Urgent Field Safety Notice

FSCA 2004

FSN 2020-002

August, 2020

Title: Potential risk of sample contamination by Emicizumab medicine on Sysmex Automated Blood Coagulation Analyzers

Product Name	CN-6000, CN-3000, CS-5100, CS-2000i, CS-2100i, CS-2400, CS-2500, CS-1600, CS-1300, CA-510, CA-520, CA-530, CA-540, CA-550, CA-560, CA-620, CA-650, CA-660, CA-1500, CA-7000, CA-8000
Product Description	Sysmex Automated Blood Coagulation Analyzer
Production Identifier (Lot No./Serial No.)	ALL
Type of Action	Advice given by manufacturer regarding use of the IVD

IMPORTANT NOTE: This Field Safety Notice (FSN) informs about a potential risk of contamination of factor VIII assays by Emicizumab medicine.

Dear Valued Customer,

This Field Safety Notice (FSN) is to inform about a potential risk of sample contamination by Emicizumab from a sample containing this drug to the next sample analyzed on one of the Sysmex Automated Blood Coagulation Analyzers listed in the table above.

Description of Situation

The Emicizumab medicine (trade name Hemlibra®) is used in the treatment for hemophilia A. Sysmex confirmed the potential risk of Emicizumab contamination from sample to sample and has assessed the impact of this contamination on coagulation tests performed on Sysmex Automated Blood Coagulation Analyzers.

Risk to Health

Hemophilia is classified according to the clinical severity as mild, moderate or severe based on the FVIII% activity in patient.
There is a possibility of making wrong clinical decisions for treatment of hemophilia patients because of Emicizumab carryover contamination of FVIII clotting and FVIII chromogenic assays. Emicizumab contamination may increase the FVIII% activity level and can lead to a change in the clinical severity from severe to moderate.

There is also a risk of data deviation in the case of the APTT and ProC global assay analysis following a sample that contains Emicizumab. The clotting times of these assays will be shortened but the clinical impact is deemed as negligible.

Other assay analyses are not affected, or the clinical impact is negligible.

Actions taken by Sysmex

To mitigate this contamination risk due to Emicizumab carryover, additional cleaning steps with CA CLEAN I and respectively CN-COAGWASHER are added to the affected analyzer FVIII assay protocols. Sysmex will take immediate action to update concerned FVIII assay protocols for CS series and CN series analyzers. For CA series analyzers a manual change of the protocol settings is required.

Actions to be taken by the customer

1. Please distribute this Urgent Field Safety Notice to all responsible persons within your organization.
2. When possible, please identify and separate samples of patients treated with Emicizumab from other patient samples for assay analysis. It is recommended to perform a rinse probe function after analysis of sample potentially containing remainders of Emicizumab. Affected assays of other patient samples should be carried out separately to prevent contamination with Emicizumab .
3. If the action as described above under point 2 is not acceptable, the assay protocol will be updated into the concerned instruments upon customer request. If the protocol update is applied, the additional cleaning steps will impact the analysis throughput specifications. Please see separate reference document for more details.
   Please return the Acknowledgement of Receipt (AoR) with your signature by the end of September 2020 if you require the assay protocol to be updated on your affected CS series, CN series and/or CA series analyzers, then our local service representatives will respond to your request.

   Please note:
   - The ProC global assay will be updated after Siemens validates the protocol because this is a Siemens application. The release date of the updated protocol disk will be determined later.
   - The protocol update does not apply to CA-1500, CA-7000 and CA-8000 because the assay protocol settings on these instruments have no sequence to add the cleaning solution before the assay analysis. Therefore, solution #2 is the only option for CA-1500, CA-7000 and CA-8000 users.

We deeply apologize for any inconvenience that this situation has caused and thank you for your patience and continued support.

Sincerely yours

Sysmex Corporation

Y. Ueda

Name: Yoshiro Ueda

Vice President / Regulatory Affairs & Quality Assurance (in case of safety issue, Safety Officer)

Urgent Field Safety Notice

FSCA 2004

FSN 2020-002

August, 2020

Title: Potential risk of sample contamination by Emicizumab medicine on Sysmex Automated Blood Coagulation Analyzers

Product Name	CS-5100, CS-2000i, CS-2100i, CS-2500, CA-500 series, CA-600 series, CA-1500, CA-7000
Product Description	Sysmex Automated Blood Coagulation Analyzer
Production Identifier (Lot No./Serial No.)	ALL
Type of Action	Advice given by manufacturer regarding use of the IVD

IMPORTANT NOTE: This Field Safety Notice (FSN) informs about a potential risk of contamination of factor VIII assays by Emicizumab medicine.

Dear Valued Customer,

This Field Safety Notice (FSN) is to inform about a potential risk of sample contamination by Emicizumab from a sample containing this drug to the next sample analyzed on one of the Sysmex Automated Blood Coagulation Analyzers listed in the table above.

Description of Situation

The Emicizumab medicine (trade name Hemlibra®) is used in the treatment for hemophilia A. Sysmex confirmed a potential risk of Emicizumab contamination from sample to sample and has assessed the impact of this contamination on coagulation tests performed on Sysmex Automated Blood Coagulation Analyzers.

Risk to Health

Hemophilia is classified according to the clinical severity as mild, moderate or severe based on the FVIII% activity in patient.

There is a possibility of making wrong clinical decisions for treatment of hemophilia patients because of Emicizumab carryover contamination of FVIII clotting and FVIII chromogenic assays (human factor based only). Emicizumab contamination may increase the FVIII% activity level and can lead to a change in the clinical severity from severe to moderate.

There is also a risk of data deviation in the case of the APTT and ProC global assay analysis with Factor V Deficient Plasma following a sample that contains Emicizumab. The clotting times of these assays may be shortened but the clinical impact is deemed as negligible.

Other assay analyses are not affected, or the clinical impact is negligible.

Actions taken by Sysmex

To mitigate this contamination risk due to Emicizumab carryover, additional cleaning steps with CA CLEAN I are added to the affected analyzer FVIII assay protocols. Sysmex will take immediate action to update concerned FVIII assay protocols for CS series analyzers. For CA series analyzers a manual change of the protocol settings is required.

Actions to be taken by the customer

1. Please distribute this Urgent Field Safety Notice to all responsible persons within your organization.
2. When possible, please identify and separate samples of patients treated with Emicizumab from other patient samples for assay analysis. It is recommended to perform a rinse probe function after analysis of samples potentially containing remainders of Emicizumab. Affected Factor VIII assays of other patient samples should be carried out separately to prevent contamination with Emicizumab(batch mode for Factor VIII assays).
3. If the action as described above under point 2 is not acceptable, the assay protocol will be updated into the concerned instruments upon customer request. If the protocol update is applied, the additional cleaning steps will impact the analysis throughput specifications. Please return the AOR with your signature to your local service representatives that will respond to your request. If you require the assay protocol to be updated on your affected CS series and/or CA series analyzers, our local service representatives will respond to your request.

   Please note:
   - The ProC global assay with Factor V Deficient Plasma will be updated after Siemens validates the protocol because this is a Siemens application. The release date of the updated protocol disk will be determined later as a facultative measure.
   - The protocol update does not apply to CA-1500and CA-7000 because the assay protocol settings on these instruments have no sequence to add the cleaning solution before the assay analysis. Therefore, solution #2 is the only option for CA-1500 and CA-7000 users.

We deeply apologize for any inconvenience that this situation has caused and thank you for your patience and continued support.

Sincerely yours

Sysmex Corporation

Name: Yoshiro Ueda

Vice President / Regulatory Affairs & Quality Assurance (in case of safety issue, Safety Officer)