Evaluation of System Carryover for the MicroWell Processing Center on the VITROS® 5600 Integrated System* and the VITROS® 3600 Immunodiagnostic System*

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ABSTRACT

BACKGROUND/OBJECTIVE

The VITROS® 5600 Integrated System and the VITROS® 3600 Immunodiagnostic System offer MicroWell technology for immunodiagnostic and infectious disease (subject to regulatory approval in local markets) assays. Carryover is eliminated from these random access analyzers ensuring accurate and reproducible results. There are four critical processes in MicroWell assay processing: sample metering, reagent metering, incubator mixing and motion, and well wash. The carryover performance of each of these processes was evaluated using elevated patient samples or horseradish peroxidase (HRP) as an indicator of elevated signal response.

METHODS

1. To eliminate carryover, sample metering uses a single-use tip for each sample. The sample metering carryover was evaluated by measuring known high positive HBsAg samples together with known negative samples. Absolute Light Units (ALU) were measured and evaluated against a no carryover goal that ensured no effect on assay performance.

2. Reagent metering also uses a single-use tip for each reagent to eliminate carryover. The MicroWell wash system uses fixed, non-disposable wash probes that are rinsed and purged throughout processing. Reagent metering, incubator mixing and motion and well washing were evaluated for carryover using high levels of HRP in conjunction with nonreactive sample diluent. Results were then either compared to a standard curve or a negative baseline run versus a test run after multiple contaminating opportunities. ALU were measured and evaluated against a no carryover goal that ensured no effect on assay performance

Process	System (VITROS® 5600 and 3600)	Base-line Pre Contamination ALU	Contaminating ALU	ALU - Post Contamination	Criteria (ALU) for 'No Carryover'
Sample Metering	1	7.4	10600	7.5	<11.4
	2	8.3	10876	7.7	<12.3
Reagent Metering	1	0.9	54,292	0.93	<4.9
	2	1.04	68,288	1.11	<5.04
Incubator- Ring 1 = outer inc ring Ring 2 = middle inc ring	1 (ring 1)	6.28	>750,000	6.02	<29.92
	1 (ring 2)	6.12	>750,000	6.26	<29.92
	2 (ring 1)	6.94	>750,000	7.21	<33.96
	2 (ring 2)	6.38	>750,000	6.35	<33.96
	3 (ring 1)	6.73	>750,000	7.02	<33.96
	3 (ring 2)	6.46	>750,000	6.46	<33.96
Wash Probes	1	1.5	>400,000	1.5	<4
	2	0.9	>400,000	1.1	<4
	3	1.4	>400,000	1.2	<4

CONCLUSION

Comparing the results of the 'Post Contamination ALU' response to the "Criteria for No Carryover," demonstrated that assay processing using elevated HRP solutions as the carryover indicator achieved the no-carryover goal for MicroWell sample and reagent metering, incubator motion and mixing, and the well wash probes on the VITROS® 5600 and VITROS® 3600 systems. The no-carryover feature on these analyzers helps ensure accurate and precise results.

INTRODUCTION

The new VITROS® 5600 Integrated System is designed to integrate clinical chemistry and immunoassay testing on a single system using all five VITROS® technologies: MicroTip, MicroSlide, MicroWell, MicroSensor, and Intellicheck®. The new VITROS® 3600 Immunodiagnostic System is a new high capacity immunoassay system for both routine and specialty immunoassay testing that uses 3 VITROS® technologies: MicroWell, MicroSensor, and Intellicheck®. Both of the new systems were designed to deliver high quality assay results that improve patient care while improving overall laboratory productivity.

It is essential that carryover in any random access analyzer be eliminated to ensure accurate, reproducible results. Potential opportunities for carryover for the MicroWell technology are evaluated in this study. These new analyzers use a single–use tip for sample and reagent metering eliminating carryover from these metering processes. Other processes important to processing MicroWell assays have eliminated carryover by design. This is critical for laboratories so as to eliminate false positive qualitative results or falsely elevated quantitative results.

OBJECTIVE

The purpose of this evaluation is to verify that carryover is eliminated on these new random access analyzers for the MicroWell technology. This study evaluated four critical processes for MicroWell assay processing: sample metering, reagent metering, incubator mixing and motion, and well wash. The carryover performance of each of these processes was evaluated using high positive patient samples or horseradish peroxidase (HRP) as an indicator of elevated signal response.

METHODS

1. Sample metering carryover was evaluated by measuring known high positive HBsAg samples together with known negative samples. High positive HBsAg samples were used because of the assay's high level of infectivity. These samples, when measured, gave very high signals resulting in high responses or signal ALU's (Absolute Light Units) that could serve as a source of contamination when run in conjunction with nonreactive samples. Internal and external sample metering was evaluated. Samples metered internally were processed in trays residing in the sample handler area of the instrument. Samples metered externally were processed from an automation track system external to the analyzer. The instrument metering system metered the sample directly from the track. It is essential that carryover does not occur, such that during sample metering and processing of known positive samples, known negative samples are contaminated and become positive.

2. Reagent metering also uses a single–use tip for each reagent to eliminate carryover. The MicroWell wash system uses fixed, non-disposable wash probes that are rinsed and purged throughout processing. Reagent metering, incubator mixing and motion, and well washing were evaluated for carryover using high levels of HRP in conjunction with nonreactive sample diluent. Results were then either compared to a standard curve or a negative baseline run versus a test run after multiple contaminating opportunities. The baseline run was processed in a batch mode where the sample was run without any opportunities for contamination. ALU were measured and evaluated against a no carryover goal that ensured no effect on assay performance.

RESULTS

SAMPLE METERING CARRYOVER

- Single–use tip eliminates carryover.
- Internal and external sample metering was evaluated. Evaluation of metering was done from the sample handler area inside the instrument and from an automation track external to the analyzer.
- HBsAg positive and negative samples were used. It is essential that positive samples do not effect negative nonreactive samples through sample metering and processing. HBsAg is a good marker for carryover detection because it has a high level of infectivity. These samples, when measured, gave very high signals resulting in high responses or signal ALU's that could serve as a source of contamination when run in conjunction with nonreactive samples.
- Multiple positive and negative samples were run, alternating high positive samples with known nonreactive negative samples in order to evaluate contamination.
- The carryover goal was selected to ensure no effect on assay performance. The carryover goal was defined as: Signal increase from a baseline ALU determination prior to contamination opportunities, not to exceed +4ALUs.
- Results indicated virtually no measurable increase in ALU.

Process	System (VITROS® 5600 and 3600)	Base-line Pre Contamination ALU	Contaminating ALU	ALU -Post Contamination	Criteria (ALU) for 'No Carryover'	Conclusion
Sample Metering	1	7.4	10600	7.5	<11.4	Pass
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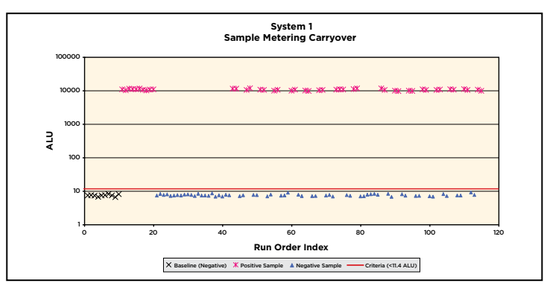

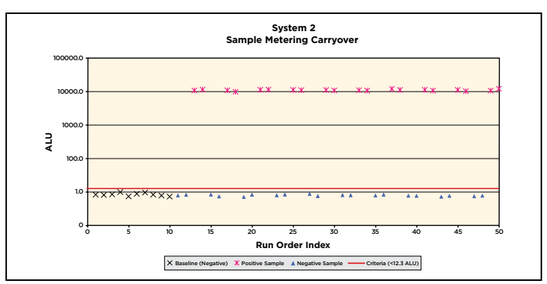

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Presented at the AACC/ASCLS Annual Meeting, July 2009, Chicago, IL

REAGENT METERING CARRYOVER

- Single–use tip eliminates carryover.
- System evaluated for dripping and splashing opportunities.
- The reagent in this evaluation was made from a high concentration of HRP and MOPS buffer. In this study, this reagent served as the contaminating fluid. Wells receiving this reagent (the potential contaminator) were interleaved with wells, not receiving this reagent. The wells not receiving the reagent, only contained fluid having minimal signal which served as the 'at risk' wells. These 'at risk' wells were then compared to a baseline run of the same fluid that has never been exposed to the potential contaminator.
- The carryover goal was selected to ensure no effect on assay performance. The carryover goal was defined as: Signal increase from a baseline ALU determination prior to contamination opportunities, not to exceed +4ALUs.
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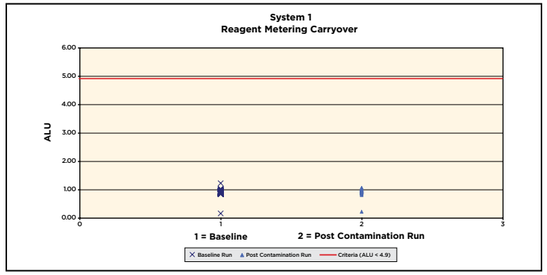

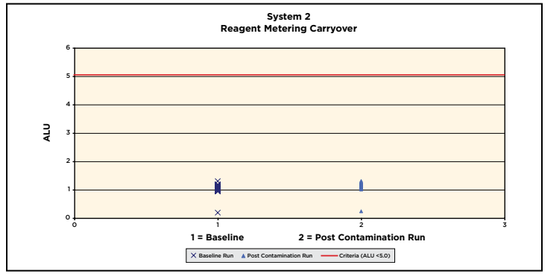

INCUBATOR MIXING AND MOTION CARRYOVER

An HRP (horseradish peroxidase) in MOPs solution (3-N-morpholino-propanesulfonicacid, 20mM, pH7.0) was used to quantify microwell incubator cross contamination.

- A serial dilution was constructed using HRP/MOPS solution with HSDB (High Sample Diluent B) as the diluent. The curve consisted of a serial dilution range of 1 part in 20; 2,000; 20,000; 200,000; 500,000; 800,000; 1,000,000; 2,000,000; 3,000,000; and 4,000,000.
- Both the outer and middle rings of the incubator were evaluated for well to well cross contamination. Both of these incubator rings were evaluated as both rings experience incubator mix moves when processing the wells.
- Undiluted HRP/MOPS solution and HSDB were alternated one after another in such a way as to fill the incubator ring and to allow for carryover opportunities. The HRP/MOPS solution generated high ALU measurements, while the wells with HSDB, if free of contamination, were to generate low ALU measurements.
- Resultant ALU measurements of the negative HSDB samples were compared to the 1:3,000,000 threshold level from the standard dilution curve.
- Results indicated that none of the ALU responses were greater than the ALU response of the 1 part to 3 million dilution, indicating that no carryover had occurred.

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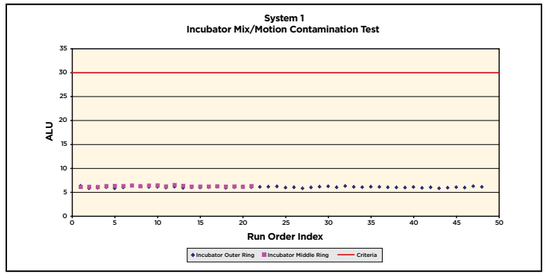

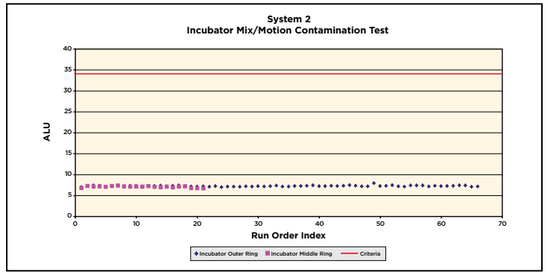

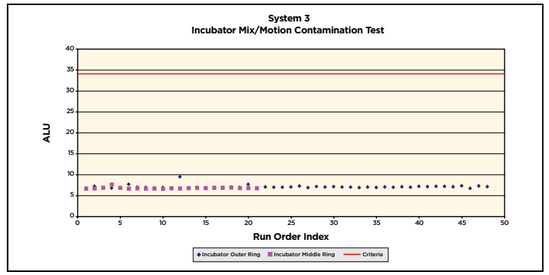

WASH PROBE CARRYOVER

In this test a potentially contaminating well (containing a high level of HRP) is washed prior to the last wash of a control well (containing low signal ALU).

- The potential carryover would present itself as unbound HRP carried over from the well wash probes, causing elevated signal in the control wells.
- The carryover goal was selected to ensure no effect on assay performance. The carryover goal was defined as: Signal increase from a baseline ALU determination prior to contamination opportunities, not to exceed +4ALUs.
- Results indicated virtually no measureable increase in ALU.

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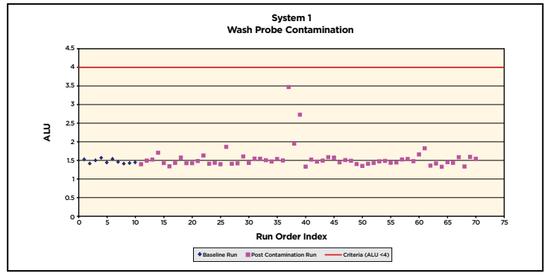

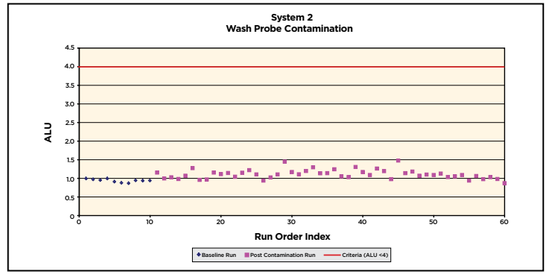

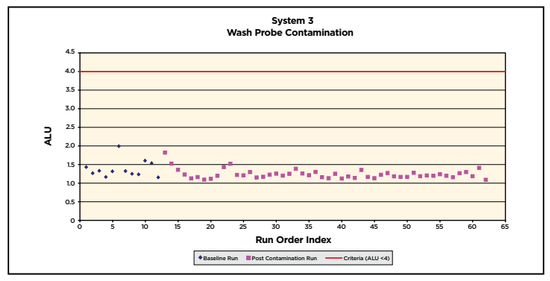

CONCLUSION

This evaluation successfully verifies that no carryover results from MicroWell sample and reagent metering, from incubator motion and mixing, and from the well wash probes on the VITROS® 5600 Integrated System and VITROS® 3600 Immunodiagnostic System. All ALU Post Contamination responses fell within the 'no carryover goals' that were chosen to ensure no effect on assay performance.

* Product Availability Subject to Local Regulatory Requirements