Field Safety Notice

SBN-RTD-2017-001

RTD / Reagents
Version 5
02-Jul-2018

Dispenser Issues with Hematoxylin II and Horseradish Peroxidase reagents

Product Name	GMMI	Lot No.
OptiView DAB IHC Detection Kit	06396500001	See Below
ultraView DAB IHC Detection Kit	05269806001	See Below
iView DAB IHC Detection Kit	05266157001	See Below
ultraView SISH DNP Detection Kit US	05572037001	See Below
CINtec PLUS Cytology Kit (CE-IVD)	06889565001	See Below
CINtec PLUS Cytology Kit (Canada/Japan)	06889549001	See Below
OptiView Amplification Kit	06396518001	See Below
OptiView Amplification Kit (250 Test)	06718663001	See Below
Hematoxylin II	05277965001	See Below
ultraView SISH DNP Detection Kit	05907136001	See Below
NEXES VEN IVIEW DAB DET KT JPN-US EXPORT	05266084001	See Below

Production Identifier (Lot No./Serial No.)

Product Name:	Roche DMS:	Lot(s):
OptiView DAB IHC Detection Kit	06396500001	Y11625 Y15571 Y19271
*ultra*View Universal DAB Detection Kit	05269806001	Y09284 Y18099 Y11687 Y18069 Y11716 Y19302 Y15384 Y22153 Y17984
*i*View DAB Detection Kit	05266157001	Y11834 No affected lot in Singapore
ultraView SISH DNP Detection Kit US	05572037001	Y15146 No affected product in Singapore
CINtec *PLUS* Cytology Kit (CE-IVD)	06889565001	Y14122 Y18107 No affected lot in Singapore

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CINtec *PLUS* Cytology (Canada/Japan)	06889549001	Y22162 Y15546 No affected product in Singapore
OptiView Amplification Kit	06396518001	Y15435 Y19322 Y22447
OptiView Amplification Kit (250 Test)	06718663001	Y19318 No affected product in Singapore
Hematoxylin II	05277965001	Y10759 Y13938 Y17402 Y17403 Y21312
*ultra*View SISH DNP Detection Kit	05907136001	Y17990 No affected lot in Singapore
NEXES VEN IVIEW DAB DET KT JPN-US EXPORT	05266084001	Y15392 No affected product in Singapore

Type of Action Field Safety Corrective Action

Dear Valued Customer,

Ventana Medical Systems, Inc. (also known as Roche Tissue Diagnostics (RTD) outside the US) has reworked five lots of reagent dispensers (referenced in the table below) that were originally included in the list of affected products above. The lots in the table below remained in Roche control and were not distributed previously to customers. Therefore they have been removed from the list of affected product above. All lots have been reworked using a validated procedure and passed final acceptance testing prior to shipping to customers.

Customers can use the lots in table below. RTD always recommends the use of same slide controls.

Product Name:	**Roche DMS:**	**Lot(s):**	**Availability**
iView DAB Detection Kit	05266157001	Y24245	Global
ultraView Universal DAB Detection Kit	05269806001	Y22147	RDG (Mannheim) served customers only. See attached list of countries.
OptiView DAB IHC Detection Kit	06396500001	Y24225	RDG (Mannheim) served customers only. See attached list of countries.
Hematoxylin II	05277965001	Y22561	RDG (Mannheim) served customers only. See attached list of countries.
*ultra*View SISH Detection Kit	05271967001	Y15133	Global

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We would like to emphasize the importance of following the instructions described in this letter in order to avoid potentially erroneous results. In the worst case, this failure mode could result in a complete or partial dispense failure of a reagent critical to the staining reaction (e.g. ultraView or OptiView HRP). This in turn could result in light or absent staining, which, discounting any mitigations (see below), could have the following health consequences:

Immediate: Diagnostic confusion leading to delay in diagnosis or in the worst case, false negative staining could lead to a false negative diagnosis.

Long Range: 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.

Description of Situation

Ventana Medical Systems, Inc. (Ventana, also known as Roche Tissue Diagnostics (RTD) outside the US) has received increased customer complaints reporting leaking and sticking reagent dispensers. These reports are currently focused on horseradish peroxidase (HRP) dispensers (part of the iView, ultraView and OptiView detection kits, as well as CINtec *PLUS* Cytology Kit) and with Hematoxylin II. Ventana has identified the cause of the issue, and is working to correct it. Additionally, Ventana has mandated specific requirements for same slide controls, detailed below, for customers with affected product in inventory.

Actions taken by Roche Diagnostics

All affected product has been placed on hold. Ventana has reworked all product in its inventory and is in the process of manufacturing new lots for distribution and replacement of customer affected kits. Customers will be notified when corrected product is available.

Actions to be taken by the customer/user

Affected kits may continue to be used by customers until corrected product is available, however Ventana is mandating that the affected IHC detection kits (iView, ultraView, OptiView) must only be used in conjunction with same-slide controls. These controls must be appropriate for each assay and capable of detecting false negative results due to a complete or partial reagent dispense failure.

For assays that directly relate to clinical therapy decision making (e.g. ER/PR, HER2, ALK, etc.), it is additionally important to select a same slide positive control tissue with sufficient sensitivity to detect small decreases in intensity that may cause borderline positive cases to appear as negative (e.g. HER2 2+ vs. 1+).

For Hematoxylin II, if the slide fails to receive hematoxylin, it should either be repeated or counterstained manually.

CINtec *PLUS* Cytology does not have the capacity for same slide controls, continue to use system-level

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controls as directed in the Package Insert. Ventana recommends that for p16/Ki-67 Dual-stain negative cases, customers evaluate slides for signs of specific DAB staining of cells, such as the staining of metaplastic cells. This will ensure that the DAB detection chemistry was properly dispensed. In cases where there is no specific brown DAB staining observed, and there are morphologic features suggesting moderate to severe dysplasia in cells showing specific red nuclear staining for Ki-67, customers should retest the specimens that may be potentially false negative as a result of a dispenser malfunction. In order to reduce the risk of this issue impacting patient care, customers should follow their local procedures and policies regarding retrospective re-testing, applying the guidance above. Any re-testing should be limited to assays performed with the affected lots. ultraView SISH Detection is used for HER2 analysis, and employs internal positive controls; no external control is required.

Although the use of same slide controls is considered optimal laboratory practice and strongly recommended by Ventana, customers may revert to standard run controls once non-impacted product is received.

In order to reduce the risk of this issue impacting patient care, customers not using same slide controls as a standard practice should follow their local procedures and policies regarding retrospective retesting, especially for IHC assays and cases that do not contain a biologic internal control. Any retesting should be limited to assays performed with the affected lots.

Communication of this Field Safety Notice

This notice must be passed on to all those who need to be aware within your organization or to any other organization/individual where the potentially affected devices have been distributed/supplied. Please pass on this notice to the Chairman Medical Board and Head of Department as well, as required by HSA.

Please maintain awareness of this notice and resulting action for an appropriate period to ensure the effectiveness of the corrective action

We apologize for any inconvenience this may cause and hope for your understanding and your support.

Sincerely,

Roche Diagnostics Asia Pacific Pte Ltd

Email: sg.regulatory@roche.com

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Appendix A – Countries receiving product from Roche Mannheim Distribution Center

Albania
Algeria
Armenia
Austria
Azerbaijan
Bahrain
Belarus
Belgium
Bosnia-Herzegovina
Bulgaria
Croatia/
Cyprus
Czech Republic
Denmark
Egypt
Eritrea
Estonia (Baltics)
Ethiopia
Finland
France
Georgia
Germany
Ghana
Greece
Hungary
Hungary
Hungary
Iceland
Iran
Iraq
Ireland
Israel
Italy
Jordan
Kazakhstan
Kenya
Kosovo
Kuwait
Kyrgyzstan
Latvia
Lebanon
Libya
Lithuania
Luxemburg
Macedonia
Maldives
Malta
Mauritius
Moldova
Mongolia
Montenegro
Morocco
Mozambique
Netherlands
Nigeria
Norway
Oman
Palestine
Poland
Portugal
Qatar
Romania
Russia
Rwanda
Saudi Arabia
Serbia,
Slovakia
Slovenia
South Africa
Spain
Sudan
Sweden
Switzerland
Syria
Tajikistan
Tanzania
Tunisia
Turkey
Turkmenistan
UAE
Uganda
Ukraine
United Kingdom
Uzbekistan
Yemen
Zambia

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