SHOT Safety Notice 03: Safe, appropriate, and timely administration of anti-D Immunoglobulin during the perinatal period

This safety notice was reviewed and approved by the Royal College of Obstetricians & Gynaecologists (RCOG) and by the Royal College of Midwives (RCM)

1. The objective of this SHOT Safety Notice

This SHOT Safety Notice has been issued to highlight the importance of appropriate administration of anti-D immunoglobulin (Ig). This includes dose, route, and administration within the correct timeframe. The aim is to reduce the risk of developing immune anti-D in mothers and birthing parents with D-negative blood type during pregnancy and following the birth of an infant with D-positive blood type. Immune anti-D can result in haemolytic disease of the fetus and newborn (HDFN). Organisations must ensure that local policies, procedures, and processes support compliance with current BSH guidelines for safe and appropriate administration of anti-D Ig following potentially sensitising events (PSE) and for routine antenatal anti-D Ig prophylaxis (RAADP) (Qureshi, et al., 2014).

This safety notice should be used as a gap analysis tool to help identify gaps in current practice and implement improvement actions to enhance patient safety.

2. Anti-D Ig errors reportable for haemovigilance

Errors relating to the request and/or administration of anti-D Ig during pregnancy and after birth are reportable to SHOT and are the focus of this safety notice. However, this reporting category (anti-D) also includes events relating to the administration of anti-D Ig following inadvertent transfusion of D-mismatched red cells or platelets or following a D-mismatched solid organ transplant (SOT).

Cases of pathological reactions to anti-D Ig such as severe allergy or local reactions are not reportable to SHOT, these are reportable via the MHRA 'Yellow Card' system for medicines using this link: https://yellowcard.mhra.gov.uk/

The SHOT definitions and reporting criteria can be accessed using this link: https://www.shotuk.org/reporting/

3. Trend in adverse events relating to anti-D Ig analysed by SHOT (2014-2023)

The number of SHOT reports relating to anti-D Ig errors between 2014 and 2023 are represented in Figure 1. These incidents have been reported with these errors occurring in both clinical and/or laboratory settings.

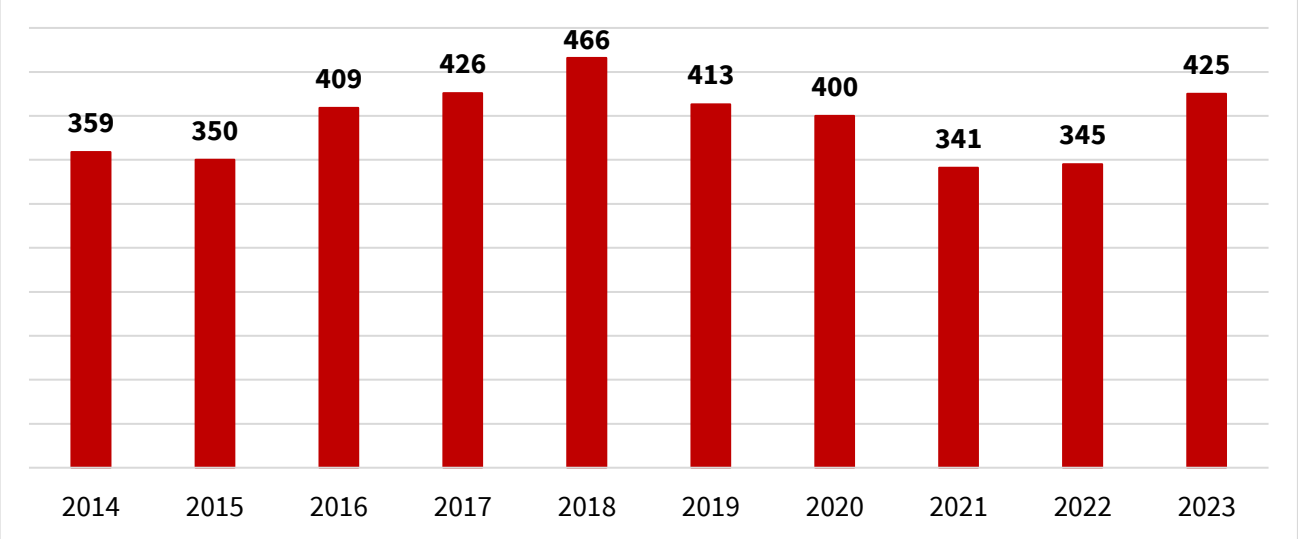

Figure 1- Number of errors reported to SHOT relating to anti-D Ig between 2014-2023

4. Number of reports from errors reported to SHOT (2021-2023)

For the last three years (2021-2023) anti-D Ig errors have represented between 22% to 24% of the total errors analysed by SHOT, being the most reported category due to errors excluding Near-Miss (Figure 2). All Annual SHOT Reports and the anti-D Ig errors chapters can be accessed using this link: https://www.shotuk.org/shot-reports/

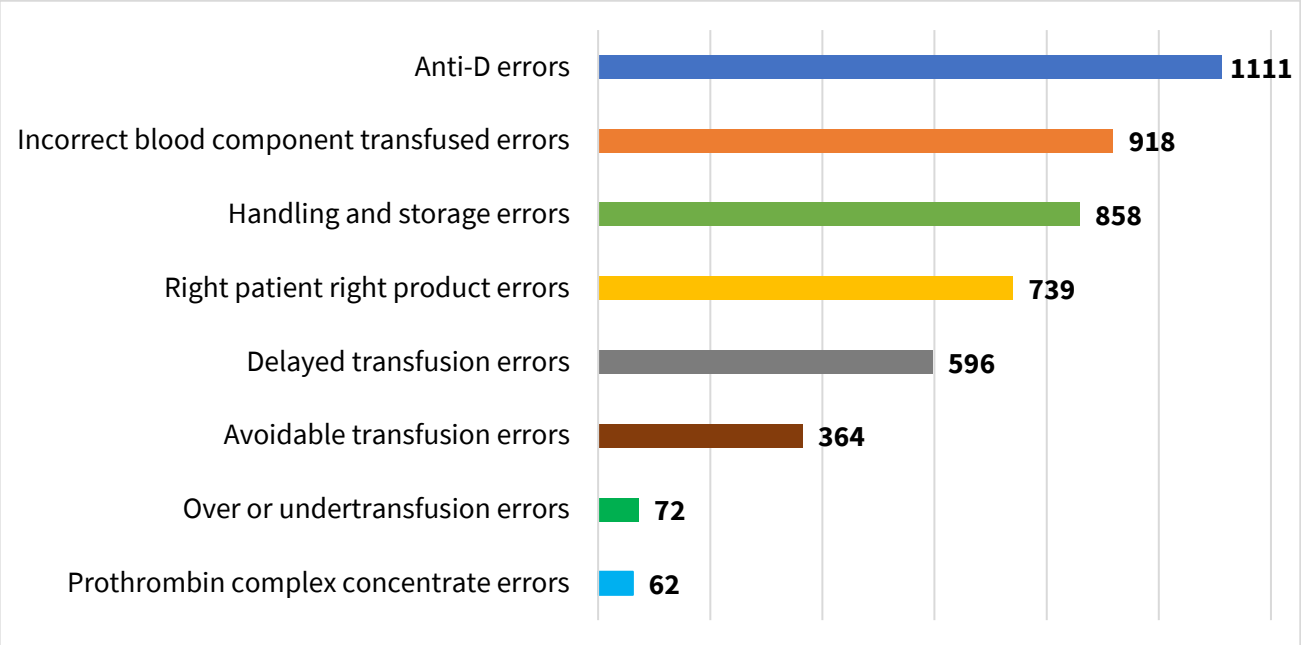

Figure 2 - Number of reports per category analysed by SHOT due to errors in the last 3 years (2021-2023).

5. Common themes relating to anti-D Ig errors reported to SHOT and key recommendations

Omission or late anti-D Ig/RAADP administration are the most common reports every year and accounted for 58% to 81% of all anti-D Ig incidents reported to SHOT between 2014-2023. These can lead to sensitisation to the D antigen and potential HDFN for future pregnancies.	
Common themes	**Key recommendation**
Transcription errors where the wrong maternal, fetal and/or cord D-types are transferred to the clinical notes can lead to incorrect decision-making.	Interoperable Information Technology (IT) systems in the laboratory and clinical settings would reduce risk of these errors by transferring data electronically.
Discharging mothers and birthing parents prior to administration of anti-D Ig is contributory in most cases of delays in administration.	Incorporating prompts when discharging mothers and birthing parents (e.g., when drafting the discharge summary); staff education and people empowerment could reduce risk.
RAADP missed or late administrated (>34 weeks gestation) when women and pregnant people **did not attend appointment and there wasn't appropriate follow-up.**	Systems should be in place to ensure that, where women/pregnant people or mothers/birthing people have not attended an appointment at any stage of pregnancy, there is a follow-up and effective communication about the risks of not having anti-D Ig administered.
Results of non-invasive prenatal testing for the *RHD* genotype using cell-free fetal DNA (ccfDNA) have led to errors when **missed or misinterpreted.**	Where these tests are performed, the results must be reviewed prior to administration of anti-D Ig/RAADP. If, after birth, the predicted D type by cffDNA is found discrepant with cord D type appropriate investigation and action should be taken by the laboratory.

6. Perinatal safety incidents due to transcription errors into maternity IT systems

Implementation and use of IT systems in healthcare must aim to reduce errors and increase safety. It is recognised that IT systems that require manual input of laboratory results, individual's demographics, or clinical data, carry a higher risk for transcription errors to occur, which can impact on safety. For example, if the D-status is incorrectly entered as D-positive, the management of anti-D Ig can be erroneous (omitted or late administrated) during pregnancy. Where the D-type is entered erroneously as D-negative, there is a risk of unnecessary administration of anti-D Ig and cffDNA testing. Transcription errors can also occur postnatally if the ABO/D group of the baby requires to be entered manually onto the IT system, leading to potential missed anti-D Ig administration.

To prevent manual transcription errors, IT systems must be improved or commissioned to support electronic transfer of data to enable safer practice. This will improve accuracy and decrease workload as manual input is not needed. This can only be achieved if the requirements for the IT systems are clearly stated before implementation with a comprehensive analysis of associated potentialities and limitations. To confirm compliance of the requirements an effective validation must be conducted *before* going live.

SHOT encourages reporters to raise awareness where gaps in IT systems are identified leading to unsafe practice. Workarounds to compensate lack of functionality and/or consideration of ergonomics in IT systems should not be accepted or regarded as normal practice.

7. SHOT categories: Anti-D immunisation vs Anti-D Ig errors

SHOT accepts and encourages reporting events where women with D-negative blood type have become sensitised to the D antigen and have developed immune anti-D detectable during pregnancy. These events are reported under a different category (immune anti-D). This category includes cases where D-sensitisation might not be related to errors in management of anti-D Ig.

The differences of reporting criteria for both categories, anti-D immunisation and anti-D Ig errors, can be find in more detail in the SHOT Bite No.29: Differences of reporting errors related to anti-D Ig and immune anti-D (https://www.shotuk.org/resources/current-resources/shot-bites/)

Gap analysis tool for anti-D Ig management in D-negative pregnancies

This template can be used to identify gaps in current practice (clinical and laboratory) where improvements can be implemented. It can also be used to identify gaps in current IT systems where development could be used to improve practice.

This gap analysis is based on the current national guidelines. Further steps or processes may be part of local policies and not reflected in this gap analysis.
While this gap analysis helps identify gaps in policies and processes, it is vital that, through observational audits/quality walkarounds and other relevant tools, to ensure work as done reflects work as agreed/prescribed/imagined.

If the answer is 'no' to any of these, then appropriate actions or appropriate risk assessment need to be taken locally to ensure patient safety.

A. General	
1. Is there a clinical policy/protocol/guideline that covers use of anti-D Ig for PSE and RAADP within maternity and gynaecology services?	Y ☐ N ☐
2. Is the clinical policy/protocol/guideline in date and easily accessible to staff?	Y ☐ N ☐
3. Is there a protocol in emergency departments to ensure all D-negative pregnant people are identified, seen by an Obstetric/Gynaecology clinician and anti-D Ig offered where appropriate?	Y ☐ N ☐
B. Decision-making processes	
1. Is the use of anti-D Ig covered in training followed by knowledge assessment for Obstetric/Gynaecology consultants, speciality doctors and resident doctors?	Y ☐ N ☐
2. Is the use of anti-D Ig covered in training and competency assessment for midwives and nurses working in gynaecology and other relevant areas?	Y ☐ N ☐
3. Does the clinical policy/protocol include instructions that anti-D Ig must be given within 72 hours of a PSE and for RAADP at 28 weeks (single dose regimen) or at 28 and 34 weeks (two-dose regimen)?	Y ☐ N ☐
4. Does the clinical policy/protocol include details of types of PSE that require anti-D Ig, including in early pregnancy?	Y ☐ N ☐
5. Does the clinical policy/protocol include instructions for use of anti-D Ig where there is a continual uterine bleeding which is clinically judged to represent the same sensitising event, with no features suggestive of a new presentation or a significant change in the pattern or severity of bleeding, such as the presence of abdominal pain or another clinical presentation, a minimum dose of 500iu anti-D Ig should be given at six weekly intervals, in accordance with BSH guidelines?	Y ☐ N ☐
6. Does the clinical policy/protocol include instructions that anti-D Ig must be given within 72 hours of diagnosis of an intrauterine death (IUD), and a subsequent dose following the birth?	Y ☐ N ☐

7. In centres where cell salvage is available, does the policy include instructions relating to requirement for minimum of 1500iu anti-D Ig where cell salvage has been used and reinfused in mothers and birthing parents with D-negative blood type?	Y ☐ N ☐ NA ☐
8. Are women and pregnant people offered both verbal and written information in a format that meets their individual needs to enable them to make an informed decision about receiving anti-D Ig?	Y ☐ N ☐
9. When RAADP or PSE indicated anti-D Ig is declined, is there a process for clearly recording this in the clinical notes and other documentation?	Y ☐ N ☐
C. Order and prescription	
1. Does the process for ordering anti-D Ig for PSE include an order for fetomaternal haemorrhage (FMH) volume estimation where gestation is greater than 20 weeks?	Y ☐ N ☐
2. Does the order process include collection of a group and screen sample to confirm the woman/pregnant individual is D-negative and does not have immune anti-D?	Y ☐ N ☐
3. Do local policies/guidelines support RAADP and post-birth anti-D Ig to be administered as a midwife exemption?	Y ☐ N ☐
4. Where IT systems are used for antenatal appointment bookings, do these include prompts for RAADP administration where appropriate?	Y ☐ N ☐
5. Postnatally, is there a process for labelling cord samples that ensures they are clearly labelled as cord blood to reduce the risk of mix-up with maternal sample?	Y ☐ N ☐
6. Does the anti-D Ig/RAADP order clearly indicate the date required for administration?	Y ☐ N ☐
7. Does the anti-D Ig/RAADP order clearly indicate the location where the mother/birthing parent is attending for anti-D Ig administration?	Y ☐ N ☐
8. Where anti-D Ig/RAADP is required for administration in community locations, is there a process for ensuring that it has been received prior to the appointment?	Y ☐ N ☐ NA ☐
9. Where anti-D Ig/RAADP is required for administration in community locations, is there a process for storing it at the correct temperature prior to the appointment?	Y ☐ N ☐
10. Are the mothers/birthing parents' ABO/D blood group results electronically transmitted to a maternity IT system?	Y ☐ N ☐
11. Where IT systems are used for anti-D Ig orders, are these configured to include clinical decision support for appropriate ordering based on D-type and admission/appointment details?	Y ☐ N ☐
12. Is there a failsafe system to ensure that D-negative women and pregnant people do not miss RAADP administration where appropriate?	Y ☐ N ☐
D. Laboratory/Pharmacy practice	
1. Are the laboratory Standard Operating Procedures (SOP) relating to estimation of FMH and release of anti-D Ig clear, concise, accurate and easy to follow?	Y ☐ N ☐
2. Is there a clear process in the laboratory that confirms that mother/birthing parent is D-negative prior to the release of anti-D Ig for PSE and RAADP?	Y ☐ N ☐
3. Is there a clear process in the laboratory that confirms absence of immune anti-D prior to release of anti-D Ig for PSE and RAADP?	Y ☐ N ☐

4. Does the laboratory have a process for review and follow up of anti-D Ig that has not been collected from storage?	Y ☐ N ☐
5. Does the training, education and competency assessment program for laboratory staff include requirements for anti-D Ig for PSE and RAADP?	Y ☐ N ☐
6. Does laboratory practice include training and regular competency assessment for manual estimation of FMH?	Y ☐ N ☐
7. Does the laboratory SOP include instructions, in accordance with BSH recommendations, for repeat FMH screening where additional doses of anti-D Ig have been required?	Y ☐ N ☐
8. Does the Laboratory Information Management System (LIMS) include algorithms to support safe release of anti-D Ig based on maternal D-type, cffDNA screening (if implemented) and absence of immune anti-D?	Y ☐ N ☐
9. Does the laboratory SOP include instructions that a minimum of 1500iu must be released where cell salvage has been used and reinfused in D-negative mothers/birthing parents?	Y ☐ N ☐
10. Do laboratory processes and procedures include release of anti-D Ig based on cord D-positive in D-negative pregnancies without an order from the clinical team?	Y ☐ N ☐
11. Do laboratory and clinical processes ensure that anti-D Ig is given within 72 hours where cord or maternal samples are rejected due to mislabelling?	Y ☐ N ☐
12. Does the LIMS include algorithms for calculation of anti-D Ig dose required based on cell counts of FMH screening/confirmatory tests?	Y ☐ N ☐
13. Where manual FMH estimation is used in the laboratory does this include a second check process?	Y ☐ N ☐
14. Does the laboratory process for FMH estimation include confirmation by flow cytometry where estimation indicates a bleed >2mL?	Y ☐ N ☐
15. Where anti-D Ig is not stored in designated blood fridges is there a process to ensure that the storage areas are maintained at the correct temperature?	Y ☐ N ☐
16. Is the date of administration of anti-D Ig/RAADP recorded in the laboratory in such a way that this is clear and accessible when maternal antibody screen indicates the presence of anti-D in antibody screening and identification?	Y ☐ N ☐
17. Is there a process for quantification, or other validated technique, of detected anti-D in maternal samples to differentiate potential immune anti-D from passively acquired anti-D?	Y ☐ N ☐
18. Does the analytical platform have a process for indicating where the mother/birthing parent's D-type may be a weak or partial D?	Y ☐ N ☐
19. Where the analytical platform indicates potential weak or partial D-type is there a process for confirmation of D-type?	Y ☐ N ☐
20. Where the D-type is equivocal and awaiting confirmation is there a process for timely and appropriate release of anti-D Ig?	Y ☐ N ☐
21. Where the D-type is equivocal and awaiting confirmation is this information relayed to the clinical team to support timely and appropriate order and administration of anti-D Ig?	Y ☐ N ☐
E. Administration	

1. Is there a process for ensuring that anti-D Ig for PSE is administered before discharge?	Y ☐ N ☐
2. Is there a clear process for administration of anti-D Ig within 72 hours where discharge occurs prior to administration?	Y ☐ N ☐
3. Does the administration process include positive patient identification prior to administration, including confirmation of patient details on label attached to the product?	Y ☐ N ☐
4. Does the administration process include confirmation that the product has not expired prior to administration?	Y ☐ N ☐
5. Is administration of anti-D Ig recorded clearly in the clinical notes and any other related documentation?	Y ☐ N ☐
6. Does the process include recording of the anti-D Ig lot number and expiry date for confirmation of correct administration and traceability?	Y ☐ N ☐
7. Does the administration process include details of site (muscle) for administration? *The deltoid muscle is an appropriate and safe site for IM administration of anti-D Ig (BSH guidelines)*	Y ☐ N ☐
8. Does the administration process include confirmation that anti-D Ig/RAADP is appropriate based on cffDNA screening results (if implemented), the D-type of the pregnant individual and absence of immune anti-D?	Y ☐ N ☐
9. Are samples for group and antibody screen at 28 weeks taken prior to administration of RAADP?	Y ☐ N ☐
10. Where stocks of anti-D Ig are held that are not labelled for a named individual does the process ensure that administration and individual details are confirmed for traceability?	Y ☐ N ☐
11. Where IT systems are used for anti-D Ig/RAADP administration are these configured to include confirmation of positive patient identification?	Y ☐ N ☐
F. Learning from incidents	
1. Are all anti-D Ig/RAADP errors and near miss events trended and investigated for learning and improvement?	Y ☐ N ☐
2. Are all anti-D Ig/RAADP errors and near miss events reported to SHOT for wider learning and improvement?	Y ☐ N ☐
3. Does the current IT system have the capability to record, track and analyse transfusion incidents including anti-D Ig errors and reactions?	Y ☐ N ☐
G. Where cffDNA screening is in place	
1. Is non-invasive prenatal screening (cffDNA) for the *RHD* genotype offered to all women and pregnant people with D-negative blood type?	Y ☐ N ☐
2. Does the screening process for cffDNA ensure that samples are not collected for analysis prior to 11+3 weeks gestation?	Y ☐ N ☐
3. Do the results of the cffDNA screening test clearly indicate whether anti-D Ig is appropriate or not?	Y ☐ N ☐
4. Are the results of cffDNA screening visible to clinical and laboratory staff at the time of order or release of anti-D Ig?	Y ☐ N ☐

5. Is it clear in the clinical notes, or IT systems, that the cffDNA results relate to the current pregnancy?	Y ☐ N ☐
6. Does the order for anti-D Ig (PSE, RAADP and postnatally) include confirmation that the woman/birthing person is D-negative and cffDNA results indicate requirement for anti-D Ig?	Y ☐ N ☐
7. Is there a clear process within the laboratory that confirms the cffDNA result prior to release of anti-D Ig for PSE and RAADP?	Y ☐ N ☐
8. Is there a laboratory procedure for investigation where cord sample has been taken and the D-type is discrepant from cffDNA predicted D-type?	Y ☐ N ☐

Useful resources and relevant guidelines

BSH guideline for the use of anti-D immunoglobulin for the prevention of haemolytic disease of the fetus and newborn https://doi.org/10.1111/tme.12091

BSH guideline for the estimation of fetomaternal haemorrhage https://b-s-h.org.uk/guidelines/guidelines/the-estimation-of-fetomaternal-haemorrhage

NICE – Technology appraisal guidance [TA156] – Routine antenatal anti-D prophylaxis for women who are rhesus D negative 1 Guidance | Routine antenatal anti-D prophylaxis for women who are rhesus D negative | Guidance | NICE

NICE – Diagnostics guidance [DG25] – High-throughput non-invasive prenatal testing for RHD genotype https://www.nice.org.uk/guidance/dg25

NICE guideline [NG126] – Ectopic pregnancy and miscarriage: diagnosis and initial management https://www.nice.org.uk/guidance/ng126/chapter/Recommendations#anti-d-rhesus-prophylaxis

NICE guideline [NG140] – Abortion care https://www.nice.org.uk/guidance/NG140

Patient Leaflet - Receiving anti-D immunoglobulin in pregnancy https://hospital.blood.co.uk/patient-services/patient-blood-management/patient-information-leaflets/

Useful SHOT resources - https://www.shotuk.org/resources/

- Aide memoire - Anti-D Ig administration to avoid sensitisation in pregnancy
- Infographic - IT supports anti-D Ig management in pregnancy
- Template for investigation of discrepant cffDNA results in hospitals
- SHOT Bite No. 2: Anti-D Ig Administration
- SHOT Bite No. 28: Cell-free DNA (cffDNA) screening errors
- SHOT Bite No. 29: Differences of reporting errors related to anti-D Ig and immune anti-D
- SHOT video: Anti-D Ig and Immune anti-D (part 1 and part 2)