URGENT FIELD SAFETY NOTICE
IMMEDIATE ACTION REQUIRED

Ref No: TD FSN SBN-RTD-2018-002

Date: 13/08/2018

Type of Action: Field Safety Corrective Action (FSCA)

Product Affected: FLO-LOK III Dispenser

System Affected: BenchMark GX BenchMark XT BenchMark ULTRA

Software Version: All Software Versions

Product Name	GMMI Number	Expanded Affected Lots	Previously Communicated Lots
OptiView DAB IHC Detection Kit	06396500001	Y24225, Y25760, E00119	Y19271, Y11625, Y15571
ULTRAVIEW UNIVERSAL DAB DETECTION KIT	05269806001	Y22147, Y25695	Y09284, Y15384, Y18099, Y22153, Y11687, Y17984, Y19302, Y11716, Y18069
iView DAB Detection Kit	05266157001	Y24245	Y11834
ultraView SISH Detection Kit	05271967001	None	Y15133
OptiView Amplification Kit	06396518001	None	Y15435, Y19322, Y22447
OptiView Amplification Kit (250 Test)	06718663001	Y26282	Y19318
ultraView SISH DNP Detection Kit	05907136001	Y26299	Y17990
Hematoxylin II	05277965001	None	Y10759, Y13938, Y17402, Y17403, Y21312
ISH iVIEW Blue Plus Detection Kit	05266181001	Y15410, Y24365	
ANTI-PAN KERATIN Primary Antibody, 25mL	05266840001	Y21610	
ultraView Universal Alkaline Phosphatase Red Detection Kit	05269814001	Y15071, Y18053, Y22469	
ISH Protease 3	05273331001	Y13927, Y18872, Y22569, Y25883	
CONFIRM anti-Progesterone Receptor (PR) (1E2) Rabbit Monoclonal Primary Antibody	05278392001	Y12992, Y18852, Y23051	
CONFIRM anti-Estrogen Receptor (ER) (SP1) Rabbit Monoclonal Primary Antibody	05278414001	Y18586, Y24472	
VENTANA ISH iView Blue Detection Kit	05278511001	Y15105, Y22455	
INFORM HPV III Family 16 Probe (B)	05278856001	Y19417	
VENTANA anti-Helicobacter Pylori (SP48) Rabbit Monoclonal Primary Antibody	06425623001	Y24119	
CINtec p16 Histology (250) CE	06695256001	Y16507, Y23040	

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Summary of Issue

FLO-LOK III Dispenser Issues – Expanded Scope and Product List

Reason for Notice

Dear Valued Customer,

Our records indicate that you received one or more of the products or lots on the expanded affected lots referenced above.

If your laboratory is utilizing same-slide controls as a routine practice, or uses assays in which a biologic internal control is always present (e.g. HER2 Dual ISH) or works with internal biological controls (e.g. CINtec PLUS) this failure mode was detectable and no look back is required. The affected products on the list above should not be used for clinical testing.

If you do not use these controls, please follow the directions per this FSN.

Description of Situation

In December 2017, Roche Tissue Diagnostics (RTD) issued a Field Safety Notification (FSN) in response to escalated complaints of leaking and sticking reagent dispensers. Roche initially attributed this failure to inadequate application of silicone oil to critical parts in the Horseradish Peroxidase (HRP) and Hematoxylin II dispensers. At that time, Roche initiated a root cause investigation.

The investigation confirmed that inadequate application of oil was the root cause. This occurred as a result of a change in manufacturing when moving from manual assembly of the dispensers to a fully automated reagent dispenser assembly (FARDA). Further, the investigation determined that the problem was not restricted to HRP and Hem II dispensers.

Two additional contributing factors were also identified:

1. Products intended for greater than 50 actuations
2. Products with emulsifiers

These two contributing factors, when combined, exacerbate the issue and its occurrence in the market.

Some products that meet the above criteria were not added to the list because they have no medical impact, and do not present a risk to patient safety (e.g. Hematoxylin II, Bluing, and RUO/Discovery products).

The root cause and contributing factors are consistent with customer complaint data. Based on this investigation we are expanding the list of affected products and lots.

The dispenser issues described above could result in a complete or partial dispense failure of a reagent critical to the staining reaction. This in turn could result in light or absent staining which, discounting any mitigations (e.g. use of same-slide controls), could cause diagnostic confusion, delay in diagnosis, or a false negative diagnosis.
In the worst case, a diagnostic error such as a false negative companion diagnostic assay (e.g. HER2) could lead to delay in treatment or inappropriate treatment that, depending on the duration of the delay, could impact patient survival.

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Actions taken by Roche Diagnostics

At the time of the initial FSN, all affected product that was in inventory was placed on hold. Further, in January 2018 RTD returned to previously established manual assembly of all dispensers.

RTD is now expanding the list of FARDA built affected products to include dispensers containing emulsifiers and those delivering over 50 actuations. Products in 50 actuation configurations, and those in any size without the presence of an emulsifier are not included in this expanded list.

RTD would like to emphasize the importance of following the instructions described in this letter in order to avoid and identify potentially erroneous results.

Action Required

Actions to be taken by the customer/user

Customers should first determine if their laboratory has any affected product lots in inventory based on the "Expanded Affected Lots" column present in this notification. **If an affected product is found, it should not be used for clinical testing.** In addition, should you have any remaining dispensers from lots listed in the "Previously Communicated Lots" column, you must not use them for clinical testing. The initial FSN required the use of same slide controls if affected product was to be used. This is because we did not have sufficient inventory of replacement product at that time. Newly manufactured products from the affected list are now readily available and should be used in place of affected product lots.

In the interest of patient safety and to identify potential diagnostic errors resulting from prior use of affected dispensers, Roche recommends a retrospective review and re-testing (if applicable) of clinical cases involving a dispenser included in the "Expanded Affected lots" column and in accordance with local hospital/laboratory procedures and policies. The ultimate scope of the re-testing is at the medical discretion of each laboratory, but should include at a minimum those assays used as the sole determinant for patient therapy or decision-making (e.g. HER2, ER/PR, ALK, PD-L1 (SP142), PD-L1(SP263) and C-Kit(9.7)).

Review/re-testing is <u>not necessary</u> for:

1) **laboratories utilizing same-slide controls as routine practice**
2) **assays in which a biologic internal control is always present (e.g. HER2 Dual ISH)**
3) **individual cases containing internal biologic controls**
4) **individual cases that were already re-tested in association with the original RTD field notification and re-testing recommendation (TD FSN-RTD-2017-001).**

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Please complete and return the Acknowledgement Form which accompanies this Field Safety Notice by **27th of August 2018.**

Please bring this notice to the attention of all personnel in your hospital or Health Care facility who need to be aware of this safety issue.

If you have forwarded the affected product(s) listed above to another laboratory, please provide a copy of this notice to them.

Attachments TD FSN SBN-RTD-2018-002 Acknowledgement Form

This action is being conducted with the knowledge of the Medicines and Healthcare Products Regulatory Agency (MHRA), the Health Products Regulatory Authority (HPRA), and other International Regulatory Agencies.

Roche Diagnostics operates a vigilance system that complies with the IVD Directive 98/79 EC

A copy of this notice can also be found on the Roche Dialog Portal

If you require any further information please contact our

Technical Support Hotline

UK: 0808 100 19 20
Ireland: 1800 40 95 64

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