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Serum work area system validation under intended user conditions

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M062

Introduction

- Here, we report on studies conducted under intended use conditions during the development of a new laboratory analyzer (cobas® pure integrated solutions; Roche Diagnostics International Ltd, Rotkreuz, Switzerland), with the aim of stress testing and enhancing the performance and reliability of the system.
- The cobas pure integrated solutions is a medium throughput laboratory analyzer developed to quantify ion selective electrolyte (ISE), clinical chemistry (CC; cobas c 303), and immunochemistry (IC; cobas e 402) parameters in biological fluids such as plasma, serum, and urine.
- During the development and validation of the cobas pure integrated solutions analyzer, operation of the study systems was undertaken by typical end-users in their own laboratories under routine-like conditions.

Objectives

- **To evaluate the overall system functionality, reliability, and user satisfaction of the cobas pure integrated solutions analyzer at various phases of development.***

*Results for analytical performance and comparability are presented in posters M061 and M040, respectively, at this congress.

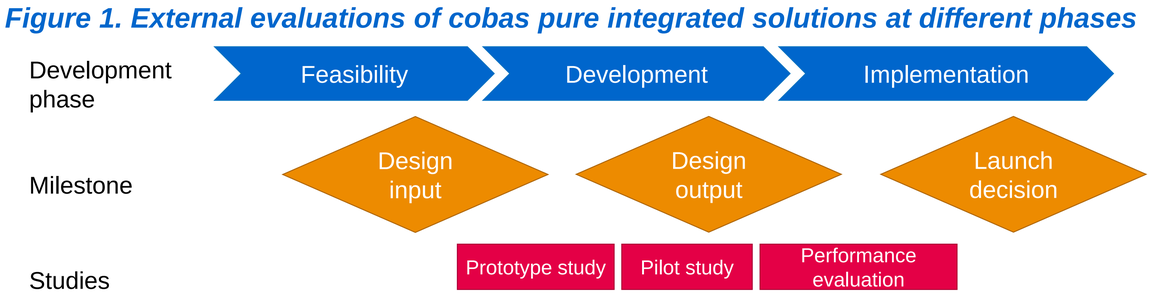
Methods

- We conducted a prototype study and a pilot study during the development phase, and a comprehensive performance evaluation study during the implementation phase (**Table 1**, **Figure 1**).
  - The goal of these multicenter studies was to stress test the overall functionality of the system and to capture user satisfaction with the design at different development phases, ending with the system performance evaluation study.
- Applications representing a selection of the available clinical chemistry and immunoassay portfolio were assessed during each study.
- Control material or anonymized leftover samples from both inpatients and outpatients of any age and health status derived from the respective study sites were used as sample material.
- Various routine simulation experiments that stress tested the overall system functionality of all components (hardware, software, assays, and samples), and supported the identification of potential deficiencies under intended use conditions, were conducted at the different development phases.[1–3]

Table 1. Evaluating cobas pure integrated solutions

Study	Study material	Study sites	Duration	No. of assays		
				ISE	CC	IC
Prototype study	Prototype hardware and software and preliminary assay applications	Visp, Switzerland	Feb–Apr 2019	3	11	6
Pilot study	Series hardware and pilot software and assay applications	Ludwigsburg, Germany; Visp, Switzerland	Apr–Jul 2020	3	30	34
Comprehensive performance evaluation study	Series hardware and software and final assay applications	Heidelberg, Germany; Ludwigsburg, Germany; Seoul, South Korea; Visp, Switzerland; Wroclaw, Poland	Aug–Dec 2020	3	30	34

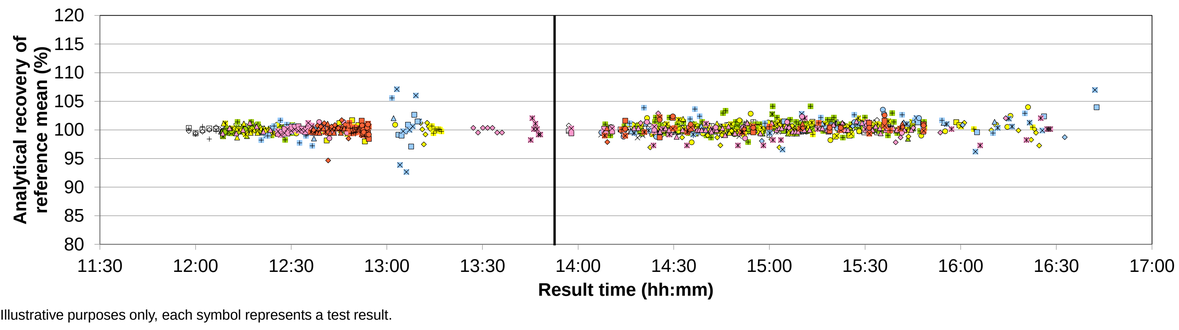
Figure 1. External evaluations of cobas pure integrated solutions at different phases



Routine-simulation experimental designs

- For testing the interaction of hardware, software, assays, and samples, routine simulation imprecision experiments tested reproducibility under various stressed routine-like conditions, including provocations (routine simulation imprecision).
  - The precision of batch type measurements were compared with precision under routine simulated random access conditions.
  - Random access coefficients of variance (CVs) that exceeded 1.5x reference batch CVs, or single measurements deviating by >10% from the batch mean, triggered in-depth analysis of the system components that contributed to the result (**Figure 2**).

Figure 2. Routine simulation imprecision: analysis concept



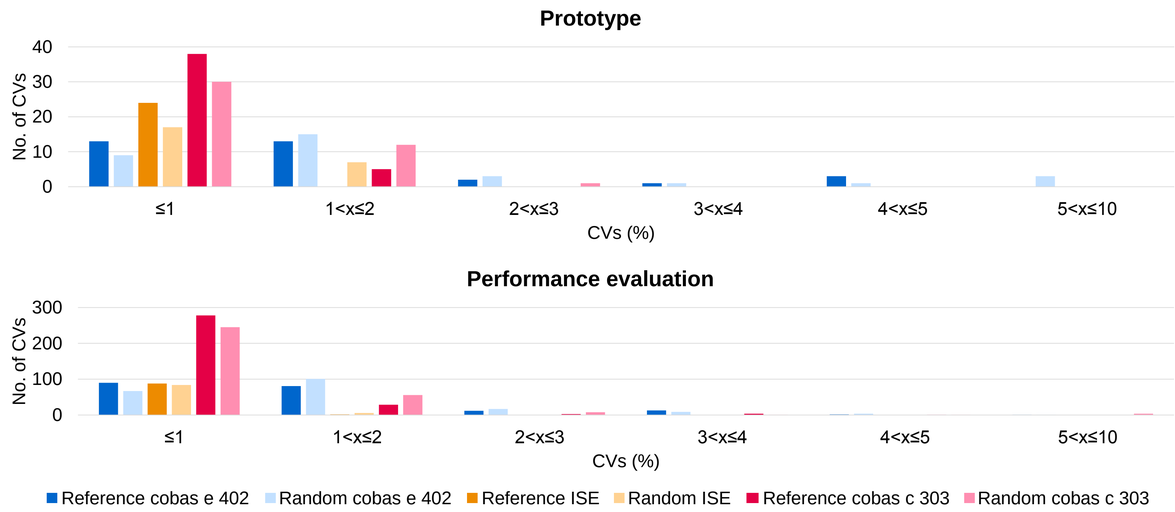
Illustrative purposes only, each symbol represents a test result.

- The workflow and performance of the study system was compared with the study laboratory routine (routine simulation download); user satisfaction, practicability, and reliability of all components were monitored and assessed, in addition to user interactions and result correctness, while repeating routine workloads on the study system.
- Overall system reliability, measured by the percentage of analysis runs completed without interruption, was compared at the different development phases.
- User satisfaction with the practicability of the system was assessed via a questionnaire, based on experience gained during routine-simulation testing.
  - The questions were graded on a 10-point scale, from 1 “does not meet expectations” to 10 “exceeds expectations”.
  - The 17 categories covered were: installation environment, location of components, operator training, user documentation and support, product design and labelling, daily workflow, reagent handling, timing/productivity, data processing, environment, quality assurance, calibration, quality control, maintenance, troubleshooting, versatility, and consolidation.

Results

- The reproducibility of results per study within a simulation experiment (batch and random CVs) showed good performance, with most CVs <1%.
- This high performance in a routine-like setting was comparable across the different development phases (**Figure 3**); this stress-testing outcome demonstrates the stability of all key components that contribute to the analytical results at a very early stage of system development.

Figure 3. Result reproducibility: prototype and performance evaluation studies

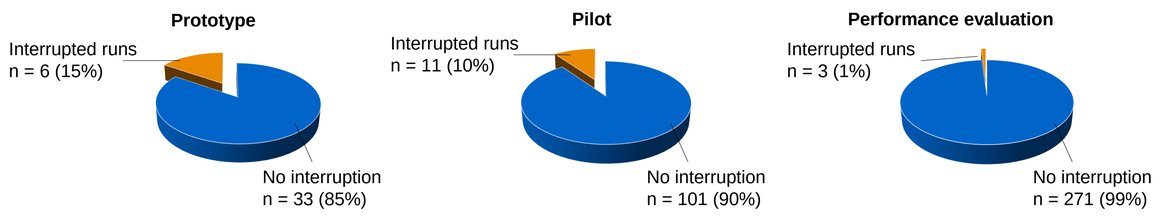


- Stress provocations introduced during randomized testing showed expected system behavior during the prototype study with two exceptions:
  - Incorrect system behavior after a provoked sample short event was identified and was reported to the development team for analysis and resolution. The root cause was traced to a software malfunction and retesting using the updated software during the performance evaluation demonstrated correct system behavior.
  - A spontaneous drain port issue also observed during the prototype study led to optimization of the fluid drain management; the fluid drain system was redesigned and the installation procedure was adjusted prior to the pilot study.

Overall system reliability

- For all studies, the reliability of the evaluation systems was closely monitored.
- System runs were classified as interrupted (unplanned stop of the system) or no interruption.
- The interruption rates of the different studies were compared, and a significant decrease in interruptions was observed as the system matured (**Figure 4**).
  - During the comprehensive performance evaluation study, high system reliability (99%) was demonstrated across study sites.

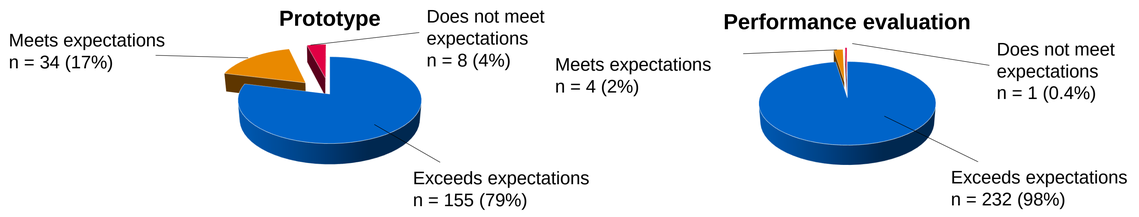
Figure 4. System performance & reliability over studies



User satisfaction

- During the prototype and performance evaluation studies, user acceptance and satisfaction was assessed across all aspects of the evaluation system.
- Results from the site that participated in all three studies (Visp, Switzerland) demonstrated an improvement in the “exceeds expectations” grading from 79% during the prototype study to 98% during the performance evaluation study (**Figure 5**).

Figure 5. Practicability grading



- Across all five sites that participated in the performance evaluation study, 80% of all questions were graded as “exceeds expectations”, 20% as “meeting expectations”, and only 0.4% as “did not meet expectations”.

Conclusions

- **The novel cobas pure integrated solutions system was thoroughly stress tested and assessed by typical end-users under routine-like conditions in their own laboratory, throughout its development.**
- **The findings presented here demonstrate improvement in the functionality, practicability, and reliability as the system matured during each development phase.**
- **The findings also show that early evaluations of new clinical chemistry and immunochemistry analyzers under varied routine-like conditions support the development process and help identify possible random and systematic errors.**

References

1. Stockmann W, et al. In Evaluation Methods in Laboratory Medicine 1993:185−201; 2. Bablok W & Stockmann W. Quimica Clinica 1995;14:239; 3. Stockmann W, et al. J Autom Methods Manag Chem 2008:183747.

Disclosures

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