February, 2014

FIELD SAFETY NOTICE (FSN)

Important Information on Fully Automated Blood Coagulation Analyzer **CS-Series**

Dear Valued Sysmex Customers,

This letter is to inform you about erroneous Factor VIII result which has occurred recently with our product, Fully Automated Blood Coagulation Analyzer **CS-Series** in conjunction with **Siemens Factor VIII chromogenic assay** (B4238).

A result of 26% for FVIII (using Chromogenic Factor VIII assay (B4238)) was questioned due to the patient being a known severe Haemophiliac under Kogenate treatment and the sample was a 72 hour trough level, therefore expected result was <0,01 IU/ml. The repeat result was given as a "no linearity" flag. Assay Protocol, which was adjusted by the customer, Calibration curve and QC were all as expected.

Result for the 26% value curve appeared flat however when zoomed in it showed a curve anomaly. No associated analyser flags were produced by the analyser to suggest abnormality. QCs and further samples were reproducible.

1. Facilities concerned

   a) Facilities which use Fully Automated Blood Coagulation Analyzer **CS-2000i/CS-2100i** with Sysmex software versions 00-61 until 00-65 and SIEMENS software versions 01-57 until 01-65.

   b) Facilities which use Fully Automated Blood Coagulation Analyzer **CS-5100** with Sysmex software versions 00-09 until 00-11 SIEMENS software versions 01-07 until 01-10

2. Phenomenon and root cause

   Irregular curves as phenomenon and associated root cause is most probably the missing algorithm sensitivity to produce flags in such cases in addition with a potential reagent stability issue.

3. Workaround (Immediate Correction)

   Until the corrective actions are available, please take a precaution by carry out the following instructions:

   Run all FVIII Chromogenic assays in duplicate and confirm result in conjunction with the patients' clinical history

4. Countermeasure (Permanent Corrective Action)

   The software improvement is expected in middle 2014. After evaluation together with SIEMENS we will release it in autumn 2014.

5. Look back statement:

Sysmex does not recommend a look back of previously generated results since the coagulation status changes over the time, and does recommend that this communication is reviewed with the laboratory medical director.

If you have any question, please feel free to contact to your local representative.

Please distribute this information to all appropriate personnel in your laboratory, retain a copy in your files and forward this information to all parties that may use this product.

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

Sincerely yours

Sysmex Europe GmbH

Thomas Kröger
Safety Officer

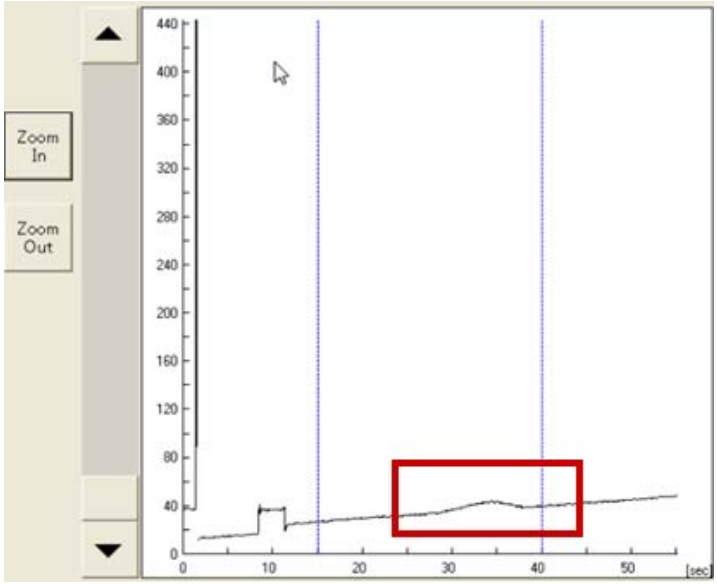
Norderstedt, 26th February 2014

Q&A

This Q & A document is to clarify open questions regarding the switch to double determination for Siemens Factor VIII chromogenic assay (B4238) on the Sysmex CS-2x00i and CS-5100 Systems. This step is necessary to identify erroneous Factor VIII results by detecting relative deviations in double determination.

Q1. What is the root cause for erroneous Factor VIII results?

A1. Erroneous Factor VIII results are caused by an unspecific increase in the evaluation window of the kinetic (bump). See Screenshot 1.



Screenshot 1: Critical kinetic with bump within evaluation window

Q2. What is the instruction to switch to double determination for F VIII chromogenic assay?

A3. The number of replications for analysis can be selected in the following way.

Login with user level "admin" to apply the modifications to the following sections of the assay group "Factor VIII chromogenic" (Management ID 6100):
Settings/Assay Group Settings
Tab "Basic" → "Analysis Condition" → "Replications" = **2**
Click the buttons "Save" and then "Close".
Shut down and restart the CS-software in order to make this change effective.

CS-2000i/CS-2100i: Please refer to chapter 8.8 – Basic settings in the "Software Guide" for a detailed description.
CS-5100: Please refer to chapter 3.5.7.1 in the "Instructions for Use" for a detailed description.

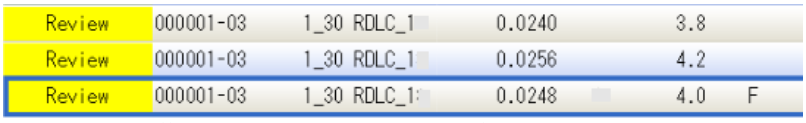
Q3. How will the customer be informed about a bigger deviation of the double determinations?

A3. We recommend activating the “Difference Limit Check” in the analyzer software.
The “Difference Limit Check” for analysis can be selected in the following way.

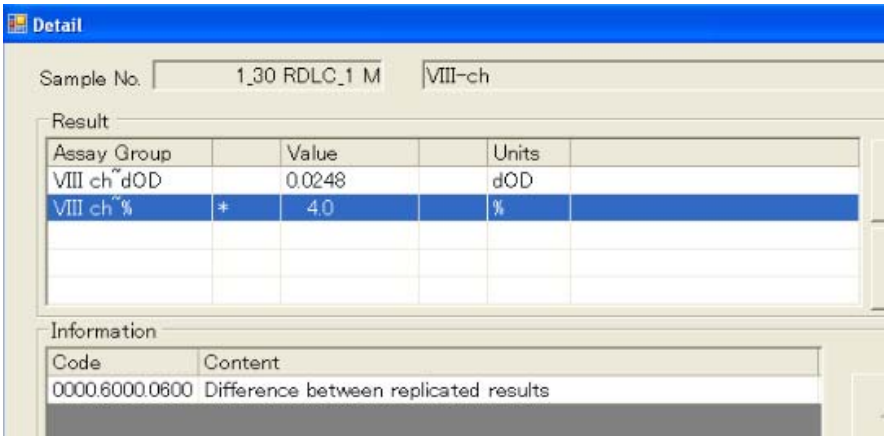
Login with user level "admin" to apply the modifications to the following sections of the assay group "Factor VIII chromogenic" (Management ID 6100):
Settings/Assay Group Settings
Tab "Basic" → Select the Assay Parameter "**VIII ch~%**" → “Edit” → Tab "Data Check"
→ Activate "Replication Difference Limit Check" → "Upper Limit" = **20%**
Click the buttons "Save" and then "Close".
Shut down and restart the CS-software in order to make this change effective.

CS-2000i/CS-2100i: Please refer to chapter 8.8 – Data Check settings in the “Software Guide” for a detailed description.
CS-5100: Please refer to chapter 3.5.7.3 in the “Instructions for Use” for a detailed description.

The customer will be informed about deviations afterwards, by a flagged result.
See the screenshots 2 & 3.



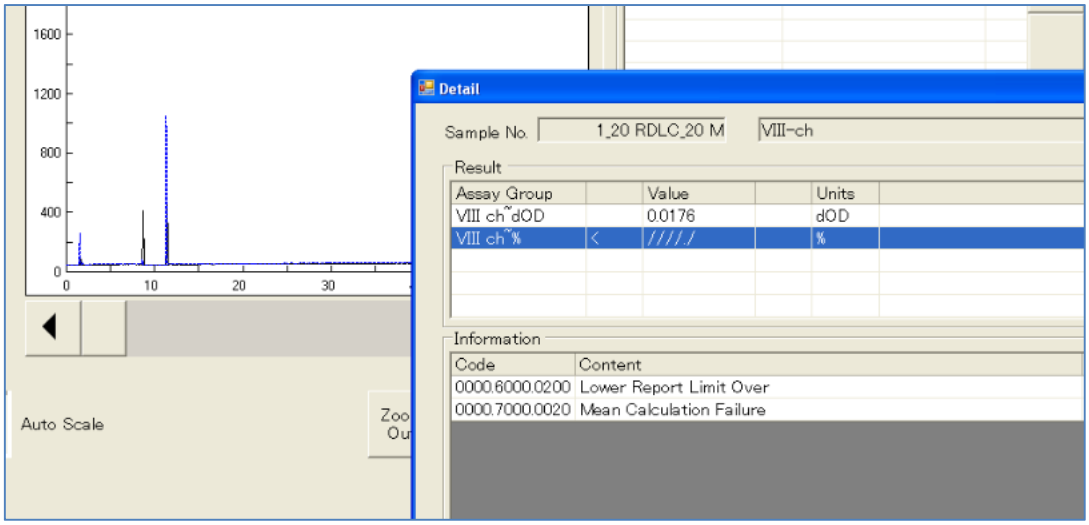
Screenshot 2: Difference Limit Check with Review flag



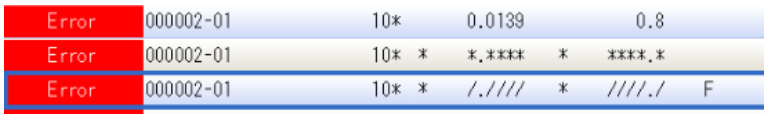
Screenshot 3: „Difference Limit Check“ detail message

Q4. What kind of result will be reported, when only one result of the double determination is valid?

A4. Double determinations with only one valid result will be marked with the review flag “Mean Calculation Failure”. The same review flag occurs when one result is out of the reportable limit. In such a case please repeat double determination for the affected sample.
See screenshots 4 and 5 for possible flag combinations.



Screenshot 4: Lower Report Limit over + Difference Limit Check triggered = Mean Calculation Failure



Screenshot 5: Double determination + “No Linearity Flag” = Flagged result with the red error message

Q5. Is it possible to create a reanalysis condition in case of “Difference Limit Check” or “Mean Calculation Failure” flag occurs?

A5. No, the software limitation does not allow an automatic reanalysis task for these errors.

Q6. Which relative deviation of the double determination is suitable for reliable detection of invalid kinetics without prompting unnecessary reanalysis?

A6. An upper replication criterion of 20% would trigger a flag by one implausible kinetic but not due to the assay/method inherent performance in terms of precision. This limit would ensure that anticipated assay/method variances will not trigger a flag, but at the same time significant deviations in the lower range will be flagged and thereby, misevaluations due a kinetic bump will be identified.

A calculation example of a low sample with 5% Factor VIII activity and a replication difference upper limit of 20 % → lowest acceptable deviation = 4%
→ highest acceptable deviation = 6%