URGENT FIELD SAFETY NOTICE

November 5th, 2014

Alere Determine HIV-1/2 Ag/Ab Combo
(7D2643, 7D2646, 7D2647)

[Click here and type the contact name]
[Click here and type the facility's name]
[Click here and type the mailing address]

Dear Valued Customer,

The purpose of this letter is to inform you of Alere Medical Co., Ltd.'s intention to update the 'Limitations of the Procedure' for Alere Determine HIV-1/2 Ag/Ab Combo (PN 7D2643, 7D2646, 7D2647). This action is being initiated as a result of Alere's post market surveillance activity. Specifically, negative results were obtained from a single sample in the EQA Ring Trial in Europe. This sample was taken from a 40 year old man with a 7 day history of fever, rash and fatigue and contained p24 antigen of a virus of subtype C at a concentration of 250 pg / mL (viral load of 2,500,000 copies / mL), corresponding to 50 IU / mL (WHO standard). A recent publication of a survey conducted in Swaziland also suggested that the antigen component of the Alere Determine HIV-1/2 Ag/Ab Combo test in a high-prevalence, high-incidence setting was unable to detect acute infection in this subtype C population (Yen T. Duong et al., J. Clin. Microbiol. 2014, 52(10):3743-3748).

Although there is published data demonstrating the ability of Determine HIV Combo to detect p24 antigen in HIV-1 subtype C viral cell culture supernatants (Beelart G. et al., J. Virol. Methods 168(2010) 218-222) others have reported a lack of detection of subtype C as well as other subtypes of lower prevalence (Vetter etal, PlosOne, October 2014). The product continues to be released to the market based on CTS criteria (2009/886/EC) for rapid HIV tests including the detection of 2 IU/ml of p24 antigen from the WHO international standard. However, external laboratories have failed to reproduce this analytical sensitivity (Beelart G. et al., J. Virol. Methods 168(2010) 218-222 , Vetter etal, PlosOne, October 2014). Based on the nature of this post market surveillance information, the following limitations **must** be considered **in addition** to those currently stated in the Instructions for Use (IFU) of the product:

- The test is designed to increase the HIV case load by improving the detection of HIV infections vs other rapid tests and 3rd generation ELISA. The sensitivity of the Determine HIV Combo is not equivalent to 4th generation HIV ELISA, p24 EIA or PCR, which will limit its ability to detect acute infections in comparison to those methods.
- Where clinical presentation or other data would suggest an inconsistent result then the patient should be tested by PCR and/or retested for antibodies to HIV >21 days after the original testing.

It is essential that users of the device follow all aspects of the IFU, but special attention must be given to the following summarised limitations listed in the Alere Determine HIV-1/2 Ag/Ab Combo IFU as our investigations have shown these may be a significant factor in the events observed.

- Alere Determine™ HIV-1/2 Ag/Ab Combo is designed to simultaneously detect antibodies to HIV-1 and/or HIV-2 and free non-immunocomplexed HIV-1 p24 antigen (Ag) in human serum, plasma and whole blood. Other body fluids or pooled specimens may not give accurate results and should not be used.

- A negative result for both antibodies to HIV and p24 antigen does not preclude the possibility of exposure to or infection with HIV-1 or HIV-2 viruses.
- A positive result for antibodies to HIV with a negative result for p24 antigen does not preclude the possibility of acute infection.
- No test provides absolute assurance that a specimen does not contain low levels of HIV-1 p24 antigen and/or antibodies to HIV-1 and HIV-2 such as those present at a very early stage of infection.

CUSTOMER/DISTRIBUTOR REQUIRED ACTION

- Review results obtained using the Alere Determine™ HIV-1/2 Ag/Ab Combo and repeat testing for any patients testing negative where clinical presentation or other data would suggest an inconsistent result. The patient should be tested by PCR and/or retested for antibodies to HIV >21 days after the original testing.
- Please share this FIELD SAFETY NOTIFICATION (FSN) with all Healthcare Providers receiving the product and maintain visibility of this FSN to them for a period of 2 months.
- If you have forwarded the product listed above to another laboratory, please provide a copy of this letter to them.
- Complete and FAX or email the enclosed Verification Form within 10 days to confirm your receipt of this notice. Only one Verification Form is required per facility.

Please FAX or e-mail the completed Reply Form to:

Alere Medical Co., Ltd.
Fax: xxxxxx
Email: xxxxxxxx

All relevant National Competent Authorities have been advised of this FSCA. Should you have any questions about the information contained in this notification, please contact:

Alere Product Support Care Centers

Region	Phone	E-Mail Address
Europe & Middle East	+44 (0) 161 483 9032	EMEproductsupport@alere.com
Asia Pacific	+ (61) 7 3363 7711	APproductsupport@alere.com
Africa, Russia & CIS	+ (972) 8 9429 683	ARCISproductsupport@alere.com
Latin America	+ (57) 2 661 8797	LAproductsupport@alere.com

Sincerely,

Aki Asahina
Quality System Manager
Alere Medical Co., Ltd.

Please complete this verification form even if you do not have any involved product and Fax Back to Technical Service at Fax Number xxxxxxxx or email to xxxxx@alere.com.

Customer/Distributor Verification Form
URGENT FIELD SAFETY NOTICE

We acknowledge receipt of the Alere Medical Co., Ltd, URGENT FIELD SAFETY NOTICE dated November 5th, 2014 for the following product:

- **Alere Determine HIV-1/2 Ag/Ab Combo (PN 7D2643, 7D2646, 7D2647). All lot numbers.**

Please check the appropriate boxes:

☐ I have no record of receipt of this product and therefore will take no further actions.

☐ I have read and understand the letter and will follow the recommended actions.

☐ I have forwarded this notification to our customers/consignees to which we have provided product.

DATE*: _____

AUTHORIZED SIGNATURE*: _____

PRINT NAME*: _____

TITLE: _____ DEPARTMENT: _____

FACILITY*: _____

ADDRESS*: _____

CITY*: _____ STATE*: _____ PHONE*: _____

POSTAL CODE*: _____ COUNTRY*: _____

EMAIL: _____

*** Mandatory field**

To satisfy global requirements for regulatory reporting, please complete and return this form within 10 business days of receipt to Technical Services at Fax Number xxxxxxxx or by email to xxxxxx@alere.com.