

## PERINATAL

## Products for Perinatal Diagnostics

### Introduction

Detection and quantification of fetal red blood cells (fRBCs) in maternal blood samples is essential for obstetrical management. Measurement of fRBCs is critical as the extent of Fetomaternal Hemorrhage (FMH), the transplacental passage of fRBCs into the maternal circulation, has consequences for further treatment of mother and child. Frequency and size of FMH is directly influenced by complications in abdominal trauma, suspected placental injury or after a caesarean section. Severe FMH may lead to intra-uterine death. In case of antigen incompatibility between mother and child FMH may result in respiratory problems or anaemia, like Haemolytic Disease of the Newborn.

Adult RBCs contain a population of HbF (F-cells), which can be very different in size. It can vary from 0 to more than 14%. The F-cells can lead to positive results in the Kleihauer-Betke acid-elution test or single HbF flow cytometry test.

These F-cells may be the result of physiological variation during pregnancy or traits such as thalassemia, sickle cell anaemia or hereditary persistence of fetal haemoglobin. The detection (and subsequent enumeration) of fRBCs is used to calculate the extent of FMH, either in case of trauma with suspected placental injury or in the situation of a RhD incompatibility between the fetus and mother. In case of the RhD incompatibility the amount of fRBCs is used to determine the (prophylactic) anti-D therapy to prevent the hemolytic disease of the newborn.

### Application

IQ Products offers a range of products for the diagnosis of Fetomaternal Hemorrhage. These products are different methods for the detection of rhesus incompatibility or Fetomaternal Hemorrhage.



### Conclusion

The FMH Kit focusses on the detection of fetal cells on the basis of a rhesus D blood group incompatibility between mother and her unborn child. The cells of the rhesus D positive child can be discriminated from the rhesus D negative erythrocytes from mother.

The FMH QuikQuant discriminates the fetal from the maternal erythrocytes on the basis of high HbF expression by the fetal cells. This method is independent of the presence of a blood group incompatibility between mother and child, and is fast to perform.

The Fetal Cell Count Kit™ is using HbF expression **in combination** with the expression of carbonic anhydrase. This method allows the discrimination of fetal cells, which have strongly reduced expression of CA, from high HbF expressing maternal F-cells, which have a high expression of CA as well. This detection is also independent of the blood group and is also recognized for its applicability with patients having high percentages of F-cells, for instance Thalassemia.

The Fetal Cell Count™ Kit is a patented and IVD/CE registered assay.

## Fetal Cell Count™ Kit

The Fetal Cell Count™ Kit assay is a flow cytometry product and is based on a patented combination of two antibodies. One is directed against HbF while the second is specific for carbonic anhydrase (CA), an enzyme present in adult RBCs and, at very detectable level, in late pregnancy stage. To circumvent the need for an arbitrary setting, the Fetal Cell Count™ Kit is designed to identify the number of fetal cells in maternal blood in a rapid and reliable way. Figure 1 shows a typical Fetal Cell Count™ Kit result emphasizing its clinical utility in the diagnosis of FMH and the subsequent treatment.

The Fetal Cell Count™ Kit is, because of the unique detection method, a good product for special applications like patients with Thalassemia. Pregnant women with Thalassemia causing interference in KB test. With the Fetal Cell Count™ Kit the F-cells are easy distinguishable from the fRBCs (see figure 2).

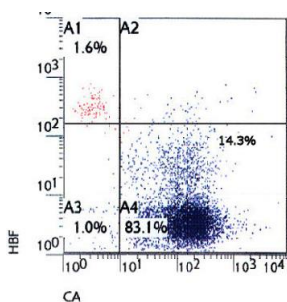


Figure 1: Results of the Fetal Cell Count™ Kit

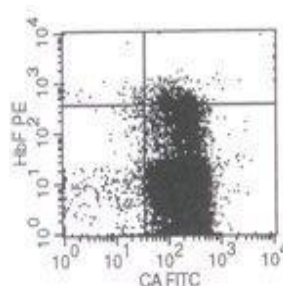


Figure 2: Example of result of a Thalassemia patient with use of the Fetal Cell Count™ Kit.

## FMH QuikQuant

Distributed for Trillium Diagnostics LLC, USA

The FMH QuikQuant is available for the flow cytometer platform.

The FMH QuikQuant uses an anti-Hemoglobin F (HbF) monoclonal antibody and Propidium Iodide reagent. The FMH QuikQuant is operative on all flow cytometers. With less than 20 minutes of technologist time needed, FMH QuikQuant is a two step wash technique requiring about 1 hour to complete. Figure 3 shows the results of the FMH QuikQuant by flow cytometer.

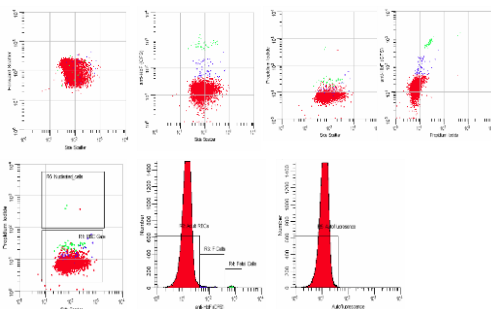


Figure 3: Results of the flow cytometer.

## FMH Kit

Distributed for IBGRL (Bristol) outside the UK.

By flow cytometry, BRAD 3 FITC can be used to do an accurate quantification of the number of RhD positive cells in a mixture of RhD positive and negative cells. Therefore FMH can be analyzed in a maternal blood sample when a RhD negative woman carries a RhD positive fetus. For optimal interpretation of the results the kit contains an anti-RhD antibody (BRAD 3) and a negative control antibody (AEVZ 5.3) both labeled with FITC. The FMH kit can only be used in case of rhesus incompatibility between mother and child.

Figure 4 shows the results of BRAD 3 FITC and AEVZ 5.3 FITC. The red histogram is AEVZ5.3 with negative cells. The blue histogram is BRAD 3 FITC with RhD positive cells.

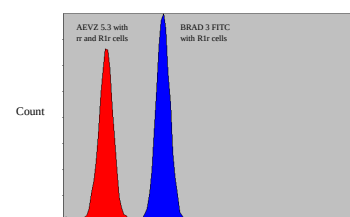


Figure 4: Results of BRAD3 FITC and AEVZ 5.3 FITC

## FETALtrol™ and FDA cleared

Distributed for Trillium Diagnostics LLC, USA.

The Fetal cell Count™ Kit, FMH Kit and FMH QuikQuant flow cytometric methods for detection of fetal cells offer a simple, reliable and more precise alternative to the KB manual technique for the assessment of Fetomaternal Hemorrhage. The method has additional potential applications for the study of HbF levels or frequency of adult red cells with low levels of HbF (F cells) in individuals with hemoglobinopathies. FETALtrol™ is a 3-level control set that can be used to validate and monitor the quality of both flow cytometric and Kleihauer-Betke manual procedures for the detection of FMH. Figure 5 shows the results of the level 3 FETALtrol™.

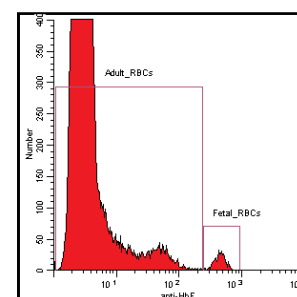


Figure 5: Results of the level 3 FETALtrol™

| Item                                                                                                                                                                                                                 | Description                                                                                           | Package size                        | Product code |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------|-------------------------------------|--------------|
| Fetal Cell Count™ Kit<br>                      | Complete assay for routine diagnosis of Fetomaternal Hemorrhage using anti-HbF and anti-CA.           | 25 tests                            | IQP-379      |
| FMH QuikQuant Flow Cytometry <sup>1</sup><br>  | Rapid assay for Fetomaternal Hemorrhage Quantification.                                               | 100 tests                           | QQF-100      |
| FMH Kit <sup>2</sup><br>                       | FITC conjugated Anti-RhD reagent for determination of Fetomaternal Hemorrhage.                        | 100 tests                           | 9447         |
| FETALtrol™ <sup>1</sup><br>  and FDA cleared   | Tri-level stabilized blood controls with known human fetal erythrocytes content in human adult blood. | 3 levels, two 2 mL vials each level | FH101        |
| FETALtrol™ <sup>1</sup><br>  and FDA cleared   | Tri-level stabilized blood controls with known human fetal erythrocytes content in human adult blood. | 3 levels, one 2 mL vial each level  | FH102        |

  In Vitro Diagnostic medical device. This product is registered as IVD in the countries belonging to the European Union.

<sup>1</sup> Distributed for Trillium Diagnostics LLC, USA

<sup>2</sup> Distributed for IBGRL (Bristol) outside the UK