tests are designed to help clinicians decide which women can be safely sent home and which need to be admitted to the hospital and given treatment to try to delay birth and improve neonatal outcomes. The results of these tests would be used in combination with clinical judgment, for example, if the test result is negative and the symptoms of preterm labor have settled, the woman would be discharged home with routine follow-up in the community and advised to return if symptoms reappear. If the test result is negative but symptoms of preterm labor continue, the woman would be admitted and monitored, and symptoms treated as appropriate and monitored. If symptoms were managed successfully, the woman would be discharged home. If the test result is positive, the woman would be admitted, and symptoms managed as appropriate and monitored. The use of these tests may result in a more accurate diagnosis of preterm labor. This could lead to improved health outcomes for women and their babies, and cost savings through reductions in the length of hospital stay, decreasing unnecessary hospital admissions, and minimizing unnecessary transfers between hospitals. The use of these tests may also enable better resource planning based on the expected need for transfers between hospitals and neonatal intensive care. The following are citations resulting from a non-biased systematic Scientific Validity literature search, using predefined search criteria after scoring and screening based on the intended uses of the device under evaluation: 1. Ehsanipoor RM, Swank ML, Jwa SC, Wing DA, Tarabulsi G, Blakemore KJ. Placental α-Microglobulin-1 in Vaginal Secretions of Women with Evidence of Preterm Labor. Am J Perinatol. 2016 Jan;33(2):208-13. 2. Çekmez Y, Kıran G, Haberal ET, Dizdar M. Use of cervicovaginal PAMG-1 protein as a predictor of delivery within seven days in pregnancies at risk of premature birth. BMC Pregnancy Childbirth. 2017 Jul 26;17(1):246.

	3. P-0250 Poster - Mechanisms for preterm labor and fetal injury - Evaluation of PAMG -1 for the Prediction of Preterm Birth in Patients Symptomatic of Preterm Labor Lotfi, G.; Faraz, S.; Al Swalhee, N.; Nasir, R.; Somini, S.; Abdeldayem, R.; Koratkar, R.; Ammar, A. Dubai Health Authority, Duba Latfa Hospital, United Arab Emirates. 4. Dawes LK, Prentice LR, Huang Y, Groom KM. The Biomarkers for Preterm Birth Study-A prospective observational study comparing the impact of vaginal biomarkers on clinical practice when used in women with symptoms of preterm labor. Acta Obstet Gynecol Scand. 2020 Feb;99(2):249-258 5. E1294 - Placental Alpha Microglobin 1 To Predict Spontaneous Preterm Birth In Symptomatic Woman Morales F. 1, Galarce V., Guerra M. (2019). 3 – Poster Presentations, Journal of Perinatal Medicine, 47(s1), eA327-eA550. 6. Ali Gokce , Erkan Kalafat , Yavuz Emre Sukur , Orhan Altinboga & Feride Soylemez (2020): Role of cervical length and placental alpha microglobulin-1 to predict preterm birth, The Journal of Maternal-Fetal & Neonatal Medicine. 7. Maryam Kashanian, Nooshin Eshraghi, Maryam Rahimi & Narges Sheikhansari (2020): Evaluation of placental alpha microglobulin-1(PAMG1) accuracy for prediction of preterm delivery in women with the symptoms of spontaneous preterm labor; a comparison with cervical length and number of contractions, The Journal of Maternal-Fetal & Neonatal Medicine. 8. Melchor JC, Khalil A, Wing D, Schleussner E, Surbek D. Prediction of preterm delivery in symptomatic women using PAMG-1, fetal fibronectin and phIGFBP-1 tests: systematic review and meta-analysis. Ultrasound Obstet Gynecol. 2018 Oct;52(4):442-451. 9. Pirjani R, Moini A, Almasi-Hashiani A, Farid Mojtahedi M, Vesali S, Hosseini L, Sepidarkish M. Placental alpha microglobulin-1 (PartoSure) test for the prediction of preterm birth: a systematic review and meta-analysis. J Matern Fetal Neonatal Med. 2019 Nov 17:1-13. 10. Nikolova T, Uotila J, Nikolova N, Bolotskikh VM, Borisova VY, Di Renzo GC. Prediction of spontaneous preterm delivery in women presenting with premature labor: a comparison of placenta alpha microglobulin-1, phosphorylated insulin-like growth factor binding protein-1, and cervical length. Am J Obstet Gynecol. 2018 Dec;219(6):610.e1-610.e9.

	11. Sergey V. Barinov, Gian Carlo Di Renzo, Antonina A. Belinina, Olga V. Koliado & Olga V. Remneva (2021): Clinical and biochemical markers of spontaneous preterm birth in singleton and multiple pregnancies, The Journal of Maternal-Fetal & Neonatal Medicine. 12. Chawanpaiboon, Saifon, Titapant, Vitaya and Pooliam, Julaporn. "Placental α-microglobulin-1 in cervicovaginal fluid and cervical length to predict preterm birth by Thai women with symptoms of labor" Asian Biomedicine, vol.15, no.3, 2021, pp.119-127. 13. Cnota W, Jagielska A, Janowska E, Banas E, Kierach R, Nycz-Reska M, Czuba B. Prediction of preterm birth using PAMG-1 test: a single centre experience - preliminary report. Ginekol Pol. 2022 Jan 24. 14. Pirjani R, Moini A, Almasi-Hashiani A, Farid Mojtahedi M, Vesali S, Hosseini L, Sepidarkish M. Placental alpha microglobulin-1 (PartoSure) test for the prediction of preterm birth: a systematic review and meta-analysis. J Matern Fetal Neonatal Med. 2021 Oct;34(20):3445-3457. 15. Konoplyannikov AG, Dikke GB, Karaganova EY. Combination of the placental alpha-1 microglobulin test and ultrasonic cervical length measurement to predict the time of preterm birth. J Matern Fetal Neonatal Med. 2022 Feb;35(3):541-545. 16. Barinov SV, Di Renzo GC, Belinina AA, Koliado OV, Remneva OV. Clinical and biochemical markers of spontaneous preterm birth in singleton and multiple pregnancies. J Matern Fetal Neonatal Med. 2021 Feb 24:1-6. 17. Dochez V, Ducarme G, Gueudry P, Joueidi Y, Boivin M, Boussamet L, Pelerin H, Le Thuaut A, Lamoureux Z, Riche VP, Winer N, Thubert T, Marie E. Methods of detection and prevention of preterm labour and the PAMG-1 detection test: a review. J Perinat Med. 2020 Oct 2;49(2):119-126. 18. Kehl S, Weiss C, Pretscher J, Baier F, Faschingbauer F, Beckmann MW, Stumpfe FM. The use of PAMG-1 testing in patients with preterm labor, intact membranes and a short sonographic cervix reduces the rate of unnecessary antenatal glucocorticoid administration. J Perinat Med. 2021 Jul 19;49(9):1135-1140.
6.2 Summary of performance data from the	Not Applicable.

equivalent device, if applicable	
6.3 Summary of performance data from conducted studies of the device prior to CE-marking	A summary of the clinical and analytical performance studies is provided below: **Clinical Performance of device under evaluation** • Expected values The PartoSure Test is a lateral flow, immunochromatographic assay designed to identify the presence of human placental alpha microglobulin-1 (PAMG-1) in amniotic fluid. PAMG-1 was selected as a marker for accurate risk assessment of preterm birth due to its unique characteristics, i.e., its high level in amniotic fluid, low level in blood, and extremely low background level (50-220 picograms/mL) in cervico-vaginal discharge. The test employs monoclonal antibodies sufficiently sensitive to detect 1 ng/mL of PAMG-1 once eluted into the solvent vial. With a dilution of 3-4-fold once eluted into the solvent vial, the cut-off concentration is 13-18 times above the maximum background PAMG-1 concentration. For the analysis, a sample of cervicovaginal discharge collected by vaginal swab is extracted into a solvent. The presence of PAMG-1 antigen is then detected by inserting a lateral-flow test strip into the vial. The sample flows from an absorbent pad to a nitrocellulose membrane, passing through a reactive area containing monoclonal anti-PAMG-1 antibodies conjugated to a gold particle. The antigen-antibody complex flows to the test region where it is immobilized by a second anti-PAMG-1 antibody. This event leads to the appearance of the test line. Unbound antigen-antibody complexes continue to flow along the test strip and are immobilized by a second antibody. This leads to the appearance of the internal control line. PartoSure detects trace amounts of human PAMG-1. PAMG-1 concentrations greater than 1 ng/mL indicate an elevated risk of delivering within the next 7 days. **Performance characteristics:** Precision and reproducibility were determined using three lots of the PartoSure Test at three sites by three different users at each site. Five

replicates of seven different PAMG-1 concentrations above and below the limit of detection of the PartoSure Test were used, including an absolute zero (0.0 ng/mL), a low-negative (0.2 ng/mL), a non-zero negative (0.5 ng/mL), the limit of detection (1.0 ng/mL), a low-positive (2.0 ng/mL).

The clinical performance of the PartoSure Test was assessed in multiple peer-reviewed publications describing the use of PartoSure in clinical studies. To be included in the review, the papers had to list methods that included performing PartoSure according to its Instructions for Use (IFU) available at the time. In total, 17 publications were included in the final analysis. The following performance estimates with corresponding 95% confidence intervals were calculated:

Table 1. Sensitivity and Specificity of PartoSure Test

Sensitivity			Specificity		
Frequency	%	95% CI	Frequency	%	95% CI
182 / 323	56.35%	(50.75%, 61.83%)	2743 / 2863	95.81%	(95.01%, 96.51%)

Table 2. Positive and Negative Predictive Value of PartoSure Test

PPV			NPV		
Frequency	%	95% CI	Frequency	%	95% CI
182 / 302	60.26%	(54.50%, 65.82%)	2743 / 2884	95.11%	(94.26%, 95.87%)

Table 3. Calculated Positive and Negative likelihood ratios

Positive Likelihood Ratio	Negative Likelihood Ratio
13.443	0.456

Note: LR+ = true positive/false positive. LR– = Probability that a person with the disease tested negative/probability that a person without the disease tested negative.

	Cross Reactivity: The PartoSure Test was evaluated using a panel of potentially cross-reactive protein substances likely to be found in vaginal specimens, including human chorionic gonadotropin, trophoblastic beta-2 glycoprotein, human placental lactogen, alpha 1 fetoprotein, IGFBP-3, and human serum albumin. Ten (10) replicates of each sample containing the potentially cross-reactive substance were tested using a non-zero negative PAMG-1 sample (0.2 ng/mL) and a low-positive sample (2.0 ng/mL). Each potentially cross-reactive substance was tested at the highest concentration of substance that was considered clinically relevant. None of the potentially cross-reactive substances tested demonstrated cross-reactivity with the PartoSure Test. **Calculation of Sensitivity, Specificity, PPV & NPV:** In order to demonstrate validation of applicable product requirements, a literature search was conducted for PartoSure clinical studies that included true negative, false negative, true positive, and false positive data. All publications for PartoSure since its launch were considered, but only those who listed methods that included performing PartoSure according to its Instructions for Use (IFU) were included in the analysis, and they must have been, at a minimum, briefly summarized in their respective Materials and Methods section. A total of 6 peer-reviewed publications included data from both PartoSure and fFN that fit the above criteria and were included in the analysis. Additionally, 11 other peer-reviewed publications examined PartoSure apart from fFN and fit the criteria listed above, so they were included in the analysis. Sensitivities, specificities, their respective frequency percentages and 95% Confidence Intervals were calculated. Additionally, PPV (Positive Predictive Value), NPV (Negative Predictive Value), and their respective frequency percentages and 95% Confidence Intervals were calculated. The different performance metrics were calculated based on a 2x2 table.

		Reference Method	
		Positive	Positive
Test methods	Positive	A	B
	Negative	C	D

Sensitivity = a / (a + c)

- Specificity = d / (b + d)
- PPV = a / (a + b)
- NPV = d / (c + d)
- Positive likelihood ratio = Sensitivity / (1 – Specificity)
- Negative likelihood ratio = (1 – Sensitivity) / Specificity

Confidence intervals were calculated using the Clopper-Pearson or exact method.

Analytical Performance of device under evaluation

A summary of the analytical performance studies is provided below:

- Precision

A panel of PAMG-1 specimens at varying concentrations were evaluated for intra-assay precision. Three different operators interpreted five (5) replicates of each panel member using three (3) different lots of the PartoSure Test for a total of 45 determinations per level. The following table below provides the percentages of negative and positive percent agreement categorized by each test sample's PAMG-1 concentration and test strip lot.

Table 4. Percentage of negative and positive agreement at each PAMG-1 concentration and test strip lot, with respective corresponding 95% confidence intervals

Agreement Measure	PAMG-1 Concentration	Lot	Frequency of Results in Agreement	% in Agreement	Lower Exact Two-sided 95% Confidence Limit	Upper Exact Two-sided 95% Confidence Limit
NPA	0.0 ng/mL	1	15/15	100.00%	78.20%	100.00%
NPA	0.0 ng/mL	2	15/15	100.00%	78.20%	100.00%
NPA	0.0 ng/mL	3	15/15	100.00%	78.20%	100.00%
NPA	0.2 ng/mL	1	15/15	100.00%	78.20%	100.00%
NPA	0.2 ng/mL	2	15/15	100.00%	78.20%	100.00%
NPA	0.2 ng/mL	3	15/15	100.00%	78.20%	100.00%
NPA	0.5 ng/mL	1	15/15	100.00%	78.20%	100.00%
NPA	0.5 ng/mL	2	15/15	100.00%	78.20%	100.00%
NPA	0.5 ng/mL	3	15/15	100.00%	78.20%	100.00%
PPA	1.0 ng/mL	1	15/15	100.00%	78.20%	100.00%
PPA	1.0 ng/mL	2	15/15	100.00%	78.20%	100.00%
PPA	1.0 ng/mL	3	15/15	100.00%	78.20%	100.00%
PPA	2.0 ng/mL	1	15/15	100.00%	78.20%	100.00%
PPA	2.0 ng/mL	2	15/15	100.00%	78.20%	100.00%
PPA	2.0 ng/mL	3	15/15	100.00%	78.20%	100.00%

- Reproducibility

A multi-center reproducibility study was conducted to evaluate performance of the PartoSure Test across study sites with multiple operators. Three sites, representing intended testing locations of hospitals and health centers, were employed for the study, and each site used three different operators to conduct the testing. Test samples consisted of a five (5) member panel of varying PAMG-1 concentrations:

Sample 1: Negative (No PAMG-1, sample is Solvent Solution)
Sample 2: Low-Negative (0.2 ng/mL of PAMG-1)
Sample 3: High-Negative (0.5 ng/mL of PAMG-1)
Sample 4: Concentration at the analytical cut-off (1.0 ng/mL of PAMG-1)

Sample 5: 2X concentration above the analytical cut-off (2.0 ng/mL of PAMG-1)
Five replicates of each concentration were tested by each operator at each site for a total of 15 replicates per site and 45 replicates for each concentration. The below table provides the percentages of negative and positive percent agreement categorized by each test sample's PAMG-1 concentration and test site.

Table 5. Percentage of negative and positive agreement at each PAMG-1 concentration and site, with respective corresponding 95% confidence intervals

Agreement Measure	PAMG-1 Concentration	Site	Frequency of Results in Agreement	% in Agreement	Lower Exact Two-sided 95% Confidence Limit	Upper Exact Two-sided 95% Confidence Limit
NPA	0.0 ng/mL	1	15/15	100.00%	78.20%	100.00%
NPA	0.0 ng/mL	2	15/15	100.00%	78.20%	100.00%
NPA	0.0 ng/mL	3	15/15	100.00%	78.20%	100.00%
NPA	0.2 ng/mL	1	15/15	100.00%	78.20%	100.00%
NPA	0.2 ng/mL	2	15/15	100.00%	78.20%	100.00%
NPA	0.2 ng/mL	3	15/15	100.00%	78.20%	100.00%
NPA	0.5 ng/mL	1	15/15	100.00%	78.20%	100.00%
NPA	0.5 ng/mL	2	15/15	100.00%	78.20%	100.00%
NPA	0.5 ng/mL	3	15/15	100.00%	78.20%	100.00%
PPA	1.0 ng/mL	1	15/15	100.00%	78.20%	100.00%
PPA	1.0 ng/mL	2	15/15	100.00%	78.20%	100.00%
PPA	1.0 ng/mL	3	15/15	100.00%	78.20%	100.00%
PPA	2.0 ng/mL	1	15/15	100.00%	78.20%	100.00%
PPA	2.0 ng/mL	2	15/15	100.00%	78.20%	100.00%
PPA	2.0 ng/mL	3	15/15	100.00%	78.20%	100.00%

- **Limit of Detection (LoD)**

Limit of Detection (LoD) is defined as the lowest concentration of analyte that can be consistently detected (typically, in ≥ 95% of the samples tested

under routine laboratory conditions and in a defined type of sample). In this context, the acceptance criteria for LoD determination is ≥ 95% positive results. The study for precision and reproducibility, included samples just below the 1 ng/mL detected by the monoclonal antibodies as the cutoff, 0.9 ng/mL and 0.7 ng/mL. They were not appropriate concentrations to measure reproducibility, due to the natural variability around an assay's cutoff, but would be appropriate to measure LoD, as the cut off concentration of 1 ng/mL was included in the dataset, so C_{95} could be measured with those samples. Below is a table that provides a summary of all data from the Precision and Reproducibility verification, including the sample concentrations noted above that were not relevant for reproducibility but are applicable to LoD determination. According to the definition for LoD, the LoD is 1.0 ng/mL, as 0.9 ng/mL was identified as a positive in 86% of the 135 replicates at that concentration

Table 6. LoD Study Results with 95% Confidence Intervals

[PAMG-1]	ALL PartoSure Lots Tested			
	Negative	Positive	%Positive	95% CI (%)
0 ng/mL	135	0	0%	(0.0, 2.7)
0.2 ng/mL	135	0	0%	(0.0, 2.7)
0.5 ng/mL	135	0	0%	(0.0, 2.7)
0.7 ng/mL	35	100	74%	(65.8, 81.2)
0.9 ng/mL	19	116	86%	(78.9, 91.3)
1.0 ng/mL	0	135	100%	(97.3, 100.0)
2.0 ng/mL	0	135	100%	(97.3, 100.0)

- **Cut-off Determination**

A risk-based approach, based on the background concentration of PAMG-1 in cervicovaginal secretions and the subsequent swab elution of the sample, was used to identify a clinical cutoff of 1 ng/mL when tested by the PartoSure Test Strip in PartoSure Solvent, as it would minimize the chance of false positives while maximizing the negative predictive value (NPV) and clinical specificity. Compared to other diagnostic tests on the market to aid the time-to-delivery prediction, the clinical cutoff of 1 ng/mL also yields comparable, if not superior, clinical sensitivity and positive

	predictive value (PPV). In parallel, verification studies have provided statistically powered data indicating an LoD of 1 ng/mL. The 1 ng/mL clinical cutoff detected by the PartoSure Test matches the LoD of ≥ 95% positive results at that concentration. • **Accuracy and Trueness** There is no reference method (gold standard) for PAMG-1 determination. There are no available standard reference materials to conduct a Trueness and Accuracy study of the PartoSure Test, and the PartoSure Test is a qualitative assay. As AmniSure detects the same biochemical marker, PAMG-1, the Trueness and Accuracy study of the PartoSure Test was performed to compare with the AmniSure Test side-by-side using the same prepared materials. Sixty (60) replicates in total were tested with both AmniSure and PartoSure (25 replicates each of PAMG-1 at a concentration of 2.0 ng/mL as positive samples and 0.2 ng/mL as negative samples). The acceptance criteria were defined as the percentage of PartoSure results in agreement with the AmniSure results to be ≥ 90.0%. For the AmniSure and PartoSure Trueness and Accuracy studies, the agreement between the AmniSure and PartoSure results was 100%. • **Interfering Substances** Endogenous substances, antibiotics, Women's health care products, therapeutic drugs used for pregnancy issues were tested for potential interference on the PartoSure Test. The study has been conducted following CLSI EP07-A2 Guidance "Interference Testing in Clinical Chemistry". The purpose of this study was to determine if the results of the PartoSure Test are impacted by interference from substances that may be found in vaginal specimens. The following potentially interfering substances were tested: naturally occurring endogenous interferent, 17-OH-progestrol, and three groups of exogenous interferents: antibiotics (used as oral pills, solutions for injections, or vaginal creams), women's health care products (shower and

	bath products), and drugs to treat pregnancy issues (used as oral pills, solutions for injections, intravenous infusion). For each interfering substance, ten (10) blinded replicate samples with 0.2 or ten (10) blinded replicates with 2.0 ng/mL of PAMG-1 levels were tested with the PartoSure Test on the same day by the same analyst. The substance was considered as not interfering in the detection of PAMG-1, if the proportion of valid and correct results is ≥ 95.0. ● The personal lubricant at 50% w/v interfered with the flow rate and the strips were invalid according to the validity criteria but were valid at 25% w/v. ● Miconazole Cream and soap were found to give potential interference for PartoSure strips. Miconazole Cream at 50% w/v did not meet the acceptance criteria of ≥ 95.0% correct calls but it did meet the acceptance criteria at 32% w/v concentration. Soap at 4% w/v did not meet the acceptance criteria. Soap at 2% w/v met the acceptance criteria of ≥ 95.0%. All of the other potential interfering substances tested did not show interference at the concentrations tested. • **Semen and Urine** A non-zero negative (0.2 ng/mL PAMG-1) sample and a low positive (2.0 ng/mL PAMG-1) sample were tested against 10 individual samples of semen and 10 individual samples of maternal urine. Neither semen nor maternal urine demonstrated interference with the PartoSure test. • **Maternal Bleeding** A non-zero negative sample (0.2 ng/mL PAMG-1) and a low positive sample (2.0 ng/mL PAMG-1) were tested against ten (10) individual maternal blood samples at the three (3) lowest admixture levels determined to represent "trace", "moderate", or "gross" levels of maternal bleeding on the vaginal collection swab. In cases of only trace amounts of blood on the collection swab, the PartoSure Test functions properly. However, moderate or gross vaginal bleeding may contribute to difficulty in interpreting the PartoSure Test results and could lead to false-positive results. See Table 7 below for the results.

Table 7. Interfering Substances Study Results (Maternal Blood)

Agreement measure	PAMG-1 Concentration	Maternal Blood Contamination Category	Frequency of Results in Agreement	% in Agreement
NPA	0.2 ng/mL	Gross	5/10	50%
		Moderate	8/10	80%
		Trace	10/10	100%
PPA	2.0 ng/mL	Gross	10/10	100%
		Moderate	10/10	100%
		Trace	10/10	100%

*Maternal blood admixture categories were determined by subjective scoring of photographed PartoSure swabs which had been inserted into solutions of various blood admixture levels; 53 healthcare professionals reviewed and scored the photographs.

- **Potentially Exogenous Microbes**

For each interfering substance, ten (10) blinded samples with 0.2 ng/mL and ten (10) blinded samples with 2.0 ng/mL of PAMG-1 levels were tested with the PartoSure Test on the same day by the same analyst. Four (4) different concentrations of the potential exogenous interfering microbes were tested for Group B *Streptococcus agalactiae* (GBS), *Trichomonas vaginalis*, *Candida albicans*, and *Gardnerella vaginalis* (exogenous interferent); $1x10^7$ cells/mL (or cfu/mL), $1x10^6$ cells/mL (or cfu/mL), $1x10^5$ cells/mL (or cfu/mL), and $1x10^4$ cells/mL (or cfu/mL). The micro-organism was considered as not interfering in the detection of PAMG-1 if the proportion of valid and correct results was ≥ 95.0% (at least 19 valid correct results out of 20 strips tested). For each PAMG-1 concentration tested, all samples with an expected negative result were negative, and all samples with an expected positive result were positive (100% correct call rate) in the presence or not of GBS.

For each PAMG-1 concentration and interfering substance concentration tested, all samples with an expected negative result were negative and all samples with an expected positive result were positive (except for *Trichomonas vaginalis* at concentrations 10^6 cfu/mL and 10^7 cfu/mL).

	These study results demonstrate that PartoSure shows no interference for GBS, *Candida albicans* and *Gardnerella vaginalis* up to 10^7cfu/mL and no interference was seen for *Trichomonas vaginalis* up to 10^5 cfu/mL. • **Cross-Reactivity** The following potential cross-reactive substances were tested: human chorionic gonadotropin, trophoblastic beta-2 glycoprotein, human placental lactogen, alpha 1 Fetoprotein, IGFBP-3, and human serum albumin. Ten replicates of each contrived sample containing each potentially cross-reactive substance were tested using a non-zero negative sample (0.2 ng/mL PAMG-1) and a low positive sample (2.0 ng/mL PAMG-1), blinded on the same day by the same analyst. Each potentially cross-reactive substance was tested at the highest concentration of substance that was considered clinically relevant. For each PAMG-1 concentration and cross-reactive substance tested, all samples with an expected negative result were negative. All samples with an expected positive result were positive, except one sample. • **High-Dose Hook Effect** The PartoSure test was evaluated for the potential of a high-dose hook effect. Sixty (60) replicates, ten (10) from each of six (6) manufactured lots of PartoSure test strips, were tested with contrived samples containing 40 µg/mL. The results of the study showed no high-dose hook effect on the PartoSure test results as all replicates tested were positive. • **Stability** o **Sample stability** The stability of samples on which the PartoSure test is used was evaluated to determine sample stability after storage for a known period of time at 2–8°C or 15–30°C. A non-zero negative sample (0.2 ng/mL PAMG-1) and a low positive sample (2.0 ng/mL PAMG-1) were used with the PartoSure test to determine the in-use stability of the samples and the effect storage time and storage duration had on the stability of the samples. The samples

used in the in-use stability study were stored at 2–8°C for a period of up to 120 hours and 15–30°C for a period of up to 24 hours; four (4) replicates were performed for each time period and test lot. The study demonstrated in-use stability for samples that were stored for 120 hours at 2–8°C and 24 hours when stored at 15–30°C, as shown in following Table 8.

Table 8. Sample Stability Study Results by Storage Time and Lot

2–8°C

Lot	Concentration	0 h	12 h	24 h	48 h	72 h	120 h
Lot 1	0.2 ng/mL (Expected Negative)	0/4	0/4	0/4	0/4	0/4	0/4
Lot 2		0/4	0/4	0/4	0/4	0/4	0/4
Lot 3		0/4	0/4	0/4	0/4	0/4	0/4
Lot 1	2 ng/mL (Expected Positive)	4/4	4/4	4/4	4/4	4/4	4/4
Lot 2		4/4	4/4	4/4	4/4	4/4	4/4
Lot 3		4/4	4/4	4/4	4/4	4/4	4/4

15–30°C

Lot	Concentration	0 h	12 h	24 h	48 h	72 h	120 h
Lot 1	0.2 ng/mL (Expected Negative)	0/4	0/4	0/4	0/4	0/4	0/4
Lot 2		0/4	0/4	0/4	0/4	0/4	0/4
Lot 3		0/4	0/4	0/4	0/4	0/4	0/4
Lot 1	2 ng/mL (Expected Positive)	4/4	4/4	4/4	4/4	4/4	4/4
Lot 2		4/4	4/4	4/4	4/4	4/4	4/4
Lot 3		4/4	4/4	4/4	4/4	4/4	4/4

- **Test Strip stability - foil pouch packaging**

The stability of the PartoSure Strip post-removal from its foil pouch was evaluated. In this test, 3 different lots of PAMG-1 test strips were removed from their foil pouches 6.5 hours ahead of the actual usage time point. The three (3) lots were tested at 2 concentrations: 0.2 ng/mL and 2.0 ng/mL. 10 strips from each lot were tested at each concentration, for a total of 60 strips. 100% of the PartoSure Test strips observed results

matched expected results. Thus, the open pouch test strip stability study demonstrated that the PartoSure test can be used within 6 hours of removal from its foil pouch packaging.

- **Test Strip Shelf-Life Stability**

The shelf-life stability of the PartoSure Strip was evaluated. The test strips were kept for ≥32 months at room temperature (15–25°C) (intended storage temperature). The samples used contained reference material representing PAMG-1 at concentrations of 0 ng/mL, 0.5 ng/mL, 1.0 ng/mL and 5.0 ng/mL, respectively. Four (4) lots of PartoSure test strips were tested, and there were 10 replicates across each level of contrived samples. Contrived samples: Negative – contained no PAMG-1; Solvent Reagent only; Non-Negative – contained PAMG-1 at 0.5 ng/mL; Positive – contained PAMG-1 at 1.0 ng/mL; High Positive – contained PAMG-1 at 5.0 ng/mL. The time points tested in strips stored at room temperature were 0, 32, 33, and 41 months.

The PartoSure test strips are stable for at least 32 months when stored per the manufacturer's intended storage condition (room temperature). Upon CE marking under the regulation of the kit, PartoSure will have a shelf-life of 32 months .

- **Transport stability**

In the transport study, the stability of PartoSure test strips and solvent were evaluated to determine stability when subjected to extreme environmental conditions (Winter and Summer stress conditions to replicate transport conditions for international shipping from the United States (72-hour international expedited airfreight transport).

Table 9: Transportation Study Results for TP6

Grouping Variable(s)		Proportion		Two-Sided 95% Confidence Limit	
Condition	**TTP**	**Fraction**	**Percentage**	**Lower**	**Upper**
Control	6	60 / 60	100.00%	94.04%	100.00%
Summer	6	60 / 60	100.00%	94.04%	100.00%

	Winter	6	60 / 60	100.00%	94.04%	100.00%

At Time Point 6, 180 of the 180 test strips tested (60/60 Control, 60/60 Winter, 60/60 Summer) gave the expected outcome for the PAMG-1 concentrations tested (negative result for 0.2 ng/ml and positive result for 2.0 ng/ml), meeting the acceptance criteria of ≥ 95.0% or greater than or equal to the proportion of correct results obtained under the Control Storage condition at the same test time point. The results presented in Table 9 demonstrate that the PartoSure Test is stable under the test conditions (Winter, Summer) when tested after exposure to temperatures outside of the recommended storage temperature for every time point of the study, including one month past expiry.

- **Reagents Shelf life stability**

This study is an ongoing study and intermediate study results are presented. Testing included three (3) lots of solvent and ten (10) blinded samples with 0.2 ng/mL and ten (10) blinded samples with 2.0 ng/mL of PAMG-1 levels were tested with the PartoSure Test. The acceptance criteria are that at each testing time point (TTP), using the data from all 3 solvent lots, the proportion of correct sample calls should be ≥90.0%.

The results (100.00%) met the acceptance criteria of ≥90.0%. Therefore, the solvent is stable for 24 months at (15°C to 25°C).

While the interim shelf life of the solvent is 24 months, QIAGEN intends to claim 32 months shelf life of the kit, and upon CE marking under the regulation of the kit, there will be approximately 48 months of data for the solvent.

6.4 Summary of performance data from other sources, if applicable

Performance Evaluation of a device consists of a combination of Scientific Validity, Analytical Performance and Clinical Performance along with Risk Analysis, Overall Risk/Benefit Analysis and planned post-market performance follow-up. Demonstration of the clinical performance of a device was based on one or a combination of the following:

- Clinical performance studies

	• Scientific peer-reviewed literature • Published experience gained by routine diagnostic testing IVDR Article 56 (4) states that clinical performance studies in accordance with Section 2 of Part A of Annex XIII shall be carried out unless it is duly justified to rely on other sources of clinical performance data. The studies suggested that PartoSure device is a more accurate method to predict spontaneous preterm delivery than the 'similar' Actim Partus test. Different tests for fetal fibronectin and phIGFBP-1, are not sufficiently relevant to recommend their use in daily practice when compared to PartoSure. PartoSure is a better predictor of spontaneous delivery within 7 days while maintaining a very high negative predictive value. The demonstration that the PartoSure test was a more accurate predictor of preterm birth when compared to cervical length was confirmed. The PAMG-1 (placental alpha microglobulin-1) test showed high PPV (Positive Predictive Value) and NPV (Negative Predictive Value) for spontaneous preterm labor in symptomatic women and the authors concluded that PartoSure could be a reliable prognostic tool in clinical obstetrics. Authors also concluded that the PAMG-1 test is statistically superior to the measurement of cervical length for PPV, NPV, and specificity for the prediction of spontaneous preterm delivery within 7 days. The PAMG-1 test showed a higher accuracy rate for prediction of delivery within <7 days in comparison with a cervical length of <25mm and the number of contractions. The PAMG-1 test had a higher positive likelihood ratio for deliveries at <37 weeks. The authors also concluded that PAMG-1 performed the same as fFN in ruling out spontaneous preterm delivery among the contemporary cohort of symptomatic women but demonstrated statistical superiority in predicting it.
6.5 An overall summary of the performance and safety	From the review of the PartoSure analytical performance as well as the clinical performance of the device, it can be concluded that the device is of overall benefit to the patient.

6.6 Ongoing or planned post-market performance follow-up	Based on the collected evidence which shows that the PartoSure Test meets the performance evaluation requirements the assay is considered safe and effective for its intended use and no acceptable residual risks remain, it was concluded that no PMPF activities are currently required for this device.
7. Metrological traceability of assigned values	
7.1 Explanation of the unit of measurement, if applicable	Not Applicable.
7.2 Identification of applied reference materials and/or reference measurement procedures of higher order used by the manufacturer for the calibration of the device	Not Applicable.
8. Suggested profile and training for users	
8.1 Suggested profile and training for users	The PartoSure Test is intended for use in a clinical setting by trained healthcare professionals and is not intended for self-testing.

9. Revision history

SSP revision number	Date issued	Change description	Revision validated by the Notified Body
01	May 2023	Generation of document	☒ Yes Validation Language: English ☐ No (only applicable for class C (IVDR, Article 48 (7)) for which the SSP is not yet validated by the NB)
02	October 2023	Classification rule was updated to: rule 3j and 4b	☒ Yes Validation Language: English ☐ No (only applicable for class C (IVDR, Article 48 (7)) for which the SSP is not yet validated by the NB)
03	January 2025	Transfer on the new template according MDCG 2022-9. 6.3 Section transport stability and reagent shelf life stability part was updated.	☒ Yes Validation Language: English ☐ No (only applicable for class C (IVDR, Article 48 (7)) for which the SSP is not yet validated by the NB)