



January 14, 2005

**UPDATE - URGENT PRODUCT RECALL NOTIFICATION**

**FETALSCREEN™ Product Code 780540**

**Lot FS451, Lot FS452 & Lot FS453**

Dear Blood Bank Medical Director:

This is a follow-up to our previous URGENT PRODUCT RECALL NOTIFICATION for FETALSCREEN™ Lots FS451, FS452, and/or FS453. Ortho-Clinical Diagnostics, Inc. (OCD) recently recalled these lots due to a possibility that tests performed with them could have produced false negative results in patient samples.

Until a root cause is identified and corrective actions instituted, we are unable to supply FETALSCREEN product. We cannot support the continued use of FETALSCREEN Lots FS451, FS452, and/or FS453. Please confirm that any and all packages of FETALSCREEN with these lot numbers have been removed from use.

**The attached communication should be immediately provided to any physician whose patient may have been tested with the affected lots.** It is intended to provide additional considerations for patient management. One option provided in the attached communication is to administer an additional dose of Rh Immune Globulin (RhIG) at no charge. Additional details regarding the remuneration for the additional RhIG dose will be provided in a subsequent communication.

***Please do the following:***

- Identify all Rh negative patients who delivered an Rh positive baby and had a negative test result with FETALSCREEN™ Lots FS451, FS452, and/or FS453. The table below indicates when these lots were distributed.

FETALSCREEN™ Product Code 780540		
Lot Number	Expiration Date	Shipping Dates
FS451	December 21, 2004	10/29/04 – 11/29/04
FS452	January 18, 2005	11/24/04 – 12/27/04
FS453	February 15, 2005	12/23/04 – 01/06/05

- Provide a copy of the attached communication and a list of potentially affected patients to their attending physicians. We have provided you with two copies of the communication for your physicians. If you require more, please make additional copies.
- If you haven't done so already, please return the Confirmation of Receipt form contained in the original communication (Ref. CL05-017).

If you have any questions concerning this package, please call Customer Technical Services at 1-800-421-3311 (Options 2, 1, 1).

Sincerely,

Donna N. Godward  
Vice President, Worldwide Quality, Regulatory,  
Compliance

Michael Waller, MD  
Vice President, Worldwide Clinical & Medical  
Affairs

Dear Physician:

**Re.: Possible false negative results with Ortho-Clinical Diagnostics (OCD)  
FETALSCREEN screening test for fetal-maternal hemorrhage**

Our records indicate that during the period from 30 October 2004 through 11 January 2005, you have ordered screening tests to identify significant fetal-maternal hemorrhage (FMH) in Rh negative mothers under your care who delivered Rh positive infants. As you know, the standard of care is to administer a 300µg dose of Rh Immune Globulin (RhIG) around week 28 to all pregnant Rh negative women and to administer a second dose of RhIG post partum to all Rh negative women who deliver Rh positive infants. A post partum dose of 300µg RhIG is indicated for prophylaxis against Rh alloimmunization from a fetal-maternal hemorrhage up to 30 mL whole blood (15 mL packed cells). In order to identify patients with an FMH volume greater than 30 mL whole blood (15 mL packed cells), we use a two-step approach to testing. The first level of testing involves a screening assay usually called the rosette test (most hospitals employ the FETALSCREEN test manufactured by OCD); the second level of testing involves a quantitative method usually the Kleihauer-Betke stain. In the event of a positive screening result, we follow up with the quantitative method to determine the FMH volume in excess of 30 mL and to define the additional dose of RhIG required for optimal protection from alloimmunization.

On January 8, 2005, OCD informed us of a recall of their screening test kit due to the possibility of false negative results. Consequently, it is possible that the test did not identify some patients who experienced FMH of greater than 30 mL whole blood (15 mL packed cells) as candidates for treatment with more than the usual post-partum RhIG dose of 300 µg.

Literature indicates that the risk of fetal-maternal hemorrhages greater than 30 mL (15 mL packed cells) is in the magnitude of less than 0.3%<sup>1,2</sup> in an unselected population at the time of delivery. Thus, patients who tested negative with one of the relevant testing lots are at a less than 0.3% risk of having received a suboptimal dose of RhIG because an FMH of greater than 30 mL went undetected.

From the literature, it is also known that the risk of Rh alloimmunization in a general population of Rh negative mothers with Rh positive infants is less than 20%,<sup>1,2</sup> and is reduced to 8% when an ABO incompatibility exists between mother and infant.<sup>1,3</sup> This low alloimmunization rate in an unselected and untreated population representing FMH volumes across the whole possible range indicates that the actual alloimmunization risk in patients who experienced FMH of greater than 30 mL whole blood (15 mL packed cells) who were treated with the full dose of RhIG at week 28 and with only 300µg of RhIG post partum is likely to be substantially below 100%. Based on this consideration, the overall risk of actually being sensitized due to a negative screening result for FMH and only receiving 300µg of RhIG after obstetrical delivery is likely to be substantially below 0.3% (< 30 per 10,000 patients).

Published data indicate that even in a population of Rh negative women who delivered Rh positive infants and were treated according to the current medical standard, the prevalence of Rh sensitization is 0.1%.<sup>4,5</sup> Thus, the possibility of existing Rh sensitization is present even when the appropriate dose of RhIG is administered. This should always be kept in mind when further pregnancies occur or are considered. Based on the considerations in this letter, the possibility of Rh alloimmunity is slightly increased in the patients who tested negative with one of the affected test kits.

Please explain the situation to affected patients and consider discussing the following information and options with them.

- When FMH in excess of 30 mL whole blood has occurred, investigators have postulated that additional RhIG could be administered with some benefit for up to 28 days after the event.<sup>1,2</sup> There is no known incremental risk of adverse drug effects associated with delayed administration of additional RhIG, but the actual benefit has not been tested or proven in prospective clinical studies. If affected patients who delivered within 28 days of receipt of this letter are informed of this information and desire to receive an additional dose of RhIG, we have arranged for cost of the drug product to be covered by our supplier.
- When concern for Rh alloimmunization exists, patients can be screened subsequently for formation of anti-D antibodies (Type and Screen). This screening should be performed no earlier than 6 months after receiving a dose of RhIG as the drug may cause the antibody screen to be positive and not accurately indicate the patient's immune status. If an anti-Rh<sub>o</sub> (D) antibody is identified, measures consistent with normal clinical management of patients at risk of Rh Hemolytic Disease of the Fetus/Newborn should be instituted. Patients with a negative antibody test should be made aware of the fact that they could be sensitized despite this test result, and that antibodies and related complications might nonetheless develop in a subsequent pregnancy involving an Rh positive fetus.
- Independent of considerations specific to this particular clinical situation, please continue informing, counseling and testing patients at risk of Rh alloimmunization consistent with usual clinical practice.

Please feel free to contact us or Ortho-Clinical Diagnostics (1-800-421-3311, Options 2,1,1) if you need further information or assistance.

#### References:

1. Bowman J. Thirty-five years of Rh prophylaxis. *Transfusion*. 2003;43:1661-1666.
2. Bowman JM. The prevention of Rh immunization. *Transfusion Medicine Reviews* 1988; Vol 2, No 3: 129-150.
3. Mollison PL., Engelfriet CP., Contreras M. *Blood Transfusion in Clinical Medicine*, 9th ed. Oxford; Blackwell Scientific Publications; 552, 557; 1993.
4. Bowman JM. Antenatal suppression of Rh alloimmunization. *Clin Obstet Gynecol*. 1991 Jun;34(2):296-303.
5. Baskett TF., Parsons ML. Prevention of Rh(D) alloimmunization; a cost-benefit analysis. *CMAJ*. 1990 Feb 15;142(4):337-339.