ADVANCED INSTRUMENTS

WHITEPAPER

EVALUATION OF COMMERCIALLY AVAILABLE OSMOMETER CONTROL SOLUTIONS

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BACKGROUND

Measured osmolality using freezing point depression is an important screening tool for the differential diagnosis of body fluid disorders. Advanced Instruments osmometers are trusted to give rapid and accurate measurements of a body fluid's osmolality. Even a slight shift in the osmolality of a patient sample can be diagnostically significant, making a robust osmometer quality control program critically important.

This paper reviews the product specifications of commercially available osmolality controls for serum and urine. These control specifications are then compared and evaluated for suitability as an osmolality control in the clinical environment.

As the instrument manufacturer, Advanced Instruments recommends using Protinol™ Protein-Based Controls and Renol™ Urine Osmolality Controls as the appropriate matrix-based control solutions to confirm osmometer performance in a clinical setting. These controls and Clinitrol™ 290 Reference Solution should be run daily prior to testing patient specimens. **Protinol and Renol verify instrument performance at the most clinically relevant osmolality levels and offer the tightest ranges amongst commercially available control solutions.**

CONTROL SOLUTIONS BEST PRACTICES

The following criteria are important to ensure a robust osmometer quality control program.

1. **Controls should challenge medical decision points.**

- **Freezing point osmometers make measurements over an extremely broad range so testing controls at medical decision points ensures the accuracy of the instrument in the clinically relevant range.**

2. **Controls should have tight ranges to quickly spot shifts in instrument performance.**

- Controls with a reliably tight acceptance range enable the detection of small shifts in instrument performance. Even a slight shift is patient osmolality values can be diagnostically significant so control ranges should have an accordingly tight acceptance range.

3. **Controls should mimic patient specimens.**

- To provide the best control for osmolality testing, a solution should be in a matrix that closely resembles the specimen being tested. The more similar a control is to the patient sample the greater confidence an operator has in the instrument performance with that sample type. [1]

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4. **Controls should support compliance to regulatory guidelines.**

- The international standard for medical laboratories (ISO 15189:2012) specifies that "The laboratory should choose concentrations of control materials, wherever possible, especially at or near clinical decision values, which ensure the validity of decisions made".[2] This standard is referenced by multiple national bodies such as UKAS.[3]
- In the United States, Clinical Laboratory Improvement Amendments (CLIA) requires the daily use of at least two different control concentrations.[4]
- The College of American Pathologists (CAP) further requires that these two concentrations be at clinically relevant decision levels.[5]

5. **Controls should have a manufacturer provided peer group for results comparison.**

- Peer group programs serve as an external quality control assessment where laboratories can compare their control solution results with those from other laboratories to identify trends.

SERUM OSMOLALITY CONTROLS

Following the regulations and guidelines previously outlined, an ideal serum control solution should mimic patient specimens and provide values at medically relevant decision points. For this paper, Advanced Instruments reviewed the product specifications of three serum control solutions: Advanced Instruments Protinol, Bio-Rad Liquid Assayed Multiqual®, and Randox Assayed Chemistry Premium Plus (Table 1).

All three brands of serum control solutions examined in this paper are formulated in a clinically relevant matrix. However, the requirement to provide values at medically relevant decision points is not universally met.

In healthy patients, a normal serum osmolality value for adults and seniors is between 285-295 mOsm/kg H_2O. In children, the normal range is 275-295 mOsm/kg H_2O. Possible critical serum osmolality values are <265 mOsm/kg H_2O or >320 mOsm/kg H_2O.[6]

The following graph (Figure 1) compares the mean values and acceptable performance ranges of serum controls from three manufacturers to clinically normal and possible critical patient serum results.

Advanced Instruments Protinol is the only serum control examined that has control levels at clinically relevant low, normal, and high values. The 240 mOsm/kg H_2O level is near the low critical value, the 280 mOsm/kg H_2O level is within the normal range, and the 320 mOsm/kg H_2O level is near the high critical value.

Bio-Rad Liquid Assayed Multiqual has only one level within the clinical range of patient values. Level one is near the critical high value, with no levels covering the critical low or normal range.

Randox Assayed Chemistry Premium Plus does not offer levels near low, normal, or high values for serum osmolality. All three levels far exceed the critical high value of 320 mOsm/kg H_2O.[6]

To ensure laboratories are confirming instrument performance at clinically relevant levels, Advanced Instruments recommends Protinol Protein-Based Osmolality Controls for use with your Advanced Instruments osmometer.

Comparison of Serum Control Ranges to Clinical Reference Ranges

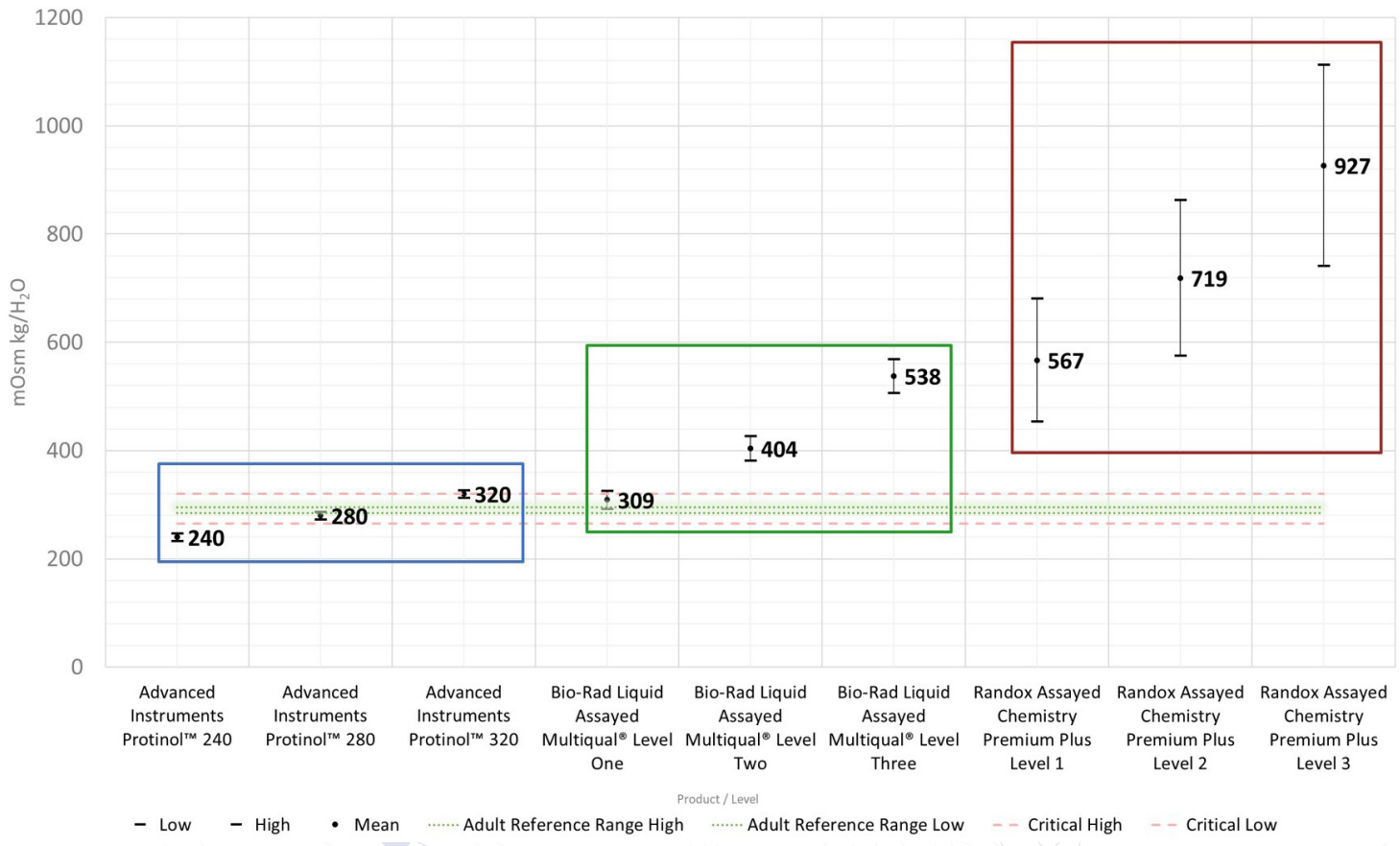

Figure 1. Shows the product insert specified mean values and ranges of serum controls from three manufacturers, averaged across recently available lots (see Table 1 in Appendix). The normal serum range is highlighted in green and possible critical values are indicated by red dotted lines.

URINE OSMOMLALITY CONTROLS

Urine osmolality values range widely depending on many variables such as hydration status. For a healthy adult, urine osmolality values can range from 50 and 1200 mOsm/kg H_2O depending on the subject's fluid intake.[6]

For this paper, Advanced Instruments reviewed the product specifications of four urine control solutions: Advanced Instruments Renol, Bio-Rad Liquichek™ Urine Chemistry Control, Quantimetrix Dropper® Urine Chemistry Control, and Thermo Scientific™ MAS™ UrichemTRAK Controls (Table 2).

The urine controls examined in this paper all fall within that range, however, not all control solutions offer reliably tight ranges. As a small difference in a patient's urine osmolality value can be diagnostically significant, it is important that controls have a tight acceptability range so operators can detect small shifts in instrument performance.

Figure 2 below shows the mean values and acceptable performance ranges of urine controls from four manufacturers.

At +/- 10 mOsm/kg H_2O, Advanced Instruments Renol offers the tightest range of urine control solutions examined. Of the evaluated controls, Renol also provides the lowest value at 300 mOsm/kg H_2O to verify performance across a wider range.

For these reasons, Renol Urine Osmolality Controls are recommended by Advanced Instruments for use with your Advanced Instruments osmometer.

Comparison of Urine Control Ranges

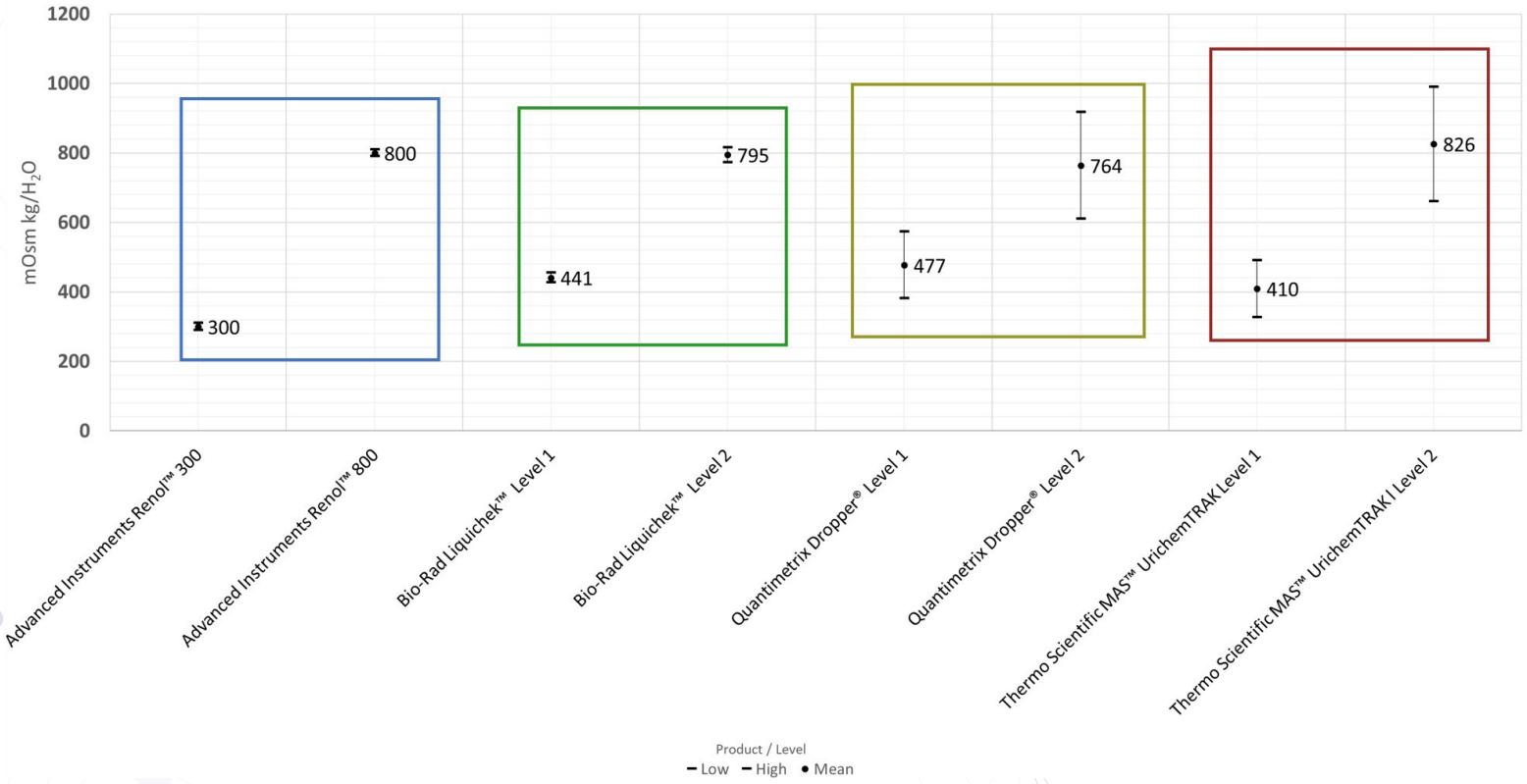

Figure 2. Shows the product insert specified mean values and ranges of urine controls from four manufacturers, averaged across recently available lots (see Table 2 in Appendix).

SUMMARY

Advanced Instruments recommends using Protinol Protein-Based Controls and Renol Urine Osmolality Controls to confirm osmometer performance prior to testing patient samples.

Protinol and Renol are designed specifically for osmolality testing and meet or exceed all of the requirements of a robust quality control program.

CRITERIA	PROTINOL	RENOL	COMMENTS
Controls should challenge medical decision points.	✓	✓	Protinol provides three levels at clinically relevant low, normal, and high values. Renol provides two levels within the expected range of human urine. Renol also provides the lowest value at 300 mOsm/kg H_2O to verify performance across a wider range.
Controls should have tight ranges to quickly spot shifts in instrument performance.	✓	✓	Protinol provides the tightest available range at +/- 7 mOsm/kg H_2O. Renol provides the tightest available range at +/- 10 mOsm/kg H_2O.
Controls should mimic patient specimens.	✓	✓	Protinol and Renol are formulated to mimic patient specimens.
Controls should adhere to regulatory guidelines.	✓	✓	Protinol and Renol both provide at least two levels at clinically relevant decision points, satisfying ISO, CLIA, CAP, and UKAS standards.
Controls should have a manufacturer provided peer group for results comparison.	✓	✓	Laboratories using Protinol and Renol have access to a free online peer group AdvancedQC™ where they can access instant and monthly peer comparison reports.

For more information on these controls please contact Advanced Instruments.

REFERENCES

1. Westguard, J.O., Ph.D., 2002, Basic QC Practices, 2nd Edition: Training in Statistical Quality Control for Heath Care Laboratories, Westguard QC, Inc., pp. 158-160.
2. International Organization for Standardization. (2012). Occupational health and safety management systems—Requirements with guidance for use (ISO Standard No. 45001:2018). https://www.iso.org/standard/63787.html
3. Medical Laboratory accreditation (ISO 15189). (n.d.). Retrieved September 30, 2020, from https://www.ukas.com/services/accreditation-services/medical-laboratory-accreditation-iso-15189/
4. 42 CFR § 493.1256 - Standard: Control procedures: https://www.govinfo.gov/content/pkg/CFR-2011-title42-vol5/pdf/CFR-2011-title42-vol5-part493-subpartK.pdf
5. College of American Pathologists: Commission on Laboratory Accreditation, 2018, Chemistry and Toxicology Checklist, College of American Pathologists, CHM.13900.
6. Pagana, K. D., Pagana, T. J., & Pagana, T. N. (2015). Mosby's Diagnostic and Laboratory Test Reference (pp. 669-672). Saint Louis, MO: Elsevier.

APPENDIX

Table 1. Serum Osmolality Control Lots Included in Analysis

Serum Osmolality Control	Level 1 Lot	Level 2 Lot	Level 3 Lot
Advanced Instruments Protinol™	16428	16429	16430
Advanced Instruments Protinol™	MW20F02089	MW20D30793	MW20D30795
Advanced Instruments Protinol™	16330	16331	16332
Advanced Instruments Protinol™	MW20C04217	MW20C11302	MW20C11307
Advanced Instruments Protinol™	16144	16145	16146
Bio-Rad Liquid Assayed Multiqual®	45871	45872	45873
Bio-Rad Liquid Assayed Multiqual®	45831	45832	45833
Bio-Rad Liquid Assayed Multiqual®	45861	45862	45863
Bio-Rad Liquid Assayed Multiqual®	45811	45812	45813
Bio-Rad Liquid Assayed Multiqual®	45801	45802	45803
Randox Assayed Chemistry Premium Plus	287UL	1272UN	986UE
Randox Assayed Chemistry Premium Plus	306UL	1363UN	1062UE
Randox Assayed Chemistry Premium Plus	332UL	1484UN	115UE

Table 2. Urine Osmolality Control Lots Included in Analysis

Urine Osmolality Control	Level 1 Lot	Level 2 Lot
Advanced Instruments Renol™	P90031	P90032
Advanced Instruments Renol™	MW20F19243	MW20G07359
Advanced Instruments Renol™	MW20D14641	MW20A20635
Advanced Instruments Renol™	MW19K04740	MW19J25623
Bio-Rad Liquichek™ Urine Chemistry Control	68601T	68602T
Bio-Rad Liquichek™ Urine Chemistry Control	68591T	68592T
Bio-Rad Liquichek™ Urine Chemistry Control	68581T	68582T
Bio-Rad Liquichek™ Urine Chemistry Control	68551T	68552T
Quantimetrix Dropper® Urine Chemistry Control	43451	43452
Quantimetrix Dropper® Urine Chemistry Control	43441	43442
Thermo Scientific™ MAS™ UrichemTRAK Controls	UC20081	UC20082
Thermo Scientific™ MAS™ UrichemTRAK Controls	UC21121	UC21122
Randox Assayed Chemistry Premium Plus	332UL	1484UN