Comparison of Technical Validation before and after Implementation of the Work Area Manager SIS 2.0 with Standard Rule Package

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Objectives: *To evaluate the work area manager "Sysmex Information System (SIS) 2.0 standard rules" for standardizing technical validation of the SYSMEX automated haematology analyser XE-2100 results in a medium sized hospital.*

Methods: *First we compared the validation time of the results (turn-around time, TAT) for 2 months before (previous validation) and 2 months after implementation (current validation) of the SIS standard rule package. The validation time is defined as "time of the results in laboratory information system (LIS)" minus "time of measurement in XE-2100". Then we compared the decisions made automatically in SIS with the decisions that were made with the previous validation criteria and we observed the quality of previous and current workflow actions and results. Finally we checked the satisfaction of the medical technologist employees after 3 months working with the SIS 2.0 standard rules work area manager.*

Results: *The validation time of the results was significantly ($p < 0.0001$) lower in the two months following introduction of the SIS 2.0 standard rules work area manager. There was a decrease in validation time with SIS which averaged 8.5 minutes for CBC (complete blood cell count) results and 37.7 minutes for CBC+DIFF (complete blood cell count plus leucocyte differential). Ninety-five percent (95%) of total validated samples were 27.8 minutes faster validated with SIS for CBC and 179.8 minutes for CBC+DIFF. The total decreased time per month with SIS was more then 700 hours for CBC and over 500 hours for CBC+DIFF. The total positive data checks and actions (repeat sample, nucleated red blood cell count, platelet optical count and smear) were clearly decreased to clinically relevant actions, with more specific information about the cause of the unreliable results. Only NRBC ADD (additional NRBC count) order was increased with the SIS rules. The quality of actions and results decided by SIS standard rules are in general at least as good as with the previous procedure. Shortly after SIS introduction acceptance of the SIS standard rules was very high. The SIS standard rules were found in general helpful both in night and day shifts, fast, safe and, most importantly, they were standardized.*

Conclusions: *The SIS software shows improvements in turn-around time (TAT) of validated results, and shows very user-friendly, standardized, specific positive results and actions with no loss of quality. It is interesting that very soon after introduction almost all laboratory technicians accepted the SIS software.*

We will continue our studies to suggest further improvements (NRBC rule) and adapt our parameters to satisfy our requirements.

(Sysmex J Int 15 : 7-12, 2005)

Key Words Work Area Manager SIS, Standard Rules, Technical Validation Criteria, Standardization, Automated Hematology Analyzer, XE-2100

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Received 6 Jan, 2005; Accepted 13 Jan, 2005

INTRODUCTION

The central haematology laboratory in Luzern services 700 beds with all major disciplines including cardiac surgery, oncology outpatients, radiotherapy and haematology. A total of about 100,000 complete blood cell counts (CBC) per year are performed, of which 15,000 include a leucocyte differential count (CBC+DIFF). Since January 2001 these CBC have been analysed using two SYSMEX XE-2100 automated haematology analysers (Sysmex Corporation, Kobe, Japan). Before installation of SIS (Sysmex Information System), the XE-2100 analysers communicated bi-directionally for all parameter combinations including CBC, leucocyte differential (DIFF), reticulocytes (RET) and nucleated red blood cells (NRBC) with the laboratory information system (LIS). The interpretation of graphics and numerical results was performed on the IPU (information processing unit) units of the XE-2100 systems and finally each parameter was manually validated in the LIS (previous validation workflow). ***Fig. 1*** shows the different validation filters with the previous validation workflow.

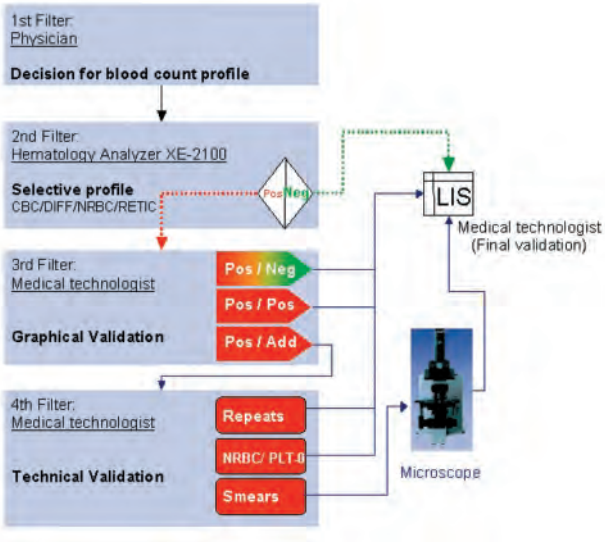

Fig. 1 *Previous validation workflow with the haematological analytical results passing through several filters (for explanation see text)*

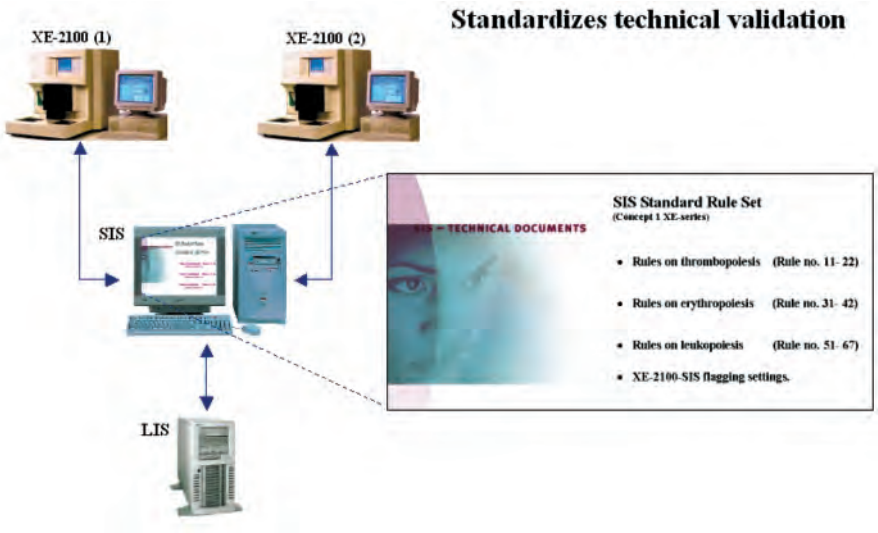

Fig. 2 *Current validation workflow pattern with SIS*

Filter 1 is the doctor at the bedside or in the outpatient clinic. Filter 2 is the haematology analyser (XE-2100) which decides between negative and positive specimens (based on abnormal numerical results and flags). Negative specimen results are reviewed and validated by the medical technologist in the LIS. Positive results are reviewed by Filter 3, the medical technologist, who proceeds on the basis of the numerical results, flags, graphics and previous results from the LIS. The interpretation of these positive results is undertaken by a medical technologist familiar with the system. The decision for a repeat sample analysis or additional tests such as NRBC (nucleated red blood cells) or PLT-O (optical platelet count) or smear depends on the expertise of the medical technologist. Filter 4 is the validation of these actions. Finally each parameter is manually validated in the LIS.

To increase the efficiency of technical validation in haematology is nowadays a great challenge which requires the centralized handling of huge amounts of information by standardized interpretation and decision.

MATERIALS

The work area manager SIS is a clinical laboratory information system which operates on a Windows platform, and has the scalability to interface multiple analysers to one connection to the LIS. The SIS can support major clinical disciplines such as haematology, coagulation and urine analysis. ***Fig. 2*** shows the configuration of the haematology workflow with SIS.

The SIS downloads all patient requisitions from the LIS and communicates bi-directionally with the two XE-2100 analysers. The intelligent solution for the first filter (***Fig. 1***) is the order-oriented real time data check. With this check it is possible to cancel or add orders (ADD order) with patient information, before analysing the data. A result-oriented real time data check is used after receiving the results (filters 3 and 4) to handle the technical validation using standardized, recommended Sysmex rules.
These consist of 42 rules (36 standardized rules and 6 customized rules). The structure of the rule set is divided into:

- Rules on thrombopoiesis:
  12 rules handle the problem of giant platelets, PLT clumps,RBC fragments, extreme RBC microcytosis, aspiration and mixing problems.
  Actions are:
  Add order for PLT-O, smear or repeat sample.
- Rules on erythropoiesis:
  12 rules handle the problem of NRBC, RBC fragments, RBC agglutination, high levels of lipids or plasma proteins, high WBC or non-lysed RBC.
  Actions are:
  Add order for NRBC count, smear or repeat sample.
- Rules on leucopoiesis:
  18 rules decide when a smear should be made or when a WBC value needs to be repeated.
  Actions are:
  Add order for smear or repeat sample.

The work area manager SIS with standard rules software simulates the knowledge of the expert for technical validation of the haematology reports. With the evaluation of this SIS standard rule packet, we want to increase the efficiency of the technical validation, regardless of who analyses the blood count, during routine daytime procedures or during a night shift.
We compared the previous LIS validation workflow (***Fig. 1***) with the current SIS validation workflow (***Fig. 2***) based on:

- TAT (turn-around time) of the validated results over periods of 2 months,
- total of positive data check results and subsequent actions, e.g. NRBC, PLT-O, repeats and smears, during a 2-month period,
- observation of the quality of previous and current workflow actions and results during a 2-week period,
- acceptance of SIS by medical technologists.

METHODS

The TAT of the validated results was calculated for two months using the previous validation workflow and 2 months with the SIS validation workflow. The TAT is defined as the time of validated result release in the LIS minus the time of measuring the blood sample on the XE-2100 analysers.

With the previous validation workflow, the final validation and release of results was done using the LIS. After SIS implementation the final validation and result release was decided by the SIS and reported to the LIS as released results. The delay in the network from XE-2100 to LIS or from XE-2100 to SIS/LIS was less than 1 second.

Over of a period of 2 months after SIS implementation we compared the total positive data check and subsequent actions decided by the SIS rules with the total positive data check and subsequent actions before implementation of SIS. The results are split up for thrombopoiesis, erythropoiesis and leucopoiesis.

Over a period of 2 weeks (3,500 samples) we compared the quality of previous and current workflow.

Finally, after 3 months of using the SIS with standard rules, 14 staff members completed a questionnaire on improvement of workflow, validation, user friendliness and general satisfaction.

STATISTICAL ANALYSIS

The TAT of the different validation workflows were analysed using Student's t-Test for independent samples with Statistica for Windows Version 6 [1]. In general, $p < 0.05$ was considered statistically significant.

RESULTS

Comparison of TAT technical validation for previous and current (SIS) workflows

The TATs were calculated during 2 separate months with the previous and current SIS validation workflows.

The previous technical validation was done for all parameters in the LIS. In total 10,977 CBC and 1,828 CBC+DIFF were processed. The number of unvalidated samples and validation times of the previous workflow are shown in figure 3. The mean TAT for the previous technical validation was 9.3 minutes for CBC and 41 minutes for CBC+DIFF. 95% of all CBC samples were validated after 28 minutes and after 3h for CBC+DIFF.

In the SIS technical validation workflow with standard rules implementation, the validation filter in the LIS was turned off, and SIS set on auto validation, only data check failed (positive rule) results not being autovalidated. In total 12,572 CBC and 1,859 CBC+DIFF were processed. The number of unvalidated samples and validation times of the current SIS workflow are also shown in ***Fig. 3***. The mean TAT for the current SIS technical validation was 0.8 minutes for CBC and 3.3 minutes for CBC+DIFF. 95% of all samples were validated after 0.2 minutes. We did not compare with the manual WBC differentials. We use our own laboratory software to handle the manual differentials and not the SIS diff pad feature.

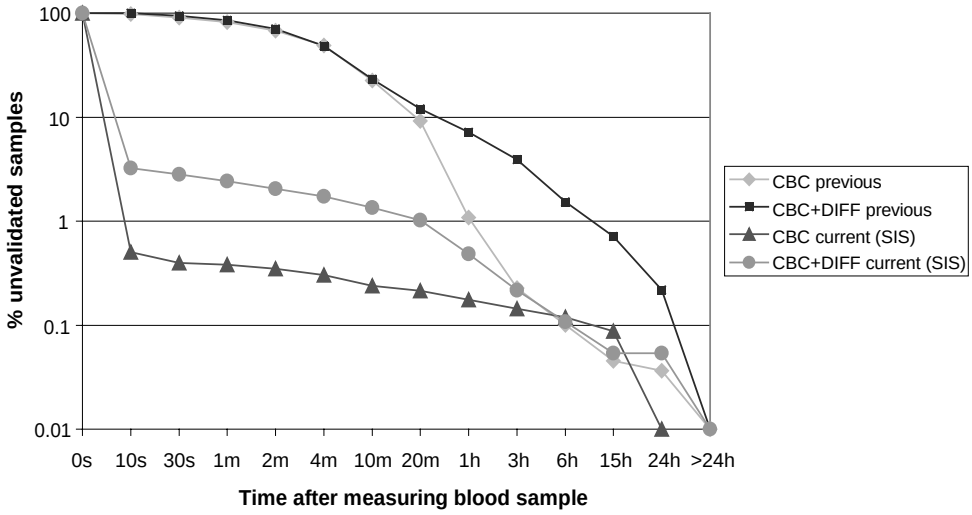

Fig. 3 *Comparison of TAT of the previous and current SIS technical validation of CBC and CBC+DIFF*

Table 1 *Comparison of total positive previous platelet rules and SIS standard platelet rules and the total of ADD order, repeat or smear actions*

Previous PLT rules		
	n	Actions
PLT Abn distribution flag	583	Total profile
PLT Clumps flag	241	Smear

SIS standard PLT rules		
	n	Actions
RBC fragment rule	79	PLT-O
RBC microcytes rule	12	PLT-O
Giant platelets rules	72	PLT-O
PLT Clumps rules	48	Smear
Mixing problem rule	0	Repeat
Aspiration problem rule	2	Repeat

Validation times show significantly different results for CBC ($p < 0.0001$) and CBC+DIFF ($p < 0.0001$) between previous and current SIS workflows. There is a decrease in validation time using SIS with a mean of 8.5 minutes for CBC results and 37.7 minutes for CBC+DIFF. 95% of samples are validated 27.8 minutes earlier with SIS for CBC and 179.8 minutes for CBC+DIFF.
The total decrease in validation time per month (= total samples per month multiplied by the mean decrease in validation time with SIS for CBC and CBC+DIFF) with SIS is more than 700 hours for CBC and over 500 hours for CBC+DIFF.

Total of positive data check results and following actions (NRBC, PLT-O, repeats and smears) over a period of 2 months

We compared the total positive data checks and following actions over a 2-month period using pre- and post-SIS implementation rules in a total of 15,414 samples.

Table 1 shows the performance of the platelet rules with the previous rules and the SIS standard rules. The previous rules had two platelet flag criteria, PLT abnormal distribution (583 of 15,414 samples) and PLT clumps (241 of 15,414 samples). The action for PLT abnormal distribution was a total profile consisting of CBC+DIFF+RET (PLT-O)+NRBC and for PLT clumps a smear was prepared. Delta-checks and user expertise contributed further to these actions. The SIS standard rules showed many fewer and more specific positive platelet rules. RBC fragments, RBC microcytes and giant platelets necessitate a repeat with an ADD order PLT-O count. PLT clumps rules require checking in a smear and aspiration or mixing problems necessitate repeat analysis.

Table 2 *Comparison of total positive previous RBC rules and SIS standard RBC rules and the total of ADD order NRBC, repeat or smear actions*

Previous RBC rules		
	n	Actions
RBC Agglutination flag	4	Smear
Turbidity/Hb interf. flag	119	Smear
NRBC flag	126	NRBC
Hb defect flag	20	Smear
Fragments flag	55	Smear
Iron deficiency flag	48	Smear

SIS standard RBC rules		
	n	Actions
RBC Agglutination rule	4	Repeat
Turbidity/Hb interf. rule	56	Check
NRBC rule I	85	NRBC
NRBC rule II	301	NRBC
Fragments rule	26	Smear
Reticulocytes rules	2	Smear

Table 3 *Comparison of total positive previous WBC rules and SIS standard WBC rules and the total of smear actions*

Previous WBC rules		
	n	Actions
Left shift flag	45	Smear
Immature Granulocytes flag	288	Smear
Blasts flag	8	Smear
Atypical lymph flag	156	Smear
Abn Lymph/ L-Blast flag	128	Smear
RBC Lyse resistance flag	0	Smear

SIS standard WBC rules		
	n	Actions
Left shift rule	3	Smear
Immature Granulocytes rule	288	Smear
Blasts rule	8	Smear
Atypical lymph rule	156	Smear
Abn Lymph/ L-Blast rule	44	Smear
RBC Lyse resistance rule	0	DIFF ch
Eosinophil rules	2	Smear

Table 2 shows the comparison for erythropoiesis rules. Again the SIS rules are less frequent (except for NRBC) and more specific.
NRBC rule II is for 'ADD order NRBC' in cases of thalassaemia or haemolytic anaemia only in a CBC order without DIFF. We checked this and came to the conclusion that 75% (n= 226) of the NRBC add order had a result of zero (false positives). Our recommendation is to alter some cut off values but without losing the 25% correct positive results.

Table 3 shows the comparison for leucocyte results. The SIS standard system shows considerable reduction of the left shift (bands) and Abn. lymph /L-blasts (abnormal lymphocytes or lymphoblasts) rule incidence.

In general, the SIS standard rules showed a reduction in positive rules and actions for all three cell lines; thrombopoiesis, erythropoiesis and leucopoiesis except for NRBC (***Table 2***).

Observation of the quality of previous and current workflow actions and results during a 2-week period

For a period of 2 weeks (3,500 samples) we checked the quality of actions and results decided by SIS standard rules. The SIS platelet rules missed one example of PLT clumps. The SIS RBC rules had no false negatives. The NRBC rule II (not used in the previous rules) showed 75% false positive NRBC add order counts (see comments erythropoiesis rules above).
Overall we were impressed by the sensitivity of the SIS system especially in the white cell line.

ACCEPTANCE OF SIS BY THE MEDICAL TECHNOLOGISTS

3 months after introduction of SIS standard rule software, 14 medical technologists who worked a minimum of one

week day and one night shift with SIS completed a questionnaire about workflow improvements, quality, standardisation and practicability. Prior to implementation of SIS, medical technologists were sceptical about its value. It is interesting to see that shortly after its introduction almost all medical technologists would miss the software. In general they found the SIS standard package safe, fast and helpful in night and weekend shifts.

DISCUSSION

Our technical validation comparison between previous rules and SIS standard rules has shown a significant improvement ($p < 0.0001$) in the TAT for validation of results with SIS. This is important for our emergency wards, our impression being that telephone enquiries for results were clearly decreased.

The total positive data checks and actions (NRBC, PLT-O, smears) were clearly decreased to clinically relevant actions with the exception of the NRBC ADD order. These SIS actions are more specific than before and they are standardised. Our previous validation showed high quality but depended on the expertise of the user. However, with the faster validation procedure and fewer positive actions the quality with SIS is at least as good as the previous procedure. Acceptance of the SIS standard rules was very high and the rules where found to be helpful, fast and safe.

We will continue with further studies to improve (the NRBC rule) and adapt our parameters and cut-off values to satisfy our clinical requirements.

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