QUALITY CONTROL APPLICATION AND VALIDATION OF 'AVERAGE OF NORMALS' FOR COMPLETE BLOOD COUNT PARAMETERS

İlknur Alkan Kuşabbi, Neslihan Cihan, Emel Çolak Samsum, Mehmet Şeneş, Vildan Fidancı, Doğan Yücel

Ankara Health Training and Research Center Health Sciences University

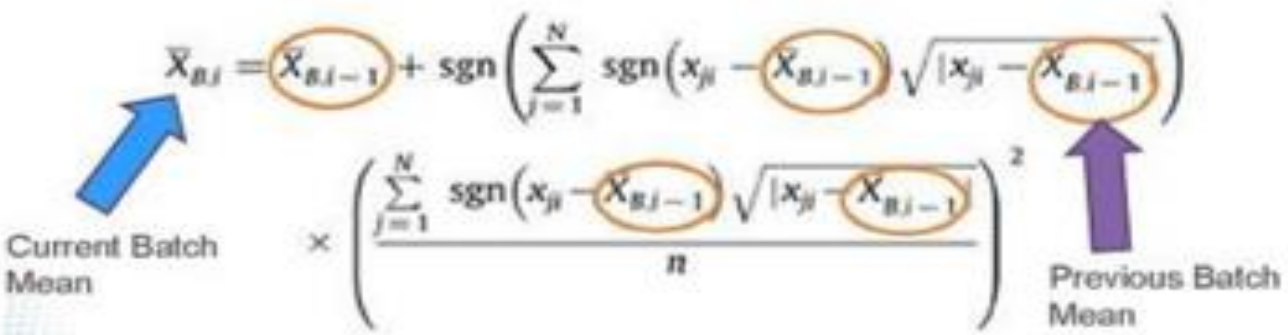
Department of Medical Biochemistry

INTRODUCTION

- The use of averaging patient results (average of normals, AON or moving averages, MA) for analytical quality control purposes was first described in 1965 by Hoffmann and Waid.
- Although their usefulness is established they are not generally implemented.
- Actually AON tools are included in the software of many analyzers, middleware and laboratory information systems (LIS), the application of MA as an internal quality control (iQC) tool is possible in many laboratories.
- One reason why MA is not widely used is the lack of readily available software to select optimal settings for each individual assay in a specific hospital.

INTRODUCTION

- Several strategies are available to perform real-time iQC using MA.
  - Simple mean
  - Weighted MA
  - Bull's algorithm
- The averages are weighted by Bull's algorithm, and both the absolute values measured and the difference between the previously calculated respective value play a decisive role.



Use of previous batch mean and square root functions in the equation help to minimize the impact of outliers which could cause one batch to go out of range

INTRODUCTION

- Major contributors to the power of error detection of MA are:
  - Ratio of biological and analytical variation
  - Number of points averaged (**batch size**) (dependent on the number of samples measured in daily routine)
  - **Control limits** used to generate MA alarms (dependent on the parameter in question)
  - **Target level** (dependent on the patient population)
  - **Truncation limits** for selection of the included assay results
  - Number of patient results falling outside the truncation limits (**Outliers**)

INTRODUCTION

- Quality control measures which use control blood samples are crucial, but may only represent a snapshot of the analyser's condition when the procedure was carried out.
- In contrast, MA control function is a long-term and **continuous** control process, which runs continuously over the entire working day and can reveal any drifts in the results much more rapidly.

METHODS- PATIENT RESULTS AND CBC MEASUREMENTS

- All reported patient complete blood count (CBC) results produced during one month on one of our Sysmex X Series analyser were included in our study.
- CBC results were extracted from our LIS in reporting time order.

METHODS-MOVING AVERAGE CALCULATION

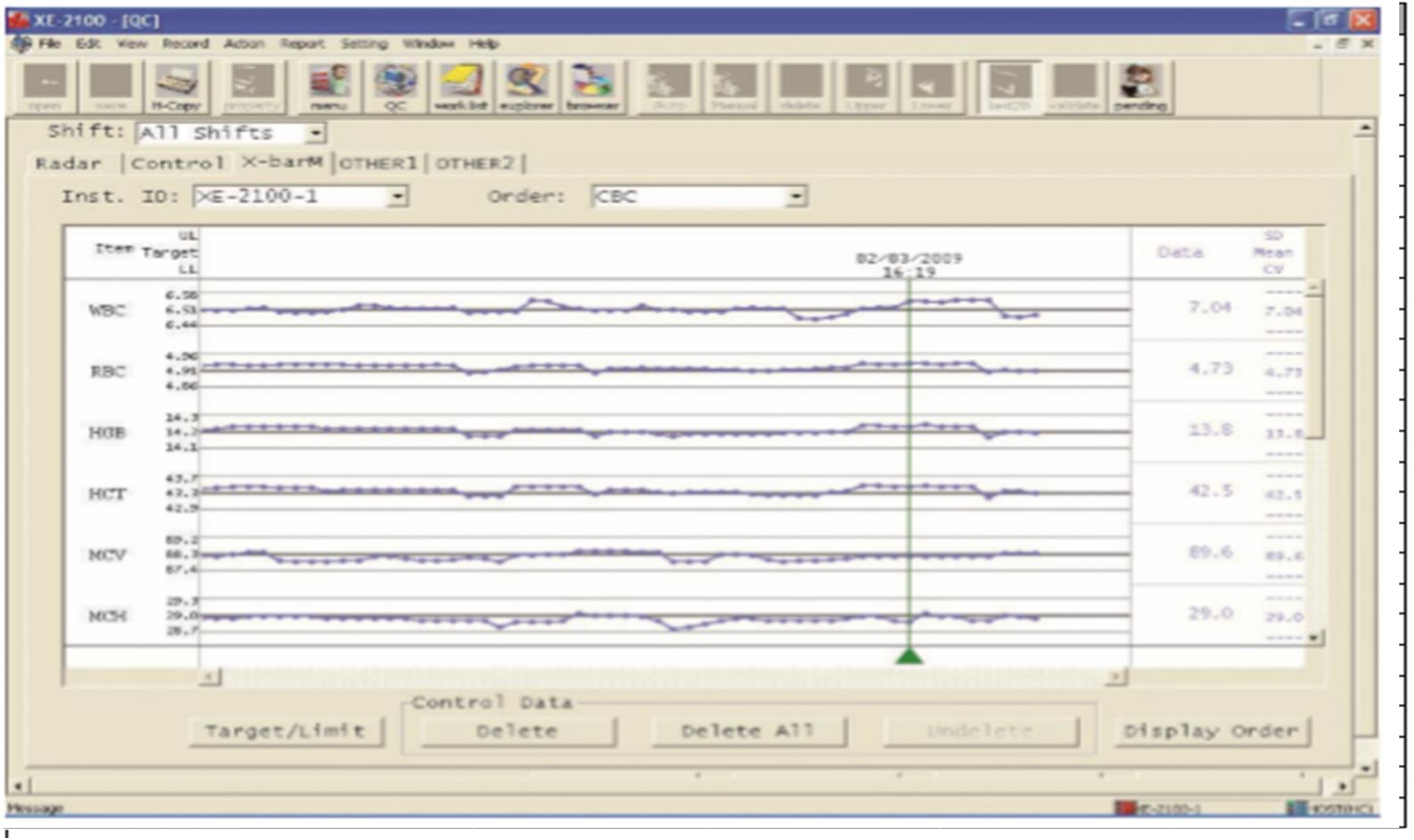
- For calculation of moving averages, a program special for Sysmex X-series hematology analysers called 'XbarM control' program was used.
- Also by Microsoft Excel program a statistical calculation was designed for calculation of moving averages using Bull's algorithm formula.

METHODS-MA CONTROL LIMIT DETERMINATION

- For control limit determination we used Sysmex X-Bar M program TARGET/LIMIT function.
- One month CBC MA data was used for calculation of target levels.
- % tolerance limits were taken from Sysmex recommended data. From this data, control limits were determined.
- Also several control limits were examined for bias detection performance comparison.

METHODS-POWER FUNCTION ANALYSIS

- Varying amounts of biases were introduced to the whole dataset, i.e.biases of −80%, −60%, −50%, −40%, −25%,−20%,−15%,−10%,−5%, −2%, 2%, 5%, 10%, 15%, 20%, 25%, 40%, 50%, 60%, 80%, 100% were introduced.
- Bull's Algorithm MA procedure was run on all bias containing datasets and the number of MA values outside the control limits as percentage of the total number of generated MA values were computed.
- Power function graphs were generated by plotting the studied bias on the x-axis and % of MA-alarms per generated MA value on the y-axis.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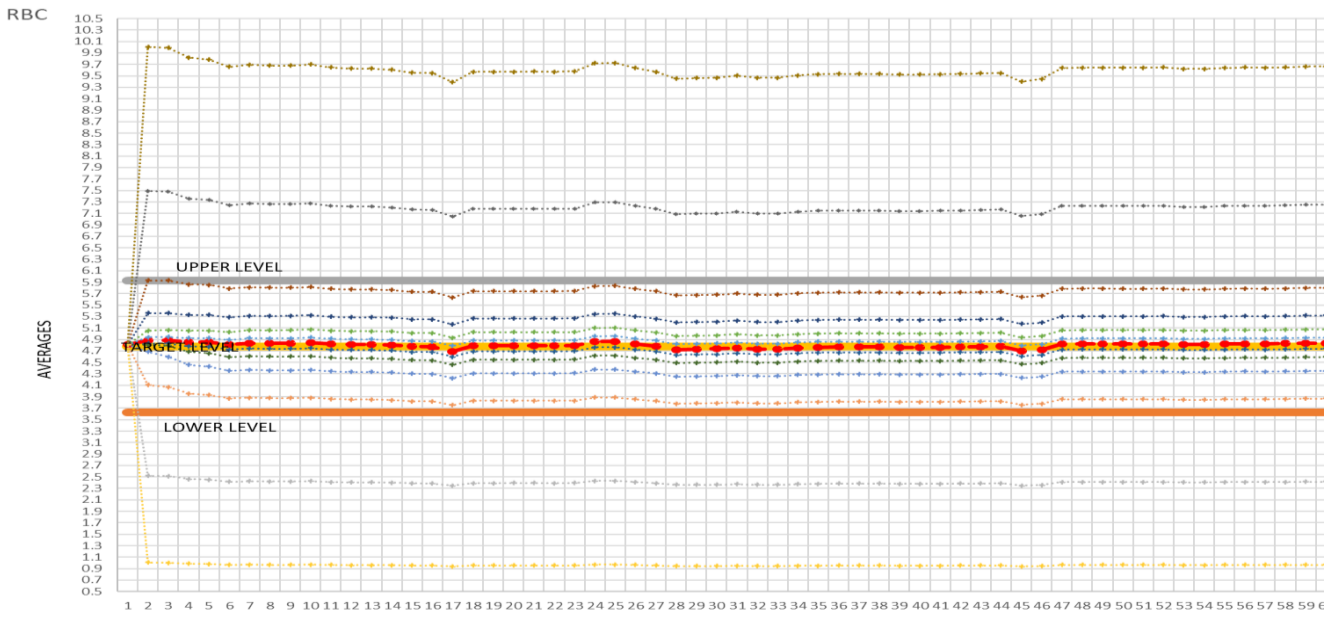
RESULTS- MA POWER FUNCTION ANALYSIS

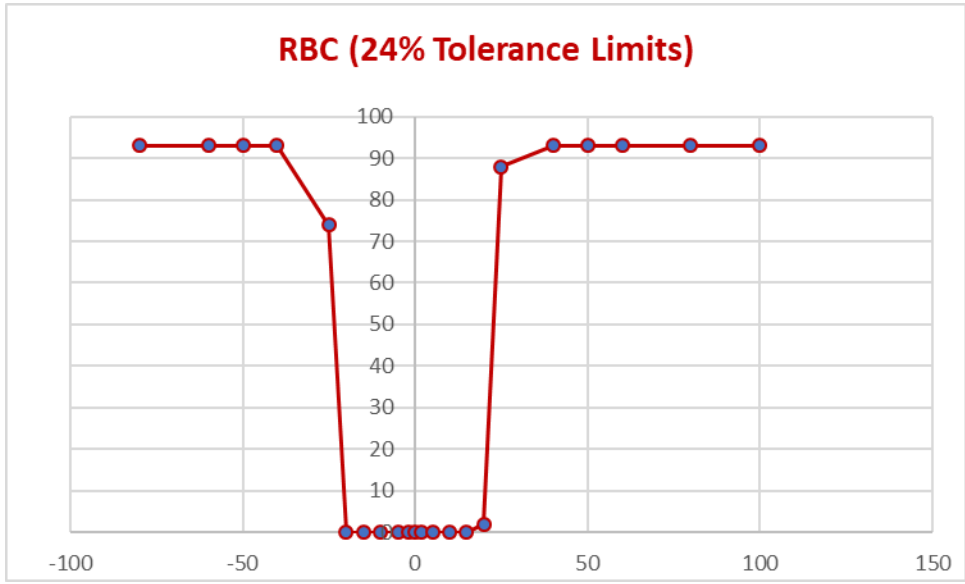
- Power function graphs were generated for all CBC parameters.
- Power function analysis shows that bias detection performance in terms of probability of MA alarm per MA value is increased by more stringent control limits.
- Additionally, larger batch sizes increase the bias detection performance of MA.

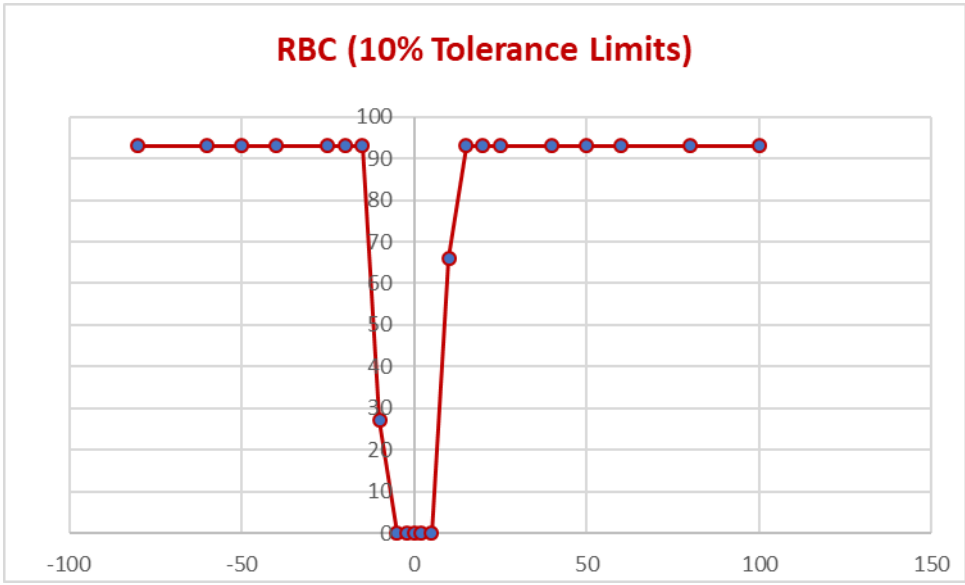
- The common count parameters of the blood count (platelets, red blood cells and white blood cells, including differential populations), hemoglobin and hematocrit, as well as some statistical parameters (distribution widths, large cell ratios) are subject to a high degree of biological variation.
- This group is therefore not the most significant of the parameters used for MA control, as it is not possible to identify changes as precisely. For this reason, traditional internal QC using control blood samples are more applicable for these parameters.
- For that reason control limits for MA alarms could be wide for these parameters.

Moving Averages by Time For RBC

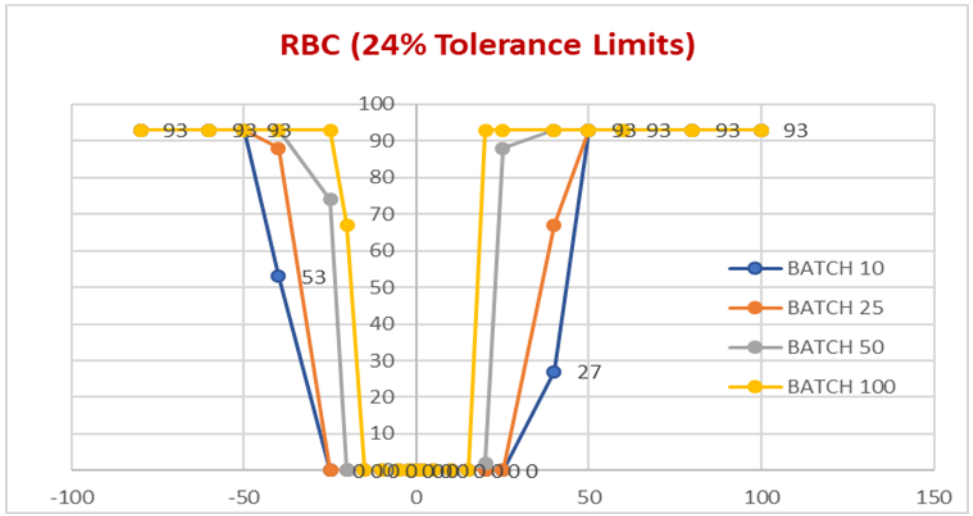


Power Function Graphs For RBC

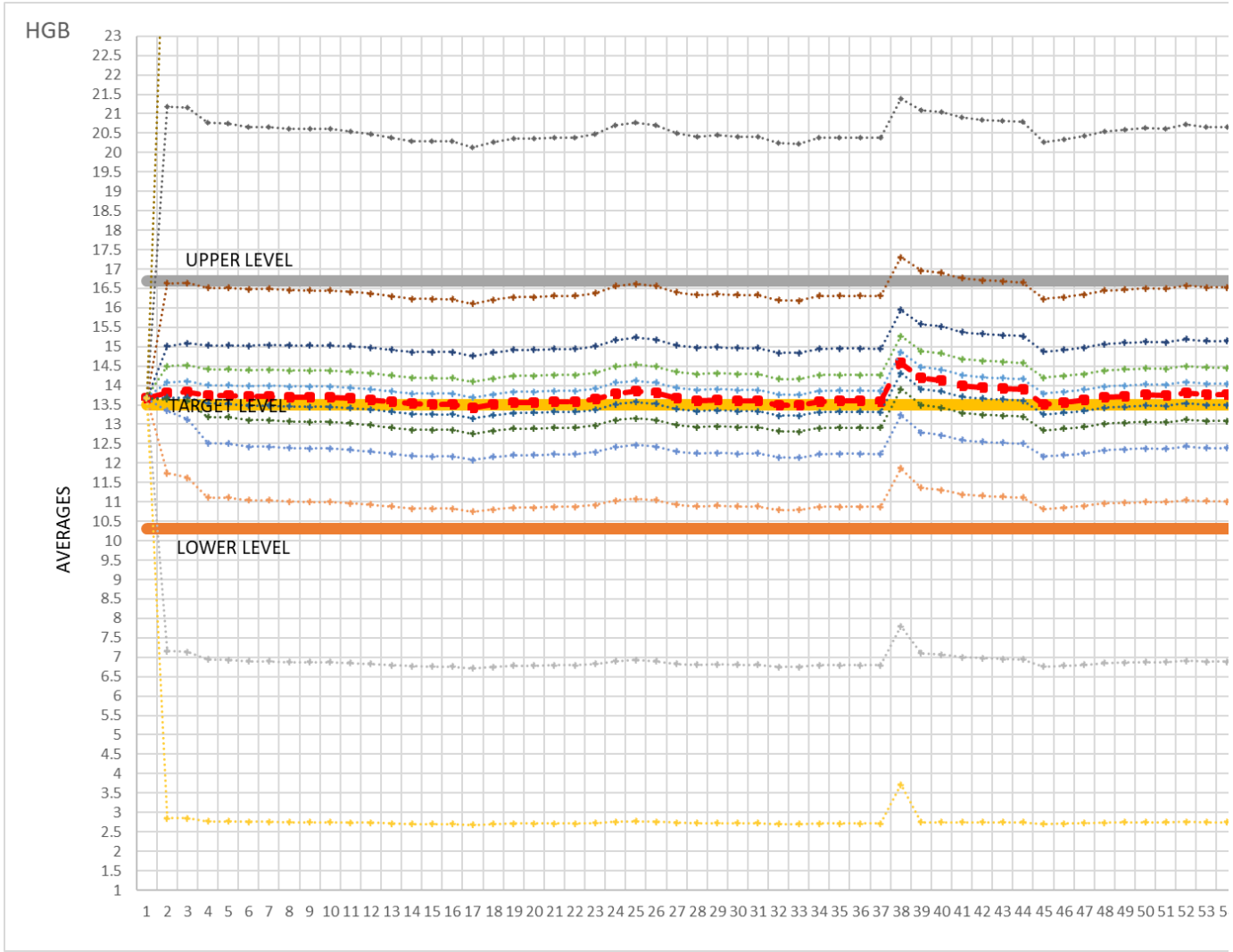




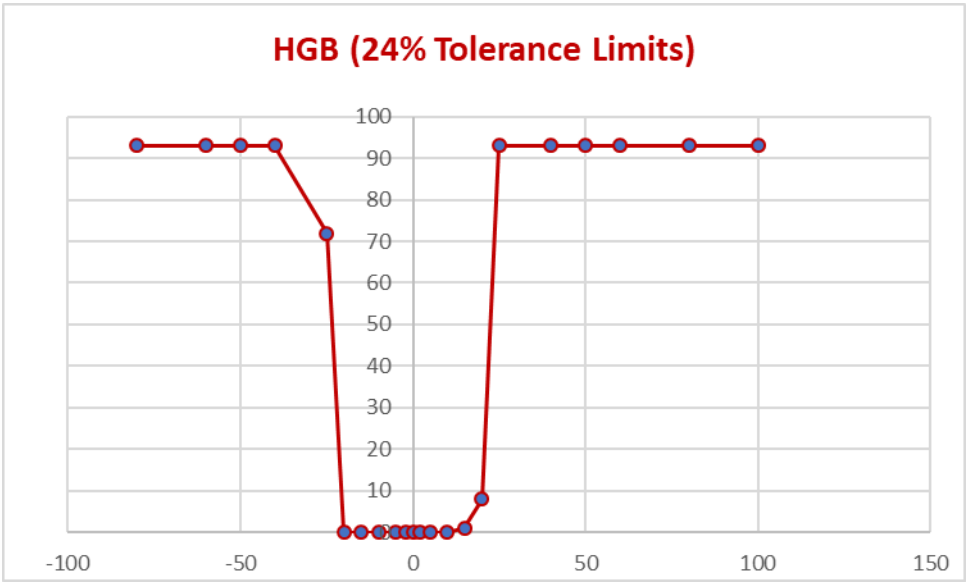
Power Function Graph for RBC with Different Batch Sizes

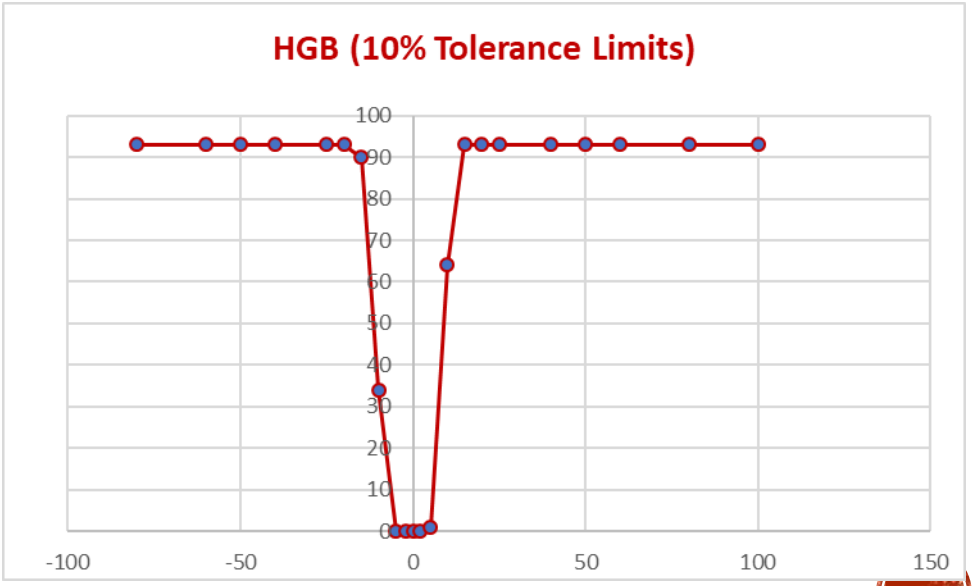


Moving Averages by Time for HGB

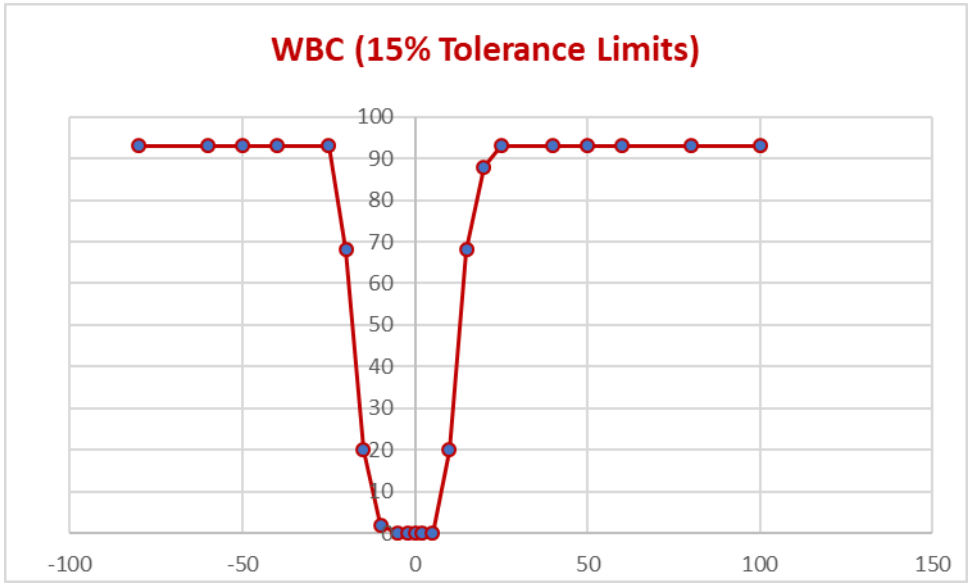


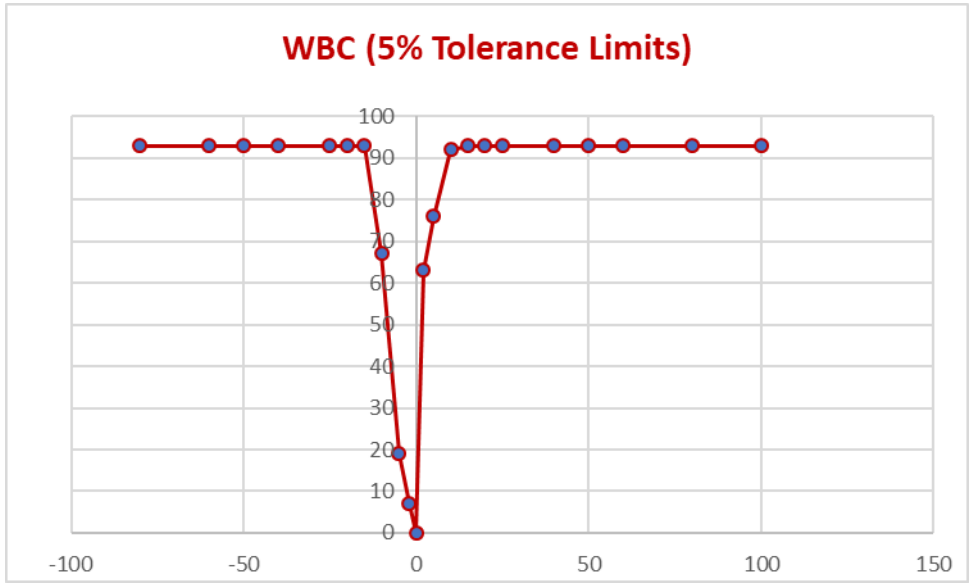
Power Function Graphs for HGB

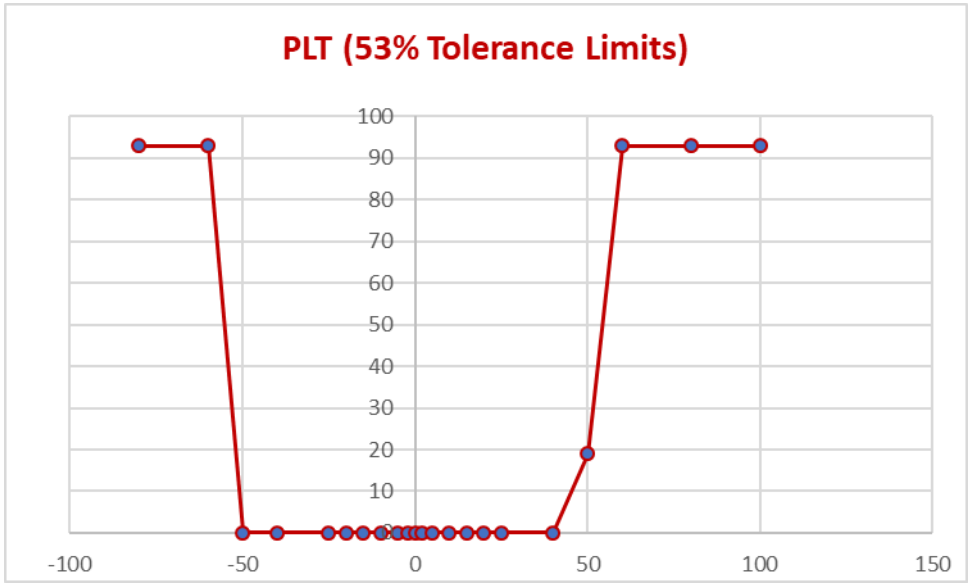


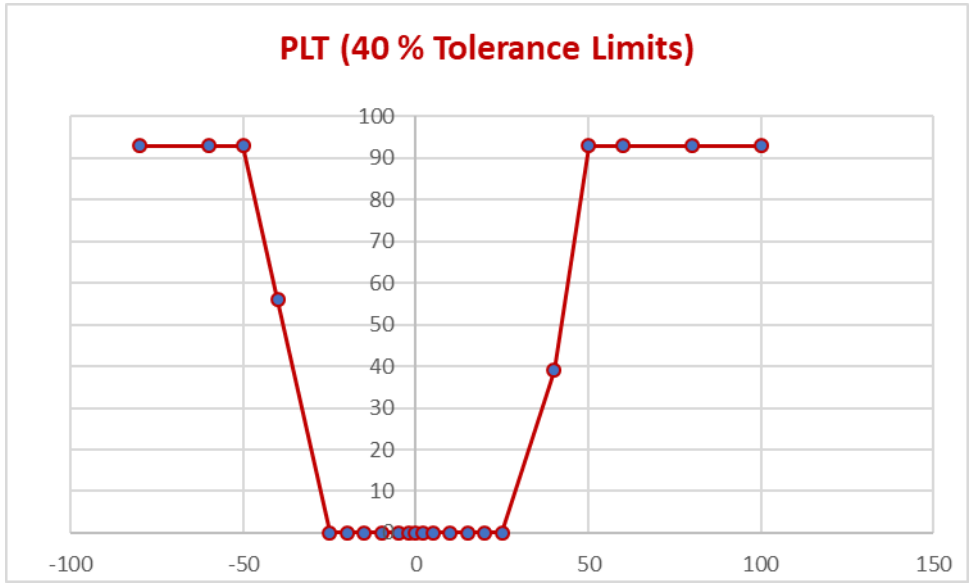


A Selection of Other Parameters' Power Function Graphs with Different Tolerance Limits



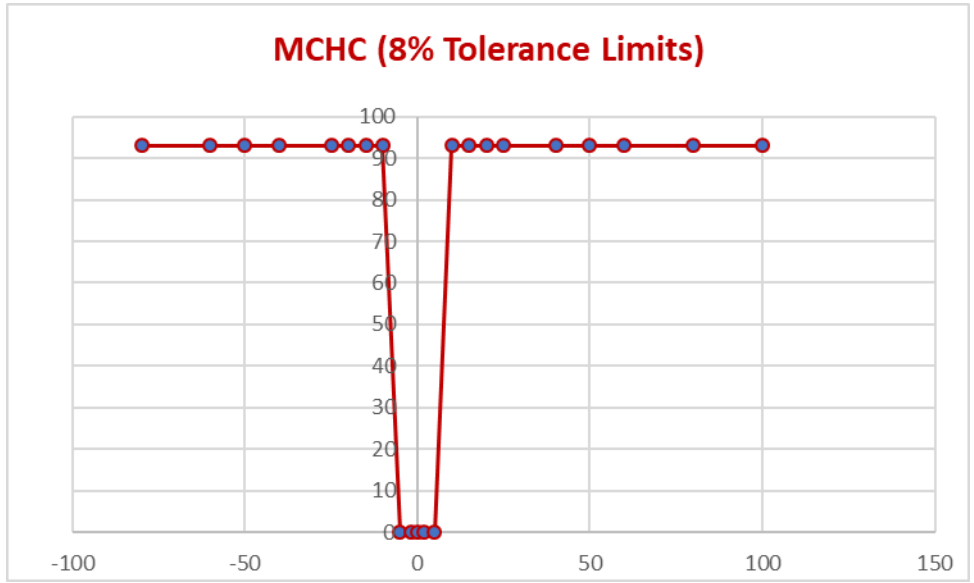


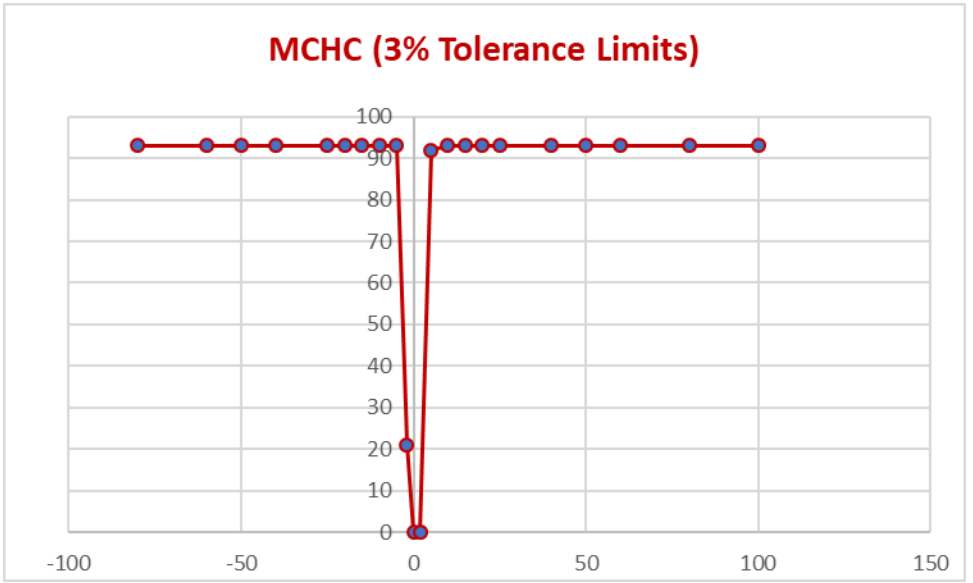


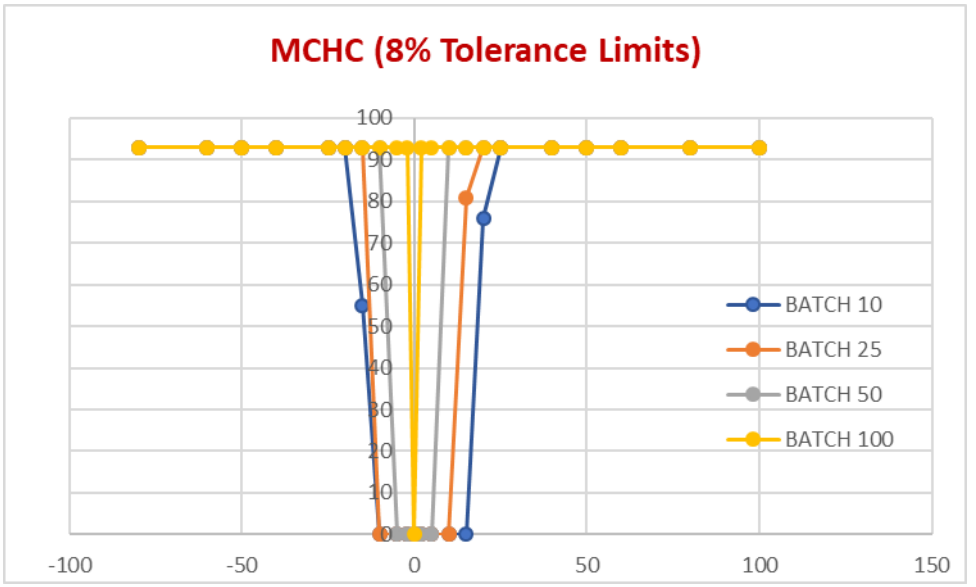


- A further group includes calculated parameters of the red blood cell count: MCV, MCH, MCHC, and also MPV.
- Using AON control algorithm, these parameters are important indicators of correct analyser operation in terms of the CBC, since they exhibit far less biological variation.
- MCHC, although known to be of lesser significance to a physician, suits as the most important parameter for the laboratory as an excellent indicator of the plausibility of results, as it naturally varies by only a very tight range.
- Furthermore, the MCHC value cannot physiologically exceed 37 g/dL (22.9 mmol/L) or fall below 27 g/dL (16.8 mmol/L).Therefore, if a value outside this range is obtained for a sample, the analysis result should always be questioned.
- A further advantage is that two different measurement channels (RBC/PLT channel and hemoglobin channel) are used to calculate the MCHC value and are therefore both monitored.

Power Function Graphs For MCHC with Different Tolerance Limits and Batch Sizes







CONCLUSIONS

- The described method investigated which bias can be detected with Bull's algorithm for CBC parameters.
- Due to laboratory-specific patient populations, logistics, analytical methods, and daily production each laboratory should determine their own specific optimal MA procedures.
- Therefore, software that can automatically perform the simulation experiments and thereby support the selection of optimal settings should be developed.

CONCLUSIONS

- In conclusion, we present a MA optimization and validation method for allowing continuous analytical quality control by MA that provides realistic insights in MA bias detection characteristics.
- In our very high volume hospital laboratory, we are planning a more comprehensive AON study for many parameters. This study is the starting point for the planned study.
- I would like to state that we will share our comprehensive study with you by completing our shortcomings in the future.

- **Thank you for your attention.**