NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Diagnostics Assessment Programme

Biomarker tests to help diagnose preterm labour in women with intact membranes

Final scope

July 2017

1 Introduction

PartoSure is manufactured by Parsagen Diagnostics Inc. and distributed in the UK by Advanced Global Health. The medical technologies advisory committee decided that PartoSure should be selected for evaluation and fulfilled the routing considerations for the diagnostics assessment programme on the basis of a briefing note that included a description of the purpose of the technology as detailed in section 2. The revised scope was informed by discussions at the scoping workshop held on 14 June 2017 and the assessment subgroup meeting held on 29 June. A glossary of terms is provided in appendix A.

2 Description of the technologies

This section describes the properties of the diagnostic technologies based on information provided to NICE from the manufacturers and on information available in the public domain. NICE has not carried out an independent evaluation of this description.

2.1 Purpose of the medical technologies

Biomarker tests (PartoSure, Actim Partus and quantitative fetal fibronectin using the Rapid fFN 10Q Cassette Kit) to help diagnose preterm labour are intended for use alongside other clinical information to assess the risk of preterm birth in women with symptoms of preterm labour who have intact amniotic membranes. These tests may be used as alternatives to qualitative fetal fibronectin testing or clinical assessment alone, where transvaginal ultrasound measurement of cervical length 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 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 judgement, for example:

- If the test result is negative and the symptoms of preterm labour have settled, the woman would be discharged home with routine follow up in community and advised to return if symptoms reappear.
- If the test result is negative but symptoms of preterm labour 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.

Use of these tests may result in more accurate diagnosis of preterm labour compared with tests currently used in NHS clinical practice. 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 minimising unnecessary transfers between hospitals. Use of these test may also enable better resource planning based on the expected need for transfers between hospitals and neonatal intensive care.

2.2 Product properties

2.2.1 PartoSure (Parsagen Diagnostics Inc.)

PartoSure is a CE marked qualitative lateral flow, immunochromatographic point-of-care test designed to identify the presence of placental alpha microglobulin-1 (PAMG-1) in vaginal secretions during pregnancy. PAMG-1 is a protein released from the lining of the uterus into the amniotic cavity throughout pregnancy. It is found in very high concentrations in amniotic fluid and in very low concentrations in normal vaginal discharge. Studies have demonstrated a strong correlation between the presence of PAMG-1 in cervico-vaginal discharge and imminent delivery. Two possible explanations for the presence of PAMG-1 in vaginal secretions are: the PAMG-1 passes through pores in fetal membranes during uterine contractions; or PAMG-1 is present because of the degradation of the extracellular matrix of fetal membranes due to inflammatory processes of labour or infection.

The PartoSure test kit contains a test strip, a vaginal swab and a plastic vial containing a solvent solution. No other instrumentation or consumables are needed. To perform the test, a healthcare professional collects a swab of vaginal discharge by inserting the sterile flocked swab 5–7 cm into the vagina

and removing it after 30 seconds. The sample may be collected with or without a speculum examination. The swab is rinsed in the solvent solution by rotating for 30 seconds and then it is removed and discarded. The test strip is then inserted into the vial for 5 mins, or until 2 lines are visible (whichever is sooner). Two lines indicate a positive result and a high risk of delivery within 7 days; 1 line indicates a negative result and a low risk of delivery within 7 to 14 days; no lines indicate an invalid result.

The test strip has a reactive area containing monoclonal anti-PAMG-1 antibodies bound to a gold particle (the detecting label). The sample flows through the reactive area and if PAMG-1 is present it binds to the anti-PAMG-1 antibodies, forming an antigen-antibody complex. This complex then flows to the test region of the strip where it is immobilised by a second anti-PAMG-1 antibody and causes the appearance of a test line if the concentration of PAMG-1 in the sample exceeds the detection limit of the test (1 ng/ml). Unbound antigen-antibody complexes continue to flow along the test strip and are immobilized by a second antibody, leading to the appearance of the internal control line.

The PartoSure test is indicated for use in in pregnant women with signs and symptoms of preterm labour, intact amniotic membranes and minimal cervical dilatation (3 cm or less), sampled between 20 weeks plus 0 days and 36 weeks plus 6 days of pregnancy. The test can be used in the presence of vaginal infections, urine, semen and trace amounts of blood, but should not be used in the presence of significant discharge of blood. It can also be used shortly after a vaginal exam. The test has a limit of detection of 1 ng/ml and a measuring range of 1 to 40,000 ng/ml.

2.2.2 Actim Partus (Medix Biochemica; distributed by Alere)

Actim Partus is a CE marked qualitative immunochromatographic test designed to detect the presence of phosphorylated IGFBP-1 (insulin-like growth factor binding protein-1) in cervical secretions during pregnancy. Phosphorylated IGFBP-1 is a protein made by the cells lining the uterus. When delivery is imminent, small amounts of phosphorylated IGFBP-1 leak into the cervix. The Actim Partus test uses monoclonal antibodies to detect human IGFBP-1.

The Actim Partus test kit contains a sterile polyester swab for specimen collection, a tube of specimen extraction buffer and a dipstick in a sealed foil pouch. No other instrumentation or consumables are needed. To perform the test, a healthcare professional collects a sample from the cervical os using the swab during a sterile speculum examination. The specimen is extracted by swirling the swab vigorously in the extraction solution for 10-15 seconds. The

swab is then discarded and the dipstick is placed into the extracted sample until the liquid front enters the results area. The dipstick is removed from the solution and left in a horizontal position for 5 minutes or until 2 blue lines are visible. Two lines indicate a positive result; 1 line is a negative result that indicates the patient will not deliver within 7-14 days; if no lines appear the test is invalid.

The dipstick contains 2 monoclonal antibodies to human IGFBP-1. One is bound to blue latex particles (the detecting label). The other is immobilized on a carrier membrane to catch the complex of antigen and latex-labelled antibody and indicate a positive result. If phosphorylated IGFBP-1 is present in the sample it binds to the antibody labelled with latex particles. The particles flow to the results area of the dipstick, and if phosphorylated IGFBP-1 is bound to them, they bind to the catching antibody. A test line will appear if the concentration of phIGFBP-1 in the sample exceeds the detection limit of the test. A control line confirms correct performance of the test.

The Actim Partus test is indicated for use in pregnant women with signs and symptoms of preterm labour and intact amniotic membranes, sampled after 22 weeks plus 0 days of pregnancy. The test can be used in the presence of vaginal infections, vaginal medications and semen; but active vaginal bleeding may cause a false positive result. The test has a limit of detection of 10 ng/ml and a measuring range of 10 to 8000 ng/ml.

2.2.3 Rapid fFN 10Q Cassette Kit (Hologic)

The Rapid fFN 10Q Cassette is a CE marked test for use in the PeriLynx System or the Rapid fFN 10Q System. It is designed for the quantitative detection of fetal fibronectin in cervicovaginal secretions to assess the risk of preterm delivery within 7-14 days. Fetal fibronectin is an adhesive glycoprotein that holds the membranes of the uterus to the fetal membranes. After the 35th week of pregnancy, it begins to break down naturally, and is detectable in vaginal secretions. Fetal fibronectin detected between 22 and 35 weeks of pregnancy is an indicator of preterm birth risk.

NICE's guideline on preterm labour and birth recommends fetal fibronectin testing to determine likelihood of birth within 48 hours for women who are 30 weeks plus 0 days pregnant or more, if transvaginal ultrasound measurement of cervical length is indicated but is not available or not acceptable. The guideline recommends a threshold concentration of 50 ng/ml to interpret the test results. However, clinical experts have noted that a quantitative fetal fibronectin test would enable alternative thresholds to be used.

The Rapid fFN 10Q Cassette test can be performed in a near patient setting. The following equipment is needed in addition to the test kit: analyser, printer, Rapid fFN Control Kit, QCette (quality control device), and pipette. To perform the test, a sample is collected from the posterior fornix of the vagina during a speculum examination and added to the specimen transport tube. The Rapid fFN 10Q Cassette is inserted into the analyser and the patient sample is pipetted into the sample application well. The sample is incubated in the analyser for 7 minutes and then the analysis is performed, which takes 2 to 3 minutes. The analyser reports fetal fibronectin concentrations ranging from 0 to 500 ng/ml; concentrations greater than 500 ng/ml are displayed as >500 ng/ml. The instructions for use do not give any thresholds, therefore laboratories would need to set and validate their own thresholds. Internal controls are performed automatically with every test.

The Rapid fFN 10Q Cassette is indicated for use in pregnant women with signs and symptoms of early preterm labour, intact amniotic membranes, and minimal cervical dilatation (less than 3 cm), sampled between 22 weeks plus 0 days and 35 weeks plus 6 days of pregnancy. Assay interference from blood, bacteria, bilirubin and semen have not been ruled out; however a negative test result (<10ng/ml) in the presence of blood or semen is valid. Further, the fetal fibronectin concentration maybe influenced by cervical disruption caused by, but not limited to, events such as sexual intercourse, digital cervical examination, or vaginal probe ultrasound.

3 Target conditions

3.1 Preterm labour

Preterm labour is defined as regular contractions of the uterus resulting in changes in the cervix that start before 37 weeks of pregnancy. Preterm labour and birth is 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 (RCOG 2014).

The World Health Organisation defines sub-categories of preterm birth, 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).

The National Perinatal Epidemiology Group splits the latter group further into moderately preterm (32 to less than 34 weeks of pregnancy) and late preterm (34 to less than 37 weeks of pregnancy).

Around 25% of preterm births are planned due to either maternal factors, such as pre-eclampsia or fetal factors, such as extreme growth restriction; but most preterm births occur because labour starts early naturally. Known risk factors for preterm labour include: previous preterm delivery; pregnancy with twins, triplets or other multiples; genital tract infections; preterm premature rupture of membranes; certain problems with the uterus, cervix or placenta; some chronic conditions, such as high blood pressure and diabetes; smoking or drug use; being underweight or overweight before pregnancy; and stressful life events.

The Department of Health's toolkit for high quality neonatal services describes 3 types of unit that provide neonatal care of preterm babies:

- Special care units (level 1) provide special care for their own local population, and may also provide some high dependency services.
- Local neonatal units (level 2) provide neonatal care for their own local population, except for the sickest babies. The majority of babies over 27 weeks of gestation will usually receive their full care, including short periods of intensive care, within their local neonatal unit.
- Neonatal intensive care units (level 3) are sited alongside specialist obstetric and feto-maternal medicine services, and provide the whole range of medical neonatal care for their local population, along with additional care for babies and their families referred from the neonatal network.

Clinical experts have noted that most babies born after 35 weeks of pregnancy will be looked after on the postnatal wards with their mothers.

Preterm birth can potentially lead to short term health problems in a newborn baby, for example, they may have problems breathing and feeding, and be at higher risk of infection. Key outcomes of concern include:

- Chronic lung disease at 36 weeks corrected age
- Intraventricular haemorrhage
- Necrotising enterocolitis
- Retinopathy of prematurity

Children who are born early, particularly those born before 28 weeks of pregnancy, may have disabilities throughout their life, including, learning disabilities, behavioural problems, and visual and hearing problems.

3.2 Diagnostic and care pathway

3.2.1 Diagnosis of preterm labour in women with intact membranes

Clinical assessment

NICE's guideline on preterm labour and birth states that women reporting symptoms of preterm labour who have intact membranes should have a clinical assessment which includes:

- clinical history taking
- observations of the woman, including: the length, strength and frequency of her contractions; any pain she is experiencing; pulse, blood pressure and temperature; and urinalysis
- observations of the unborn baby, including: asking about the baby's movements in the last 24 hours; palpation of the woman's abdomen to determine the fundal height, the baby's lie, presentation, position, engagement of the presenting part, and frequency and duration of contractions; and auscultation of the fetal heart rate for a minimum of 1 minute immediately after a contraction
- a speculum examination (followed by a digital vaginal examination if the extent of cervical dilatation cannot be assessed).

If the clinical assessment suggests that the woman is in suspected preterm labour and she is 29 weeks plus 6 days pregnant or less, treatment for preterm labour is recommended.

Clinical experts have noted that, in practice, not all women in suspected preterm labour that are 29 weeks plus 6 days pregnant or less are treated for preterm labour. They stated that diagnostic testing is often performed in this group for the following reasons: they do not have the resource available to admit or transfer all women; they are concerned about the impact of unnecessary treatment; and patients may prefer to avoid hospital admission and transfer when possible.

Transvaginal ultrasound measurement of cervical length

If the clinical assessment suggests that the woman is in suspected preterm labour and she is 30 weeks plus 0 days pregnant or more, transvaginal ultrasound measurement of cervical length should be considered to determine likelihood of birth within 48 hours. If cervical length is more than 15 mm, it is unlikely that the woman is in preterm labour. If cervical length is 15 mm or less, preterm labour should be diagnosed and treatment offered.

NICE's guideline on preterm labour and birth notes that ultrasound scans should be performed by healthcare professionals with training in, and

experience of, transvaginal ultrasound measurement of cervical length. The guideline committee also noted that transvaginal ultrasound scanning is not routinely available across the NHS because of limitations of equipment or expertise, and that investment in technology and training may be required for its universal implementation in the NHS.

A 2014 survey of all 198 consultant-led maternity units in the UK showed that only 35% used transvaginal ultrasound of cervical length to assess the risk of preterm labour (Stock 2015). Clinical experts consulted during scoping have confirmed that transvaginal ultrasound measurement of cervical length is not currently routinely performed on women presenting with symptoms of preterm labour, and that this is because of a lack of equipment or availability of trained staff 24 hours a day.

Fetal fibronectin testing

If transvaginal ultrasound measurement of cervical length is indicated but is not available or not acceptable, fetal fibronectin testing should be done to determine likelihood of birth within 48 hours for women who are 30 weeks plus 0 days pregnant or more. If the fetal fibronectin test result is negative (concentration 50 ng/ml or less) it is unlikely that the woman is in preterm labour. If the fetal fibronectin test result is positive (concentration more than 50 ng/ml), preterm labour should be diagnosed and treatment offered. The guideline notes that if a swab for fetal fibronectin testing is anticipated, the swab should be taken before any digital vaginal examination.

If a woman in suspected preterm labour who is 30 weeks plus 0 days pregnant or more does not have transvaginal ultrasound measurement of cervical length or fetal fibronectin testing to exclude preterm labour, treatment should be offered consistent with her being in diagnosed preterm labour.

A women with suspected preterm labour, but with a negative diagnostic test result suggesting that preterm labour is unlikely, may go home or may continue to be monitored and treated in hospital. If the women goes home she is advised to return to hospital if symptoms suggestive of preterm labour persist or recur.

NICE's guideline on preterm labour and birth notes that transvaginal ultrasound measurement of cervical length and fetal fibronectin testing should not be used in combination to diagnose preterm labour.

The recently published recommendations on preterm labour and birth management from the European Association of Perinatal Medicine state that 2 methods can be used to improve the accuracy of the diagnosis of preterm labour in women presenting with symptoms:

- transvaginal ultrasound cervical length measurement;
- measurement of biochemical markers in cervical-vaginal secretions (fetal fibronectin / PAMG-1 / IGFBP-1)

3.2.2 Management of diagnosed preterm labour in women with intact membranes

Tocolysis to supress preterm labour
NICE'S guideline on preterm labour and birth makes the following recommendations on tocolysis:

- consider nifedipine for tocolysis for women between 24+0 and 25+6 weeks of pregnancy who have intact membranes and are in suspected preterm labour
- offer nifedipine for tocolysis to women between 26+0 and 33+6 weeks of pregnancy who have intact membranes and are in suspected or diagnosed preterm labour
- If nifedipine is contraindicated, oxytocin receptor antagonists for tocolysis should be offered.

NICE's quality standard on preterm labour and birth makes the following quality statement: women between 26+0 and 29+6 weeks of pregnancy who are in suspected preterm labour are offered tocolysis.

Maternal corticosteroids to reduce the risk of neonatal complications
NICE's guideline on preterm labour and birth makes the following recommendations on maternal corticosteroids:

- consider maternal corticosteroids for women between 24+0 and 25+6 weeks of pregnancy who are in suspected or established preterm labour
- offer maternal corticosteroids to women between 26+0 and 33+6 weeks of pregnancy who are in suspected, diagnosed or established preterm labour
- consider maternal corticosteroids for women between 34+0 and 35+6 weeks of pregnancy who are in suspected, diagnosed or established preterm labour
- Do not routinely offer repeat courses of maternal corticosteroids.

NICE's quality standard on preterm labour and birth makes the following quality statements:

- women between 26+0 and 29+6 weeks of pregnancy who are in suspected preterm labour are offered maternal corticosteroids.

- women between 30+0 and 33+6 weeks of pregnancy who are in diagnosed preterm labour, are having a planned preterm birth or have preterm prelabour rupture of membranes are offered maternal corticosteroids.

Maternal corticosteroids are most effective in babies who are delivered between 2 and 7 days after the administration of the drugs, with the greatest benefit being within 48 hours after the administration of treatment. Clinical experts consulted during scoping noted that there is less evidence that maternal corticosteroids have any sustained beneficial effect after 7 days, and they may be harmful to the baby if given to a woman who then delivers at full term. As repeat courses of maternal corticosteroids are not routinely recommended, it is important to accurately assess the risk of delivery within 7 days before administration of treatment.

Magnesium sulphate for neuroprotection of the baby
NICE's guideline on preterm labour and birth makes the following recommendations on magnesium sulphate:

- Offer intravenous magnesium sulfate to women between 24+0 and 29+6 weeks of pregnancy who are in established preterm labour.
- Consider intravenous magnesium sulfate for women between 30+0 and 33+6 weeks of pregnancy who are in established preterm labour.
- Give a 4 g intravenous bolus of magnesium sulfate over 15 minutes, followed by an intravenous infusion of 1 g per hour until the birth or for 24 hours (whichever is sooner).
- For women on magnesium sulfate, monitor for clinical signs of magnesium toxicity at least every 4 hours by recording pulse, blood pressure, respiratory rate and deep tendon reflexes.
- If a woman has or develops oliguria or other signs of renal failure: monitor more frequently for magnesium toxicity; and think about reducing the dose of magnesium sulfate.

NICE's quality standard on preterm labour and birth makes the following quality statement: women between 24+0 and 29+6 weeks of pregnancy who are in established preterm labour or having a planned preterm birth within 24 hours are offered magnesium sulfate.

Other guidelines are also available, including:

- WHO recommendations on interventions to improve preterm birth outcomes (2015)

- The International Federation of Gynecology & Obstetrics (FIGO) and the International Pediatric Association (IPA) Joint Statement: Prevention and treatment of preterm births (2012)
- The American College of Obstetricians and Gynecologists Practice bulletin: Prediction and prevention of preterm birth (2012)
- The American College of Obstetricians and Gynecologists Practice bulletin: Management of preterm labor (2016)

3.3 Patient issues and preferences

An accurate test for diagnosing preterm labour could prevent women being unnecessarily admitted to hospital for treatment and monitoring, or unnecessarily transferred to a specialist unit. An accurate test should also ensure: that women with true preterm labour are offered treatment to help ensure the best possible short and long term outcomes for babies; and that appropriate transfers of women to specialist units are made, so that babies born preterm are delivered at a location where specialist care is available.

Complications associated with preterm birth can lead to stillbirth, neonatal death, short term health problems in a newborn baby, and long term disabilities. These would have an impact on the mental wellbeing of a woman and her family.

4 Comparators

4.1 Fetal fibronectin

Fetal fibronectin testing, to determine likelihood of birth within 48 hours for women who are 30+0 weeks pregnant or more, is recommended in NICE's guideline on preterm labour and birth if transvaginal ultrasound measurement of cervical length is indicated but is not available or not acceptable. NICE's guideline on preterm labour and birth recommends a cut-off of 50 ng/ml.

The fetal fibronectin test is available as a quantitative enzyme-linked immunosorbent assay (ELISA), and as a qualitative membrane immunosorbent assay. Examples include:

- Fetal Fibronectin Enzyme Immunoassay; a quantitative assay with a recommended threshold of 50 ng/ml (Hologic)
- Rapid fFN for the TLi$_{IQ}$ System; a qualitative immuno-chromatographic assay with a limit of detection of 50 ng/ml (Hologic)
- QuikCheck Fetal Fibronectin Test; a qualitative test with a limit of detection of 50 ng/ml (Hologic).

4.2 Clinical assessment

Clinical assessment is described in NICE's guideline on preterm labour and birth, and includes:

- clinical history taking
- observations of the woman
- observations of the unborn baby
- a speculum examination.

5 Scope of the assessment

Table 1 Scope of the assessment

Decision question	What is the clinical and cost effectiveness of tests used to help diagnose preterm labour in women with intact membranes?
Populations	Women with signs and symptoms of preterm labour and intact amniotic membranes who are 36+6 weeks pregnant or less, who are not in established labour, and for whom a transvaginal ultrasound is not available or acceptable. Where data permit subgroups based on gestational age will be considered.
Interventions	PartoSure with clinical assessment of symptoms Actim Partus with clinical assessment of symptoms Rapid fFN 10Q Cassette Kit, used with thresholds other than 50 ng/ml, with clinical assessment of symptoms
Comparator	Fetal fibronectin, used with a threshold of 50 ng/ml, with clinical assessment of symptoms Clinical assessment of symptoms alone
Healthcare setting	Secondary care
Outcomes	Intermediate measures for consideration may include: • Diagnostic accuracy for preterm birth within 48 hours and 7 days • Time to test result • Test failure rate • Number of women admitted to hospital • Number of re-presentations to hospital within 48 hours and 7 days • Number of women who have tocolytics / corticosteroids • Length of inpatient hospital stay

	• Number of transfers of pregnant women and neonates between hospitals • Time to delivery from presentation • Number of women treated appropriately (that is, they deliver within 7 days following treatment) • Number of women treated inappropriately (that is, they do not deliver within 7 days following treatment) • Impact on neonatal intensive care resource planning • Gestational age at birth
	Clinical outcomes for consideration may include: • Perinatal mortality • Neonatal morbidity and mortality • Long term health problems in the child • Maternal morbidity and mortality
	Patient-reported outcomes for consideration may include: • Health-related quality of life • Anxiety associated with confidence in the test results
	Costs will be considered from an NHS and Personal Social Services perspective. Costs for consideration may include: • Cost of the test kit • Cost of staff time to undergo training and perform the testing • Costs associated with resource use, such as hospital admissions and length of stay, treatments, and transfers between hospitals • Costs associated with the treatment of short term neonatal health problems • Costs associated with the treatment of long term effects of preterm birth
	The cost-effectiveness of interventions should be expressed in terms of incremental cost per quality-adjusted life year.
Time horizon	The time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared.

6 Other issues for consideration

The scope will not include assessment of women who have no symptoms of preterm labour, but have a history of spontaneous preterm birth or mid-trimester loss between 16+0 and 34+0 weeks of pregnancy.

The scope will not include women with multiple pregnancy, as care of these women differs from the care of women with singleton pregnancy, and is described in NICE's guideline on multiple pregnancy.

The treatment of preterm prelabour rupture of membranes (P-PROM) is different to the treatment of preterm labour. NICE's guideline on preterm labour and birth states that women with P-PROM should be treated with prophylactic antibiotics and that a combination of clinical assessment and tests should be used to diagnose intrauterine infection. Maternal corticosteroids should also be considered or offered depending on the gestation.

The diagnosis of P-PROM is also described in NICE's guideline on preterm labour and birth. It states that if a woman reports symptoms suggestive of P-PROM, a speculum examination to look for pooling of amniotic fluid should be offered, and:

- if pooling of amniotic fluid is observed, care consistent with the woman having P‑PROM should be offered
- if pooling of amniotic fluid is not observed, an IGFBP-1 test or PAMG-1 test of vaginal fluid should be considered.

Two tests for PROM are available. The AmniSure ROM Test (Qiagen) uses the PAMG-1 biomarker with a limit of detection of 5 ng/ml. The Actim PROM test (Medix Biochemica) uses IGFBP-1 as a biomarker at a limit of detection of 25 µg/ml.

During the development of the NICE clinical guideline on preterm labour and birth, the review question on diagnosing preterm labour in women with intact membranes was prioritised for economic analysis. The evaluation compared alternative diagnostic strategies to identify preterm labour in women with suspected preterm labour and intact membranes between the gestational ages of 24 and 34 weeks. It took a 'what-if' approach to diagnostic accuracy to determine what combinations of sensitivity and specificity were cost effective for a given prevalence, diagnosis and treatment cost.

7 Potential equality issues

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others.

Pregnancy and maternity are protected characteristics under the Equality Act 2010. Children born before 37 weeks gestation are at increased risk of

developing disabilities which would lead to them being protected under the Act.

8 Potential implementation issues

The NICE Adoption team collated information from healthcare professionals working within NHS organisations who have experience of using PartoSure to help diagnose of preterm labour. They considered the benefits and difficulties that may be faced by organisations when planning to adopt the technology into routine NHS use.

8.1 Adoption levers

8.1.1 Ease of use of PartoSure

PartoSure was reported by experts to be very easy to use. A speculum examination is not required, therefore the sample collection can be done by midwives. In comparison the sample for a fetal fibronectin test has to be obtained during a speculum examination performed by a consultant. Experts noted that after the sample has been collected the PartoSure test is simple to complete and the result is easy to interpret as it is qualitative. The test can be used in the presence of blood or gel.

8.1.2 Costs and resource use

Experts noted that the cost per test for PartoSure is less than the cost per test for fetal fibronectin. They also noted that using the PartoSure test results in a decrease or a similar number of unnecessary admissions compared with using the fetal fibronectin test. Experts stated that changing to PartoSure from fetal fibronectin had led to a 30% decrease in the use of tocolytics and a decrease in the use of maternal corticosteroids.

8.2 Adoption barriers

Adoption barriers noted by experts were related to internal governance and procurement processes, which were reported to be challenging and time consuming.

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Appendix A Glossary of terms

Chronic lung disease
Lung disease most commonly seen in premature infants who required mechanical ventilation and oxygen therapy for acute respiratory distress.

Diagnosed preterm labour
A woman is in diagnosed preterm labour if she is in suspected preterm labour and has had a positive diagnostic test for preterm labour.

Established preterm labour
A woman is in established preterm labour if she has progressive cervical dilatation from 4 cm with regular contractions.

Intraventricular haemorrhage
Bleeding into the fluid-filled areas (ventricles) inside the brain.

Necrotising enterocolitis
A serious illness in which tissues in the intestine become inflamed and start to die. This can lead to a perforation developing, which allows the contents of the intestine to leak into the abdomen.

Retinopathy of prematurity
A disease that occurs in premature babies. It causes abnormal blood vessels to grow in the retina, which can cause the retina to detach from the back of the eye, leading to blindness.

Suspected preterm labour
A woman is in suspected preterm labour if she has reported symptoms of preterm labour and has had a clinical assessment (including a speculum or digital vaginal examination) that confirms the possibility of preterm labour but rules out established labour.

Appendix B References

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