For the attention of the Head of Laboratory

Reference: RIS-19-0037

FIELD SAFETY NOTICE

Emicizumab medicine and factor VIII assays on Stago instruments

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Dear Customer,

According to our lot traceability records, you are using the STA - Deficient VIII (ref. 00725) or STA - ImmunoDef VIII (ref. 00728) reagent. This Field Safety Notice (FSN) is about a potential risk of contamination by Emicizumab - of factor VIII assays on the following Stago instruments : STA® Compact, STA® Compact Max, STA-R® Evolution or STA-R® Max.

✓ Description:

The Emicizumab medicine (trade name Hemlibra®), used for hemophilia A treatment, has recently entered the market. According to the manufacturer, “laboratory tests based on the extrinsic coagulation pathway should not be performed on patient samples that contain Emicizumab, either for the substitution factor assay, anticoagulant factor assay or to titrate for anti-factor VIII inhibitors".

Diagnostica Stago has detected there is a risk of sample to sample carry-over of this molecule on Stago instruments, and, has assessed this contamination impact on coagulation tests.
A risk has been identified in the case of factor VIII assay on hemophilia A patients. If factor VIII assays are performed following a sample that contains Emicizumab, the factor VIII results may be affected. In this case, the clotting times will be shortened, and the factor VIII levels will falsely increase.
For other coagulation tests, impact is negligible (others factors, lupus, APC-R …).

✓ Actions:

To remove this contamination risk, a special wash has been developed for the concerned Stago methodology. It involves special washing of needle 1 before every factor VIII assay in order to eliminate any residual quantities of Emicizumab.

This pre-wash feature has been implemented and activated in the following software versions:

- STA-R® Max: from version 4.05.04 with an update of factor VIII methodology (from MS217 or a specific MU)
- STA-R® Evolution with serial number higher than 8012756 : from version 3.04.09
- STA® Compact Max: from version 110.05 (included in 110.06)

You will find in Appendix 1 details of this new functionality for the instrument(s) installed in your laboratory.

Pending update of this new functionality which needs to be completed by your Stago representative Factor VIII assays should be closely monitored. Patients samples treated with Emicizumab must be identified and isolated, and, Factor VIII assays of other patients samples must be carried out separately in order to avoid contamination.

According to our risk analysis regarding Emicizumab contamination, the most critical clinical case would be a factor VIII assay on a hemophiliac A patient preceded by testing on a patient sample treated by this new medicine. The probability of this combination of tests is estimated to be very low. As a consequence of patient results being interpreted in a global clinical and biological context, along with the low probability of this sequence of testing it is unlikely this defect could have resulted in an

adverse patient event. Therefore, it is not necessary for previous patient results reported to be reassessed.

Please return to us, by fax or by e-mail, the completed enclosed form confirming that you have read this letter and will apply the instructions.

The Competent Administrative Authority of the country of origin (France) has been informed.

Please accept our apologies for this inconvenience. We thank you in advance for your support.

For additional information, please contact us.

Yours sincerely,

FIELD SAFETY NOTICE

APPENDIX 1:
NEW PRE-WASH FEATURE
FOR FACTOR VIII ASSAYS

There are cases for which the special wash is not activated and have to be:

STA-R® MAX from version 4.05.04:

- When using the factor VIII Stago methodology if it was not updated from MS217
- When creating and using Factor VIII User Test
- When using low curve Factor VIII Stago methodology

STA-R® EVOLUTION (with serial number higher than 8012756) from version 3.04.09:

- When copying Factor VIII Stago methodology
- When creating and using Factor VIII User methodology
- When using low curve Factor VIII Stago methodology

STA® COMPACT MAX from version 110.05:

- When copying Factor VIII Stago methodology
- When creating and using Factor VIII User methodology
- When using low curve Factor VIII Stago methodology

Stago representative intervention is required to install these versions and activate this functionality in the cases described above.

STA-R® Evolution with serial number equal or below than 8012756 and STA® Compact will not benefit from this correction.
Consequently, if you have one of these instruments and if you performed Factor VIII assays, you must pay particular attention to it.
Therefore, you need to identify and isolate patients samples treated with the molecule and carry out testing separately from other patients samples Factor VIII assays in order to avoid contamination.