Trust Guideline for the use of Fetal Fibronectin and AmniSure

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Version History:

Version	Date	Author	Reason/Change
5	April 2020	Consultant Obstetrician	Change of brand of swab used to diagnose preterm labour from Actim Partus to Fetal Fibronectin
6	June 2020	Consultant Obstetrician	Change of brand of swab used to diagnose PROM from Actim PROM to AmniSure
7	April 2023	Charles Bircher	Updated to new Trust Docs template
8	August 2024	Charles Bircher	Addition of Actim Partus as an option if Fetal Fibronectin unavailable

Previous Titles for this Document:

Previous Title/Amalgamated Titles	Date Revised
None	Not applicable

Distribution Control

Printed copies of this document should be considered out of date. The most up to date version is available from the Trust Intranet.

Consultation

The following were consulted during the development of this document:

- Beth Gibson, Chief of Service – Obstetrics
- Maternity Guidelines Committee.
- Clinical Guidelines Assessment Panel

Monitoring and Review of Procedural Document

The document owner is responsible for monitoring and reviewing the effectiveness of this Procedural Document. This review is continuous however as a minimum will be achieved at the point this procedural document requires a review e.g. changes in legislation, findings from incidents or document expiry.

Relationship of this document to other procedural documents

This document is a clinical guideline applicable to Norfolk and Norwich University Hospitals (NNUH); please refer to local Trust's procedural documents for further guidance.

Guidance Note

This guideline has been approved by the Trust's Clinical Guidelines Assessment Panel as an aid to the diagnosis and management of relevant patients and clinical circumstances. Not every patient or situation fits neatly into a standard guideline scenario and the guideline must be interpreted and applied in practice in the light of prevailing clinical circumstances, the diagnostic and treatment options available and the professional judgement, knowledge and expertise of relevant clinicians. It is advised that the rationale for any departure from relevant guidance should be documented in the patient's case notes.

The Trust's guidelines are made publicly available as part of the collective endeavour to continuously improve the quality of healthcare through sharing medical experience and knowledge. The Trust accepts no responsibility for any misunderstanding or misapplication of this document**.**

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1. Introduction

1.1. Rationale

- Correctly diagnosing pre-term labour is difficult when using clinical history and examination alone, and many women will be admitted to hospital, transferred or treated unnecessarily.
- Diagnosis of Pre-term labour and / or Pre-term rupture of membranes is important because there are targeted interventions that can be given to the mother which have been proven to improve perinatal mortality and/or morbidity. For example, antenatal corticosteroids, magnesium sulphate and tocolysis.
- Fetal Fibronectin and AmniSure are simple and quick bed-side tests which can be used to aid diagnosis, with high sensitivity. A negative test can be safely relied upon to rule out Pre-term labour or PROM respectively and therefore reduce unnecessary intervention and hospital admissions.
- The supply of Fetal Fibronectin is difficult, so if not available, Actim Partus can be used as a test of preterm labour. Of note, a cervical length is a better test of threatened preterm labour than Actim Partus, but is outside the scope of this guideline.

1.2. Objective

To direct the appropriate use of Fetal Fibronectin in the assessment of women with symptoms of preterm labour and intact membranes (or if not available, Actim Partus) and of AmniSure in the assessment of women with suspected PROM in whom there is no obvious evidence of rupture of membranes, with a resultant improvement in care of these women.

1.3. Scope

This guidance is concerned with the indication, use and interpretation of Fetal Fibronectin (or if not available, Actim Partus) and Actim PROM tests. For management of PROM and pre-term labour please refer to separate relevant guidelines.

1.4. Glossary

The following terms and abbreviations have been used within this document:

Term	Definition
NNUH	Norfolk and Norwich University Hospitals
SROM	Pre-labour spontaneous rupture of membranes
PROM	Premature rupture of membranes
fFN	Fetal Fibronectin
PAMG-1	Placental alpha microglobulin-1
VE	Vaginal examination
NICU	Neonatal Intensive Care Unit
GBS	Group B Streptococcus
NICE	National Institute for Health and Care Excellence

ROM	Rupture of membranes
EIA	Equality Impact Assessment

2. Responsibilities

Charles Bircher, consultant obstetrician and labour ward lead, responsible to make sure the local guidance is up to date and in line with national guidance

3. Processes to be followed

3.1. Use of FETAL FIBRONECTIN: Threatened pre-term labour with intact membranes.

Fetal fibronectin (fFN) is a fibronectin protein produced by fetal cells. It is found at the interface of the chorion and the decidua (between the fetal sac and the uterine lining). Fetal fibronectin "leaks" into the vagina if a preterm delivery is likely to occur and can be measured in a screening test.

A fFN test result <200 ng/mL gives providers confidence that preterm labour is not imminent, as less than 1% of women with this result will deliver within 7 days.

3.1.1. Criteria for using Fetal Fibronectin

- Women with signs and symptoms of pre term labour from 24 weeks of gestation to 35+6 weeks
  - fFN is validated from 22 weeks so can be used between 22 and 23+6 with senior doctor (Tier 3 or Consultant) involvement in the decision and if a result would affect patient care.
- Intact membranes
- Do not use if cervix is 3cm dilated or greater

3.1.2. Contraindications

- Ruptured membranes
- Cervix 3cm dilated or greater
- Any contraindication to tocolysis
- Moderate- severe vaginal bleeding. This is because moderate-severe vaginal bleeding is a reason to admit a patient, therefore fFN will not change the decision.
  - NB Testing a bloody sample can give a falsely positive result. Therefore if done in this situation and the result is <200ng/mL it can still be interpreted as a valid negative result
- Sexual intercourse (with no lubricant) within the previous 24 hours
  - NB Semen increases the fFN level by 5-6 times. Therefore if the test is done in this situation and the result is <200ng/mL it can still be interpreted as a valid negative result. If the test is done and >200ng/mL it may be a false positive but this cannot be determined. Clinical judgement is advised. If the

patient is admitted then a fFN level can be done >24 hours after intercourse to give an accurate result.

- Use of lubricant for VE or internal ultrasound scan within the previous 24 hours
    - The use of lubricant can interfer the fFN sample giving an invalid result. Therefore after either you must wait >24 hours to get an accurate result.

3.1.3. Method for carrying out Fetal Fibronectin

1. Specimen must be collected **PRIOR** to digital examination or collection of culture specimens.
2. Perform speculum examination (**using only water as a lubricant**) and rotate swab across posterior fornix for 10 seconds to allow for absorption of secretions.
3. Thoroughly mix swab in liquid extraction buffer provided for 10 seconds
4. Squeeze swab against inside of tube
5. If not testing immediately, snap the swab shaft and replace cap onto test tube until it clicks. This sample is valid for testing for up to 8 hours at room temperature.
6. When testing, remove swab and discard and place tube into stand
7. At PeriLynx analyser – select test patient on main menu, scan user ID (barcode) and press next
8. Enter rapid fFN Cassette lot number and press next.
9. Enter patient ID and press next.
10. Insert the rapid fFN cassette and prepare pipette with 200µl (0.2ml) from the patient sample collected in the buffer solution and press next.
11. Pipette 200µl (0.2ml) from the sample collected in the buffer solution into the well of the rapid fFN cassette and press Start Test
12. When testing is complete, the system will display and print the result.
13. Result will be given in ng/mL and should be interpreted and managed according to table 1 below:

Table 1: Results

FFN Value ng/mL	% who will deliver within 1 week	% who will deliver within 2 weeks	% who will deliver at <34/40	Suggested Management
0-9	1	1.8	1.5	Discharge with routine midwife follow-up
10-49	0	1.6	8.2	Discharge with routine midwife follow-up
50-199	0	7.7	11.5	Discharge but advise the woman to re-present if symptoms worsen. Make sure woman is aware of risk of delivery between days 7 and 14
200-499	14	29	33	Admit and inform NICU Antenatal steroids Tocolysis GBS antibiotics if in labour MgSO4 if in labour and <30/40
>500	38	46	75	Admit and inform NICU Antenatal steroids Tocolysis GBS antibiotics Magnesium Sulphate if <30/40

(Abbott DS et al 2012)

3.2. Use of Actim Partus: Threatened pre-term labour with intact membranes

The Actim Partus test is a rapid bed side test that measures phosphorylated Insulin-like Growth factor Binding Protein – 1 (phIGFBP-1) in cervicovaginal secretions to identify the risk of preterm delivery in women with intact membranes.

The level of phIGFBP-1 in the cervix increases considerably as the cervix matures and this aids identification of the patients with an increased risk of delivering preterm. More specifically, a negative test result is a safe indication that imminent delivery or delivery within two weeks is highly unlikely. The principal utility of the Actim Partus test lies in its **high negative predictive value** (over 99 percent in symptomatic patients in populations with low prevalence of preterm birth within seven days); the positive predictive value is much lower (39-46%).

3.2.1. Criteria for using Actim Partus

- Women with signs and symptoms of pre term labour from 24 weeks of gestation to 36 +6 weeks
- Intact membranes

- Do not use if cervix is 4cm dilated or greater

The test **<u>can</u>** be used for those women who have recently had sexual intercourse.

3.2.2. Contraindications

- Ruptured membranes
- Moderate or heavy vaginal bleeding

These situations can increase the false positive result, do <u>not</u> use in these circumstances.

3.2.3. Method for carrying out Actim Partus

- A cervical swab is taken during a speculum examination using the included polyester swab.
- The swab should be left at the cervical os for 10-15 seconds to let the specimen absorb.
- Then place the swab into the extraction sample for 10 seconds swirling it around and remove it.
- Place the yellow part of the dipstick into the extraction solution until the liquid reaches the result area.
- Place the dipstick in a horizontal position.
- A positive test can be seen as two blue lines - a control line and a positive line, which appear in the result area.
- The time to read the result is between 1 and 5 minutes later. Results interpreted after 5 minutes may be inaccurate.

3.2.4. Negative Actim Partus result

Withhold tocolysis and steroids if the Actim Partus test is negative. Instead, the woman should be observed on the labour ward according to clinical need.

- Analgesia should be prescribed as required.
- Inform and discuss with the woman and her partner, that her risk of delivering in the next 10 days is 1%, ie 1 in 100.
- Educate on signs and symptoms of pre term labour.
- Discharge home if clinically well.

3.2.5. Positive Actim Partus result

A symptomatic woman with a positive swab has an increased chance of delivering her baby preterm.

- If less than 30+0 weeks monitor closely and if reaches 4-8cm cervical dilation commence IV Magnesium sulphate according to protocol.
- Offer antenatal corticosteroids and tocolysis according to protocol.
- Inform NICU and neonatal sister in charge.

Consider in utero transfer if no cots available in NICU

3.3. Use of AmniSure: Equivocal findings with history of PROM

The AmniSure test is a rapid, non-invasive strip test for the detection of the placental alpha microglobulin-1 protein (PAMG-1). It is used to help diagnose whether patients have ruptured membranes in patients presenting with signs and symptoms of PROM/PPROM. **It can be used on patients at any gestation.**

In commenting on the evidence for PAMG-1, NICE states “One prospective cohort study (n=100) found that placenta alpha-microglobulin-1 is a useful test in diagnosing P-PROM. Positive and negative likelihood ratios were very useful.” The sensitivity in this trial was 92% and the specificity 99%. This is better performing than other products on the market, including Actim PROM (a test for insulin-like growth factor binding protein-1 – IGFBP-1)

3.3.1. Criteria for using AmniSure

- Women who present with history of rupture of membranes but there is **no** clinical evidence of membrane rupture**.** Women *with* clinical evidence of PROM should be treated as such without the need for this test.
- Can be used at *any* gestation.
- AmniSure can be used in the presence of semen, minimal amounts of blood, vaginal infection, after intercourse, after a vaginal examination, and in the presence of a minimal amount of water-based lubricant.

3.3.2. Contraindications

- Do NOT use in women with a history of threatened preterm labour where there is no history suggestive of rupture of membranes.
- Additional diagnostic testing is usually not necessary to confirm risk for women with advanced cervical dilatation.
- Active vaginal bleeding as this can affect the result and it is a reason to keep the patient in hospital. As above, AmniSure can be used with minimal amounts of blood.
- In rare cases, when a sample is taken 12-24 hours or later after a rupture has occurred and the leakage of amniotic fluid has stopped, the test may not detect

ROM due to several factors including (but not limited to) resealing of the rupture, denaturing antigen etc. Periodic retesting in such cases may be advisable.

3.3.3. Method for carrying out AmniSure

3.3.3.1. Collecting the sample:

- Have the patient lie on her back, speculum is optional, but the test can be performed without a speculum. Have a timer/stop clock ready.
- Take the solvent vial by its cap and ensure all liquid in the vial has dropped to the bottom. Open the solvent vial and place it in a vertical position to prepare.
- Use only the sterile flocked swab provided with the AmniSure Test kit. Remove the swab from its packet holding the shaft, not the tip.
- The tip of the swab should not touch anything prior to insertion into the vagina.
- Hold the swab in the middle of the shaft and with the patient lying on her back, carefully insert the tip of the sterile swab into the vagina until your fingers contact the skin (no more than 5-7cm deep) for **1 minute**.
- Remove swab from the vagina and ensure swab tip does not touch anything after removal prior to inserting into the solvent vial.
- If the swab is light pink or spotted with blood (trace amounts), this is okay and can still be tested. If the swab is red and saturated with blood, the test should not be used.

3.3.3.2. Testing the sample:

- Remove the swab from the vagina, immediately place the tip into the provided solvent vial, and rotate swab for **1 minute**.
- Remove the swab from the vial and discard swab.
- Tear open the foil pouch at the tear notches and remove the AmniSure test strip holding the blue end.
- Insert the white end of the test strip with the two arrows facing downwards into the vial with the solvent.
- Wait for **5 minutes** or until you see 2 lines (whichever is sooner) and remove the test strip.

3.3.3.3. Reading results:

- Extract test strip from the vial and read the results on a clean, dry, flat surface and immediately record the results.
- **POSITIVE** = 2 lines visible. This indicates the membranes have ruptured. Even if the second line is faint or broken, this result is still positive.

- **NEGATIVE** = 1 line visible. This indicates there is NO rupture of membrane.
- **NO LINES =** The test is not valid.
- Do not interpret the result based on the intensity of the lines.
- AmniSure is a qualitative test, do not interpret a quantitative result from the test.
- Do not read results 10 minutes after dipping the test strip into vial.

3.3.4. Negative AmniSure Result

- Women found to be negative using the AmniSure test will no longer require admission and can be safely discharged home.
- These women will no longer require USS to assess liquor volume and avoid repeated visits to the hospital for maternal and fetal well being monitoring.

3.3.5. Positive AmniSure Result

- Women who are pre-term will have targeted interventions according to the duration of pregnancy to improve perinatal mortality and morbidity (antenatal corticosteroids +/- tocolysis or induction of labour if term) See PPROM Guideline Trustdocs Id: 873.
- Women who are term will be offered induction of labour. See Pre-labour rupture of membranes >37 weeks Guideline Trustdocs Id: 872.

4. Training and Competencies

If midwifery staff wish to perform these tests, there is a “Competency for use of Fetal Fibronectin and AmniSure” – Trust i.d. 15553

5. References / Source documents.

1) Rapid fFN for the TLiIQ System [package insert]. AW-04196-002, Rev. 003
2) Martinez et al, BJOG (2006) 113: 1096-1099
3) Rutanen et al, Clinica Chimica Acta (1993) 214: 73-81
4) NICE (2015) CG25 Preterm labour and Birth pp.
5) Abbott DS, Radford SK, Seed PT, et al. Evaluation of a quantitative fetal fibronectin test for spontaneous preterm birth in symptomatic women. AM J Obstet Gynecol 2012;208.
6) Ramsauer et al 2013. The diagnosis of rupture of fetal membranes (ROM): a meta-analysis. DOI 10.1515/jpm-2012-0247 J. Perinat. Med. 2013; 41(3): 233–240
7) Ramsauer et al 2014. Effect of blood on ROM diagnosis accuracy of PAMG-1 and IGFBP-1 detecting rapid tests J. Perinat. Med. 2014; aop

6. Audit of the service to be delivered

Compliance with the process will be monitored through the following:

Key elements	Process for Monitoring	By Whom (Individual / group /committee)	Responsible Governance Committee /dept	Frequency of monitoring
Fetal fibronectin has been used as component of preterm birth risk assessment in cases resulting in preterm birth	Case reviews occur monthly through perinatal optimisation project	Perinatal Optimisation	Maternity Clinical Governance	Monthly

The audit results are to be discussed at Maternity Clinical Governance meetings to review the results and recommendations for further action. The Maternity Clinical Governance meeting ensures that the actions and recommendations are suitable and sufficient.

7. Equality Impact Assessment (EIA)

Type of function or policy	Existing

Division	Women's and Children's	**Department**	Obstetrics
Name of person completing form	Charles Bircher	**Date**	24/4/23

Equality Area	Potential Negative Impact	Impact Positive Impact	Which groups are affected	Full Impact Assessment Required YES/NO
Race	No	No	No	No
Pregnancy & Maternity	No	No	No	No
Disability	No	No	No	No
Religion and beliefs	No	No	No	No
Sex	No	No	No	No
Gender reassignment	No	No	No	No
Sexual Orientation	No	No	No	No
Age	No	No	No	No
Marriage & Civil Partnership	No	No	No	No
EDS2 – How does this change impact the Equality and Diversity Strategic plan (contact HR or see EDS2 plan)?	It does not			

- **A full assessment will only be required if: The impact is potentially discriminatory under the general equality duty**
- **Any groups of patients/staff/visitors or communities could be potentially disadvantaged by the policy or function/service**
- **The policy or function/service is assessed to be of high significance**

IF IN DOUBT A FULL IMPACT ASSESSMENT FORM IS REQUIRED

The review of the existing policy re-affirms the rights of all groups and clarifies the individual, managerial and organisational responsibilities in line with statutory and best practice guidance.