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Taunton and Somerset NHS Foundation Trust	**Guideline Haematology/Obstetrics**

Title: Guidelines for the use of anti-D for the prevention of haemolytic disease of the fetus and newborn

key words : HDN, anti-D, RAADP, haemolytic disease, free fetal DNA

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Applies to: Staff involved in care of D negative pregnant women	**Exclusions:** None

Purpose; To prevent haemolytic disease of the newborn

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Key recommendations

- All RhD negative women who have had free fetal DNA screening (cffDNA), and given a result which predicts the fetal group as negative, do not require anti-D to be administered during the pregnancy, unless requested by the woman.

- All D negative women and those where the cffDNA result has shown the fetus to be positive or who are not previously sensitised should be offered routine anti-D immunoglobulin (1500 anti-D Ig) (RAADP) at 28 - 30 weeks.

- All D negative women who are not previously sensitised to D should be offered an appropriate dose of anti-D Ig following a potentially sensitizing event.

- Anti D Ig should be administered as soon as possible and always within 72 hours of the event.

- Appropriate tests for fetomaternal haemorrhage (FMH) should be performed if the potentially sensitising event occurs after 20 weeks gestation and additional anti D Ig given if necessary.

- Following birth all babies of negative mothers should have RhD typing performed on cord blood. If the newborn is positive all previously negative non-sensitised women should be offered 1500 iu anti-D IgG within 72 hours of delivery. Maternal samples should be tested for FMH and additional anti-D given as guided by results.

1. Background

This guideline applies to RhD negative non-sensitised pregnant women who are not participating in free fetal DNA screening, or whose screening results have predicted the fetus to be Rh D positive.

Non-sensitised women are those who have not developed immune anti-D antibodies. Routine antenatal anti-D prophylaxis has reduced the incidence of Rh alloimmunisation in Rh D negative women to less than 0.3%. Prior to the availability of anti- D Ig the incidence of Rh D alloimmunisation in D negative women following two deliveries of D positive ABO compatible infants was approximately 16% and haemolytic disease of the fetus and newborn (HDN) due to anti-D was a significant cause of morbidity and mortality.

2. Free Fetal DNA Test (cffDNA)

In approximately 1:3 pregnancies the fetus will be Rhesus Negative in such cases Anti D would have been unnecessary. Since 2001 there have been developments enabling the mothers blood to be tested for free fetal DNA. This test is now offered routinely at MPH.

2.1 Management

- At the booking appointment the woman will be offered a blood test for RhD status. This should be offered even if the woman is aware of her status.

- The midwife is responsible for obtaining and informing the woman of the test results at the next antenatal contact.

- Women who are RhD negative should be offered bloods for cffDNA at 15-16 weeks gestation.

- Bloods must not be obtained before 12 completed weeks gestation, as the result will be inaccurate and a repeat sample will be required.

- The result of the cffDNA test is only valid for the current pregnancy. The test needs to be repeated for each pregnancy.

- Women with a multiple pregnancy may be offered cffDNA test.

Information leaflets should be made available to pregnant women to help with the informed consent process. Maternal consent should be obtained prior to taking blood for cffDNA.

2.2 Process for screening the fetus of D negative women

If the woman is RhD negative the process within Appendix A should be instigated.

3. Routine prophylaxis

3.1 Administration of routine antenatal anti-D IgG prophylaxis (RAADP)

RAADP must be offered to all D negative non sensitised pregnant women (NICE 2002 and 2008), not participating in free fetal DNA screening, or whose screening results have predicted the fetus to be Rh D positive Information leaflets should be made available to pregnant women to help with the informed consent process. Maternal consent should be obtained prior to administration of anti D Ig. The communication and maternal decision, with her reason to accept or decline, must be recorded in the woman's hand held or hospital notes. This is most easily done when the woman's blood group is recorded in her antenatal notes.

A single dose of anti-D Ig 1500 iu should be administered IM at 28 - 30 weeks. The dose and timing is unaffected by previous anti-D prophylaxis for a sensitising event earlier in the same pregnancy. The deltoid muscle is the preferred site for IM injection. If the gluteal region is used absorption may be delayed and efficacy reduced by inadvertent subcutaneous administration.

The following details of the injection should be recorded in the woman's maternity record (hand held or hospital clinical notes)

- Product description and batch number
- Dosage and route
- Site
- Date and time of administration

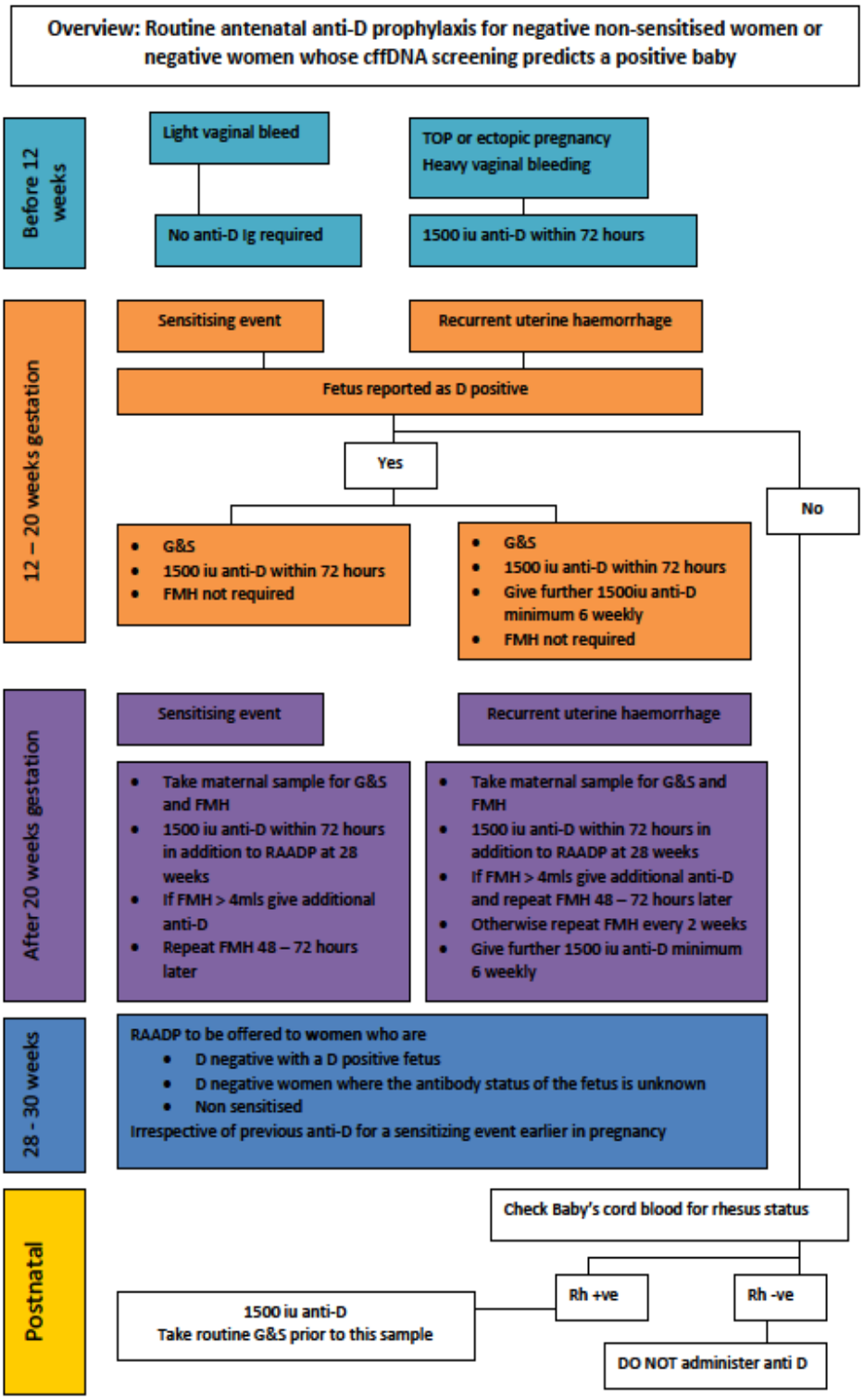
On every occasion that anti-D Ig is administered always confirm the following:

- Woman's identity
- That the woman is Rh D negative using the latest laboratory report
- That the woman does not have immune anti-D using the latest laboratory report
- That informed consent for administration of anti-D Ig is recorded in notes

3.2 Documentation of anti-D administration

- Anti D Ig is a blood product. There must therefore be clear documentation and record keeping to ensure full traceability and compliance with BSQR 2005. This requires prompt return of completed transfusion forms to the Transfusion laboratory in all cases. This also means that this information is available should a pregnant women require pre-transfusion testing. This is essential as it is impossible to differentiate between administered prophylactic anti-D and immune anti-D in laboratory tests. For this reason the 28 week sample for blood group and antibody screen should be taken prior the first routine prophylactic anti-D Ig.

3.3 Overview of anti D prophylaxis for negative non-sensitised women or negative women whose baby predicts a positive baby


Overview: Routine antenatal anti-D prophylaxis for negative non-sensitised women or negative women whose cffDNA screening predicts a positive baby
Before 12 weeks
Light vaginal bleed
No anti-D Ig required
TOP or ectopic pregnancy
Heavy vaginal bleeding
1500 iu anti-D within 72 hours
12 – 20 weeks gestation
Sensitising event
Recurrent uterine haemorrhage
Fetus reported as D positive
Yes
No
G&S
1500 iu anti-D within 72 hours
FMH not required
G&S
1500 iu anti-D within 72 hours
Give further 1500iu anti-D minimum 6 weekly
FMH not required
After 20 weeks gestation
Sensitising event
Recurrent uterine haemorrhage
Take maternal sample for G&S and FMH
1500 iu anti-D within 72 hours in addition to RAADP at 28 weeks
If FMH > 4mls give additional anti-D
Repeat FMH 48 – 72 hours later
Take maternal sample for G&S and FMH
1500 iu anti-D within 72 hours in addition to RAADP at 28 weeks
If FMH > 4mls give additional anti-D and repeat FMH 48 – 72 hours later
Otherwise repeat FMH every 2 weeks
Give further 1500 iu anti-D minimum 6 weekly
28 - 30 weeks
RAADP to be offered to women who are
D negative with a D positive fetus
D negative women where the antibody status of the fetus is unknown
Non sensitised
Irrespective of previous anti-D for a sensitizing event earlier in pregnancy
Postnatal
Check Baby's cord blood for rhesus status
Rh +ve
Rh -ve
1500 iu anti-D
Take routine G&S prior to this sample
DO NOT administer anti D

4. Potentially Sensitising Events

Additional prophylactic anti-D Ig should be offered in the event of any of the following potentially sensitising events

- Amniocentesis, chorionic villous sampling and cardiocentesis
- Antepartum haemorrhage or PV bleeding in pregnancy
- External cephalic version
- Fall or abdominal trauma
- Ectopic pregnancy
- Intrauterine death and still birth
- In-utero therapeutic interventions (transfusion, surgery, insertion of shunts)
- Miscarriage or threatened miscarriage
- Termination of pregnancy

Anti-D Ig should be given as soon as possible after the potentially sensitising event but always within 72 hours. If it is impossible to give before 72 hours every effort should still be made to administer anti-D Ig as a dose given within 10 days may provide some protection.

See algorithm on page 5.

4.1 Before 12 weeks gestation

Recurrent uterine bleeding

Anti-D Ig is unnecessary in women with threatened miscarriage with a viable fetus where bleeding stops completely before 12 weeks. If bleeding is heavy or repeated or where there is associated abdominal pain and gestation approaches 12 weeks a dose of 1500 iu anti-D Ig may be considered.

4.2 Between 12 and 20 weeks gestation

Recurrent uterine bleeding

D negative women with recurrent PV bleeding between 12 and 20 weeks gestation should be given 1500 iu anti-D Ig at a minimum of 6 weekly intervals.

4.3 At and after 20 weeks gestation

Recurrent uterine bleeding

A 1500iu anti-D Ig should be given at 6 weekly intervals. FMH should be estimated when anti-D is first given and thereafter every 2 weeks. If positive, additional anti-D Ig should be given to cover the volume of fetal red cells. Any additional dose should be offered regardless of the presence or absence of passive anti-D in maternal plasma and FMH should be retested after 48 – 72 hours.

Additional anti-D dose calculation

A dose of 1500 iu IM is sufficient to treat a FMH of up to 15mls fetal red cells. Where it is necessary to give additional doses of anti D Ig the following dose calculations apply:

- Rhophylac: 100 iu anti-D per 1 ml fetal red cells administered IM or IV

4.4 At or after 28 weeks gestation

For any potentially sensitising event 1500 iu anti-D Ig should be given within 72 hours of the event even if the woman has received RAADP at 28 weeks. The antibody screen will be positive if anti-D has been given as part of RAADP and hence routine blood group and antibody screen are unnecessary after 28 weeks gestation if the antibody screen was negative at 28 weeks. A G&S sample should be taken if blood component support may be necessary e.g. Antepartum haemorrhage. A sample for FMH must be sent. Additional anti-D will be necessary if the volume of FMH exceeds that covered by the standard anti-D dose. If this is the case further maternal blood samples will be needed 48 – 72 hours after additional anti-D dosing to ensure fetal cells have cleared.

Recurrent uterine bleeding

1500iu anti-D Ig should be given at 6 weekly intervals. FMH should be estimated every 2 weeks. If positive additional anti-D Ig should be given to cover the volume of fetal red cells. Any additional dose should be offered regardless of presence or absence of passive anti-D in maternal plasma and FMH should be retested after 48 – 72 hours.

Additional anti D dose calculation

A dose of 1500 iu IM is sufficient to treat a FMH of up to 15mls fetal red cells. Where it is necessary to give additional doses of anti D Ig the following dose calculations apply:

- Rhophylac: 100 iu anti-D per 1 ml fetal red cells administered IM or IV

5. Post Natal anti D

Following birth a cord sample should be taken to test the ABO and D group of the baby for all RhD negative women, even those who have been previously screened for cffDNA and there is a 0.1% chance that the predicted blood group is incorrect. A direct antiglobulin test should not be performed routinely as it may be positive in a proportion of cases because of antenatal anti D prophylaxis. Maternal samples for confirmatory ABO and D type and FMH should be collected within 2 hours but no earlier than 30 minutes post delivery to allow any FMH to be dispersed in the maternal circulation.

If the infant's blood group is D positive 1500 iu anti D IgG should be administered im to previously non-sensitised D negative women within 72 hours of delivery. If the confirmed FMH volume exceeds the standard dose of anti-D Ig already given an additional dose must be given within 72 hours of delivery The minimum dose to be administered should be calculated as 100 iu for each additional ml of fetal cells.

When intra-operative cell salvage is used in Caesarean section the reinfused blood may contain up to 20ml fetal blood. It is therefore recommended that a minimum anti-D dose of 1500 iu is administered immediately after reinfusion of salvaged red cells. Maternal sample for FMH should be taken 30 – 45 minutes after re-infusion to allow additional anti-D to be given if required.

A dose of 1500 iu im is sufficient to treat a FMH of up to 15 mls fetal red cells. Where it is necessary to give additional doses of anti D Ig the following dose calculations apply:

- Rhophylac: 100 iu anti-D per 1 ml fetal red cells administered im or iv

If the pregnancy is non-viable and no sample can be obtained from the baby prophylactic anti-D Ig should be administered to D negative non-sensitised women.

Some protection may be offered if anti-D Ig is given up to 10 days after the sensitising event.

6. Management of discordant cffDNA result and cord blood group result

In the event of there being a difference between the cffDNA result and the cord blood group following the birth of the baby, before administering anti D take repeat bloods from the mother for:

- antibody screen
- cffDNA (X2 6mls EDTA bottles)

An incident form should be completed and the Blood Transfusion laboratory informed as soon as is reasonably practicable. Although there is a false negative rate for the cffDNA test (1:800) an incident investigation will be raised to ensure there was no failure within the process.

The mother should be informed of the finding and if any maternal antibodies are found on screening advice should be sought from the Haematologist.

7. Management of transfusion of D positive blood components

7.1 D positive platelet transfusions

The dose of 1500 iu anti-D Ig is sufficient to cover up to five adult therapeutic doses of D positive platelets given within a six week period. In severely thrombocytopenic patients (platelet count < 30 x 10^9/l) anti-D Ig should be given subcutaneously or if an intravenous preparation is available, intravenously to avoid the risk of intramuscular bleeding following im injection.

7.2 Inadvertent transfusion of D positive blood to D negative pre-menopausal women

When less than 15ml have been transfused, the appropriate dose of anti-D immunoglobulin should be given. When more than 15ml have been transfused use the larger anti-D immunoglobulin IM preparation (1500 iu). The dose should be calculated on the basis that 1500 iu anti-D Ig will suppress sensitisation by 15 ml of D positive red cells.

When more that one unit of D positive red cells have been transfused, a red cell exchange transfusion should be considered. Contact On call Haematologist for further advice.

8. Side effects

Probable or possible adverse events are rare (< 1 per 80,000 doses of anti-D Ig). There is no evidence that anti-D administered to the mother during pregnancy is harmful to the fetus. Allergic reactions are very rare but severe hypersensitivity including anaphylaxis may occur. Anti-D preparations may contain trace amounts of IgA. Consequently patients with anti-IgA antibodies have a risk of severe hypersensitivity or anaphylactic reactions.

9. Training and audit

All staff involved in the administration of anti-D should complete the e- learning package: “Anti-D clinical module” (learnPro NHS - Login). Midwives must complete this package every 3 years.

Audits will be performed to assess compliance with this guideline. Audit topics include the following:

- Proportion of non-sensitised D negative pregnant women offered anti-D for sensitising events during pregnancy
- Availability of information leaflet for RAADP
- Proportion of non-sensitised D negative women given anti D within 72 hours of sensitising event
- Documentation to ensure traceability of anti-D Ig from source to recipient
- Documentation of reasons given by women who decline RAADP

10. Incident reporting

Incidents relating to the administration of anti-D Ig should be reported to the Serious Hazards of Transfusion (SHOT) via the MHRA incident reporting website. It is the responsibility of the senior blood transfusion staff to report these in a timely manor, but it is also the responsibility of the clinician who identifies the incident to report it the Blood Transfusion Department through the Trust incident reporting mechanism.
The following incidents should be reported

- Omission or late administration

- Anti-D given to a D positive patient or a patient with immune anti-D
- Anti-D given to the wrong patient
- Incorrect dose of anti-D given
- Anti-D given that has expired or out of temperature control
- **discordant cffDNA result and cord blood group result**

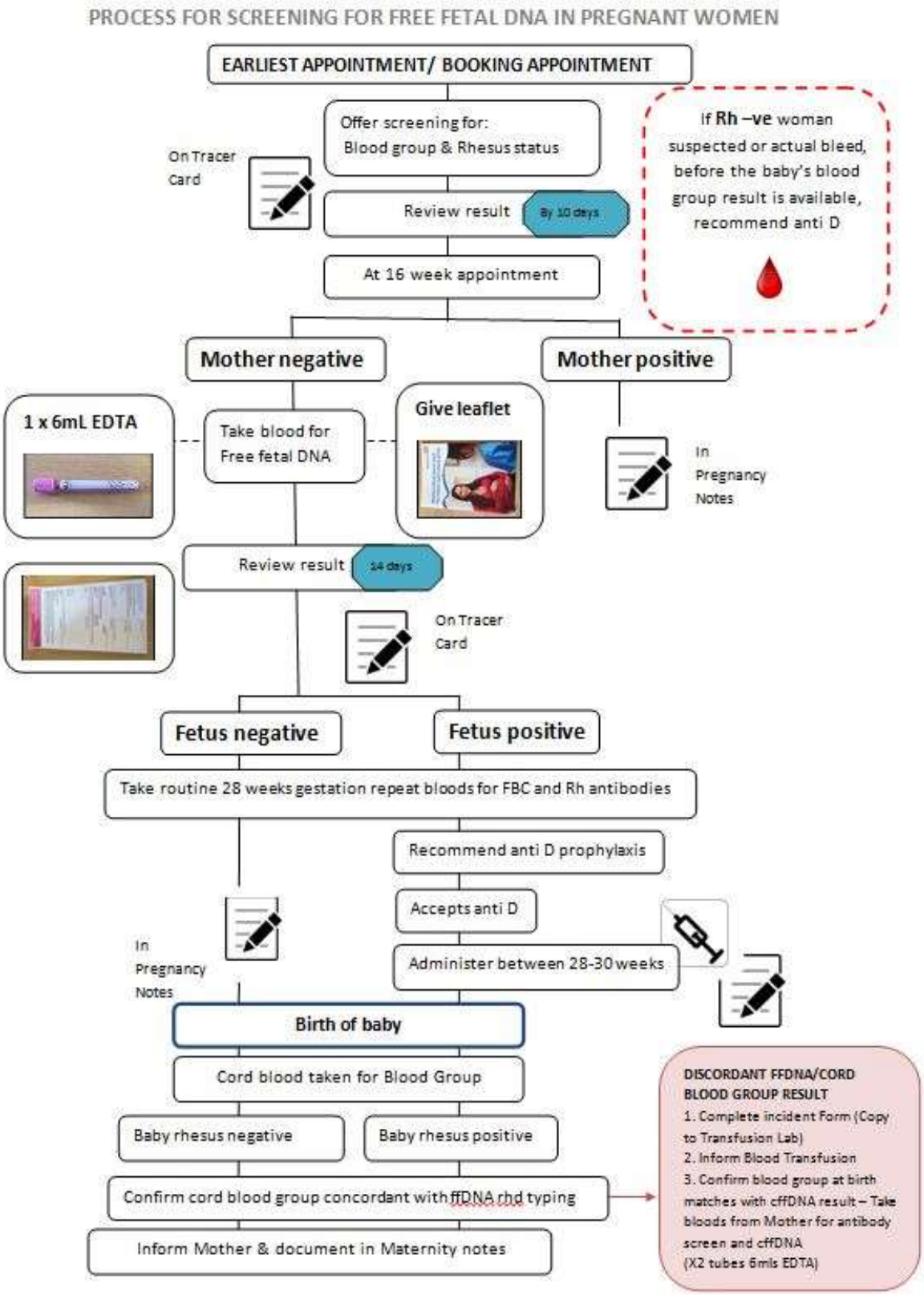
In addition SHOT is expected to introduce an additional category for incidents where women who have become sensitised and have subsequently developed D antibodies. Please therefore identify any such incidents to the Transfusion Laboratory staff.

11. References

RCOG Green top guideline No 22, March 2011.

National Institute for Health and Clinical Excellence: Routine antenatal anti-D prophylaxis for women who are rhesus D negative (TA156). London: NICE 2008.
British Committee for Standards in Haematology: Guidelines for use of prophylactic anti-D immunoglobulin 2006.

Appendix A


PROCESS FOR SCREENING FOR FREE FETAL DNA IN PREGNANT WOMEN
EARLIEST APPOINTMENT/ BOOKING APPOINTMENT
Offer screening for:
Blood group & Rhesus status
On Tracer Card
Review result
By 10 days
At 16 week appointment
If Rh –ve woman suspected or actual bleed, before the baby's blood group result is available, recommend anti D
Mother negative
Mother positive
1 x 6mL EDTA
Take blood for Free fetal DNA
Give leaflet
In Pregnancy Notes
Review result
14 days
On Tracer Card
Fetus negative
Fetus positive
Take routine 28 weeks gestation repeat bloods for FBC and Rh antibodies
Recommend anti D prophylaxis
Accepts anti D
Administer between 28-30 weeks
In Pregnancy Notes
Birth of baby
Cord blood taken for Blood Group
Baby rhesus negative
Baby rhesus positive
Confirm cord blood group concordant with ffDNA rhd typing
Inform Mother & document in Maternity notes
DISCORDANT FFDNA/CORD BLOOD GROUP RESULT
1. Complete incident Form (Copy to Transfusion Lab)
2. Inform Blood Transfusion
3. Confirm blood group at birth matches with cffDNA result – Take bloods from Mother for antibody screen and cffDNA
(X2 tubes 6mls EDTA)