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White Paper

Evaluation of an Automated Humidity Check for Instrument-Read Urinalysis Strips: A Comparative Study of Three Urinalysis Analyzers

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Introduction

The integrity of urine strips is essential in obtaining accurate test results. The improper handling of strips, regardless of brand, can lead to false results and possible incorrect diagnosis. If strip bottles are not recapped or tightened completely, the contents can be exposed to humidity in room air, potentially compromising strip integrity and leading to reagent degradation and false results.

A study by Crolla et al.[1] compared three manufacturer's reagent strips and instruments after test strips were exposed to room air. Room air exposure occurs if strip containers are not closed after use as directed by the manufacturer. This white paper reports the results of that study, which compared the Siemens CLINITEK Status®+ Analyzer and MULTISTIX® 10SG urine strips to two other manufacturers' offerings.

Auto-Checks—Improving Clinical Information and Urinalysis Workflow

Novel identification (ID) bands on the Siemens MULTISTIX® family of urine reagent strips (Figure 1) provide a range of automatic quality checks (Auto-Checks) when used with the CLINITEK Status family[a] of urine chemistry analyzers (Figure 2).

Proprietary Auto-Checks technology automatically:

• Detects test strip humidity overexposure[b] —the analyzer does not report results for this condition, minimizing false-positive results

• Checks for common sample interferences[c] (high specific gravity, elevated glucose, visibly bloody urine, high pH)—the operator alerts to these interfering conditions and documents if results may be impacted

• Identifies the Siemens reagent strip type—eliminating manual data entry and saving time

Figure 1:
MULTISTIX 10 SG reagent strips with ID bands.

Figure 2:
CLINITEK Status family of analyzers employs an algorithm for humidity-compromised reagent strip detection that helps ensure quality results.

(a) CLINITEK Status® Connect, and CLINITEK Status® legacy analyzers upgraded to version 2.0 or greater.

(b) Only available with test strips that have the leukocyte pad.

(c) Feature not available in the U.S.

Materials and Methods

The Crolla et al. study evaluated results generated by three manufacturers' reagent strip and analyzer combinations:

• MULTISTIX 10 SG strips read on the CLINITEK Status+ Analyzer (Siemens Healthcare Diagnostics)

• CHEMSTRIP® 10 MD strips read on the Urisys 1100® Analyzer (Roche Diagnostics)

• Clarity® UROCHECK strips read on the Urocheck 120 Analyzer (Diagnostic Test Group)

Two sets of strips were prepared for each manufacturer. In set one, the bottle was opened and left exposed for 40-plus days to room air (22°C to 26°C) and room humidity (26% to 56%) to simulate the exposure the strips could receive by an operator not properly closing the strip container (stressed strips). The second set of bottles was left sealed until urine sample testing was conducted (unstressed strips).

Approximately 200 patient urine samples were tested across all three brand combinations. Sample numbers vary slightly because of errors/insufficient volume that occurred during testing. Table 1 details the total number of samples tested, by manufacturer. Strips were tested with patient samples for the following analytes: occult blood, leukocytes, nitrate, protein, ketone, bilirubin, urobilinogen, specific gravity, pH, and glucose.

Urine samples were tested over three months. The samples were tested across all instrument systems in duplicate for each set of strips, stressed and unstressed. These duplicate samples were run consecutively for each combination of strips and analyzers.

The study setting was an outpatient treatment center in an urban area. Nursing personnel and medical assistants completed a majority of the testing, with an occasional test being conducted by a trained (ASCP) laboratorian. This mix of operators simulated actual testing conditions in the center. All operators were trained and their competency assessed on all three analyzers before data was collected.

Results and Discussion

The study by Crolla et al. evaluated the analyte performance agreement between stressed and unstressed strips by examining the first replicate of each set tested. This agreement was then compared to the agreement between the results from the unstressed (control), replicate 1, and replicate 2.

MULTISTIX 10 SG strips read by the CLINITEK Status+ Analyzer are designed to return an error flag rather than an actual result when the system detects that the strips have been potentially compromised due to excessive exposure to environmental humidity. More than 95% (95% confidence interval: 95.9% to 99.7%) of the stressed MULTISTIX 10 SG strips returned error flags when tested on the CLINITEK Status+ Analyzer, correctly suggesting that the strips had been compromised and were no longer suitable for use (Table 1).

Table 1: Error-flagged results for unstressed and stressed (humidity compromised) test strips, by manufacturer.

Manufacturer	Condition	Sample Size	# Flagged Results	Percent Flagged Results
Siemens	Unstressed	207	4	1.9%
	Stressed	212	209	98.6%
Roche	Unstressed	198	0	0.0%
	Stressed	212	0	0.0%
Diagnostic Test Group	Unstressed	206	1	0.5%
	Stressed	214	1	0.5%

The flagged sample rate for environmentally stressed MULTISTIX 10 SG strips was 98.6%. Therefore, all subsequent analysis of stressed performance in this study included only those strips manufactured by Roche and Diagnostic Test Group, as the Siemens strips did not provide performance data post-stress.

The performance of the unstressed strips (control condition) was the percent agreement (both exact and ±1 group) between two replicates of unstressed strips for all three manufacturers' materials. The authors used a ±1 block scale, as this is the usual acceptable variance for urine strips.

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The results summarized in Tables 2 and 3 demonstrate no significant difference ($p>0.05$) in replicate agreement among the three manufacturers' strips in an unstressed condition, using either exact or ±1 block scale. Based on replicate agreement rates for unstressed strips of the other manufacturers, there were only two instances of significantly different % agreements for the two replicates of unstressed strips. These instances are highlighted.

For Diagnostic Test Group and Roche, performance of environmentally stressed strips was assessed by determining the percent agreement between the first replicate of the unstressed strip and the first replicate of the stressed strip. Results are summarized in Tables 4 and 5 for each of the analytes. Those analytes where the percent agreement for the stressed conditions differs significantly from the percent agreement for the control conditions are flagged as "Significant" ($p<0.05$) in the tables.

Table 2: Unstressed strips—replicate agreement (exact).

Test	Vendor	Percent Exact Agreement
Bilirubin	Diagnostic Test Group	96.1%
	Roche	84.8%
	Siemens	96.6%
Occult Blood	Diagnostic Test Group	94.1%
	Roche	94.4%
	Siemens	89.7%
Glucose	Diagnostic Test Group	96.6%
	Roche	97.0%
	Siemens	97.5%
Ketone	Diagnostic Test Group	96.6%
	Roche	93.9%
	Siemens	95.1%
Leukocytes	Diagnostic Test Group	87.3%
	Roche	84.3%
	Siemens	88.7%
Nitrates	Diagnostic Test Group	98.0%
	Roche	96.5%
	Siemens	99.0%
pH	Diagnostic Test Group	77.6%
	Roche	91.4%
	Siemens	86.2%
Protein	Diagnostic Test Group	92.2%
	Roche	87.9%
	Siemens	95.1%
Specific Gravity	Diagnostic Test Group	80.0%
	Roche	74.7%
	Siemens	78.3%
Urobilinogen	Diagnostic Test Group	92.7%
	Roche	86.4%
	Siemens	96.6%

Table 3: Unstressed strips—replicate agreement (±1 group).

Test	Vendor	Percent Within 1 Group Agreement
Bilirubin	Diagnostic Test Group	99.51%
	Roche	100.0%
	Siemens	100.0%
Occult Blood	Diagnostic Test Group	99.5%
	Roche	99.5%
	Siemens	100.0%
Glucose	Diagnostic Test Group	99.0%
	Roche	99.5%
	Siemens	100.0%
Ketone	Diagnostic Test Group	100.0%
	Roche	99.5%
	Siemens	100.0%
Leukocytes	Diagnostic Test Group	99.5%
	Roche	91.4%
	Siemens	98.0%
pH	Diagnostic Test Group	97.6%
	Roche	99.5%
	Siemens	99.5%
Protein	Diagnostic Test Group	100.0%
	Roche	98.0%
	Siemens	100.0%
Specific Gravity	Diagnostic Test Group	98.0%
	Roche	94.9%
	Siemens	96.6%
Urobilinogen	Diagnostic Test Group	99.0%
	Roche	99.0%
	Siemens	98.5%

Table 4: Performance of stressed vs. unstressed strips (exact).

Test	Manufacturer	Second Replicate Condition	Percent Exact Agreement	Significant (P<0.05)
Bilirubin	Diagnostic Test Group	Unstressed Stressed	96.10% 79.44%	Significant
	Roche	Unstressed Stressed	84.85% 83.02%	
Occult Blood	Diagnostic Test Group	Unstressed Stressed	94.1% 76.5%	Significant
	Roche	Unstressed Stressed	94.4% 85.8%	Significant
Glucose	Diagnostic Test Group	Unstressed Stressed	96.6% 24.3%	Significant
	Roche	Unstressed Stressed	97.0% 70.8%	Significant
Ketone	Diagnostic Test Group	Unstressed Stressed	96.6% 21.1%	Significant
	Roche	Unstressed Stressed	93.9% 77.4%	Significant
Leukocytes	Diagnostic Test Group	Unstressed Stressed	87.3% 17.4%	Significant
	Roche	Unstressed Stressed	84.3% 62.3%	Significant
Nitrates (binary response)	Diagnostic Test Group	Unstressed Stressed	98.0% 14.1%	Significant
	Roche	Unstressed Stressed	96.5% 11.3%	Significant
pH	Diagnostic Test Group	Unstressed Stressed	77.6% 66.2%	
	Roche	Unstressed Stressed	91.4% 83.0%	
Protein	Diagnostic Test Group	Unstressed Stressed	92.2% 89.7%	
	Roche	Unstressed Stressed	87.9% 49.1%	Significant
Specific Gravity	Diagnostic Test Group	Unstressed Stressed	80.0% 80.3%	
	Roche	Unstressed Stressed	74.7% 48.6%	Significant
Urobilinogen	Diagnostic Test Group	Unstressed Stressed	92.7% 7.5%	Significant
	Roche	Unstressed Stressed	86.4% 33.0%	Significant

Table 5: Performance of stressed vs. unstressed strips (±1 group).

Test	Vendor	Condition	Percent Within 1 group Agreement	Significant (P<0.05)
Bilirubin	Diagnostic Test Group	Unstressed Stressed	99.5% 99.5%	
	Roche	Unstressed Stressed	100.0% 100.0%	
Occult Blood	Diagnostic Test Group	Unstressed Stressed	99.5% 85.9%	Significant
	Roche	Unstressed Stressed	99.5% 95.3%	
Glucose	Diagnostic Test Group	Unstressed Stressed	99.0% 57.5%	Significant
	Roche	Unstressed Stressed	99.5% 96.7%	
Ketone	Diagnostic Test Group	Unstressed Stressed	100.0% 100.0%	
	Roche	Unstressed Stressed	99.5% 99.1%	
Leukocytes	Diagnostic Test Group	Unstressed Stressed	99.5% 27.7%	Significant
	Roche	Unstressed Stressed	91.4% 79.2%	Significant
pH	Diagnostic Test Group	Unstressed Stressed	97.6% 98.6%	
	Roche	Unstressed Stressed	99.5% 99.1%	
Protein	Diagnostic Test Group	Unstressed Stressed	100.0% 100.0%	
	Roche	Unstressed Stressed	98.0% 91.5%	Significant
Specific Gravity	Diagnostic Test Group	Unstressed Stressed	98.0% 98.6%	
	Roche	Unstressed Stressed	94.9% 88.2%	
Urobilinogen	Diagnostic Test Group	Unstressed Stressed	99.0% 11.3%	Significant
	Roche	Unstressed Stressed	99.0% 97.6%	

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Nitrate tests return a binary (positive/negative) result and, therefore, are not a candidate for analysis using the ±1 group criterion. For nitrate, Roche and Diagnostic Test Group stressed strips had only 11.3% to 14.1% agreement between the nitrate results from replicate 1 of the stressed and replicate 1 of the unstressed conditions as opposed to 96.5% to 98% agreement between the replicates of unstressed condition (control).

For non-binary analyte responses (responses that are numeric), the greatest percentage of disagreement between the unstressed and stressed strips for exact block output was observed with glucose, ketone, leukocyte, and urobilinogen tests on both Diagnostic Test Group and Roche strips. When the agreement criterion was expanded to ±1 group, the disagreement was reduced to a large extent for the Roche strips with the exception of leukocyte (79.2% agreement) and protein (91.5% agreement), both agreement rates still being significantly different from the unstressed (control) agreement. For the Diagnostic Test Group strips, the percentage agreement for glucose (57.5%), leukocytes, (27.7%), and urobilinogen (11.3%) remained significantly lower than their respective unstressed conditions.

Based on the data for the Diagnostic Test Group and Roche strip and analyzer combinations, there were significant differences between stressed and unstressed results because of exposure to room air and humidity. The possibility then exists for an inaccurate diagnosis and treatment based upon the erroneous results generated from the exposed strips. The Siemens analyzer has an automatic warning mechanism that prevents results from being reported when humidity exposure is detected. In this controlled study, approximately 98% of the time, this system would have prevented inaccurate reporting and generated an error message instead of generating a result.

Conclusion

Auto-Checks technology provided with Siemens MULTISTIX 10 SG urinalysis strips and the CLINITEK Status+ Analyzer allows for the automatic detection of strips that may have been affected by excess humidity.

The CLINITEK Status+ Analyzer was able to detect MULTISTIX 10 SG strips that had been compromised by humidity, and prevented potentially erroneous results from being reported.

Neither the Roche nor Diagnostic Test Group analyzers incorporate a humidity detection system. Both of these analyzers reported results for patient samples despite the test strips being compromised by humidity. These reported results are likely to be inaccurate, as analyte results differed between exposed (stressed) and unexposed (unstressed) test strips for the same patient sample.

During numerous inspections of laboratories, Crolla et al. have observed that it is not uncommon to see urine-strip bottles with the cover ajar or completely removed. Their study has shown the need for testing entities to strongly enforce the individual manufacturer's recommendation to keep strip containers capped when strips are not being removed for analysis. It also would be advantageous in situations where there are multiple operators, which makes it difficult to ascertain compliance, to use a system that would notify the tester of a compromised strip and not allow testing.

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