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Performance Evaluation of Commercially Available Osmometer Control Solutions

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“Even a slight shift in the osmolality of a patient sample can be diagnostically significant, making an accurate control system extremely important.”

BACKGROUND

Freezing point osmometry is a widely applied clinical diagnostic tool primarily used for the differential diagnosis of many water balance disorders. Human serum and urine specimens are commonly measured using freezing point depression osmometers which measure osmolality in terms of concentration of particles in solution. This measurement can be used clinically as a STAT measurement for the screening of toxins. Because it must be trusted to give an accurate, rapid response for patient diagnosis, high performance of the instrument must be certain at all times. This is achieved with a control system. Even a slight shift in the osmolality of a patient sample can be diagnostically significant, making an accurate control system extremely important. To provide the best control for osmolality testing, a matrix control solution should be used. Matrix refers to the substances from which the control solution is prepared, and an appropriate matrix control will closely resemble the human specimen being tested. This close relationship between control solution and human sample provides assurance that the control and the human specimen will behave the same way when tested[1]. Matrix controls come in either liquid or lyophilized form.

CLIA regulations provided by the Centers for Disease Control simply require the daily use of two different control concentrations[2]. This regulation is expounded upon by the College of American Pathologists (CAP) to require that these two concentrations be at clinically relevant decision levels[3].

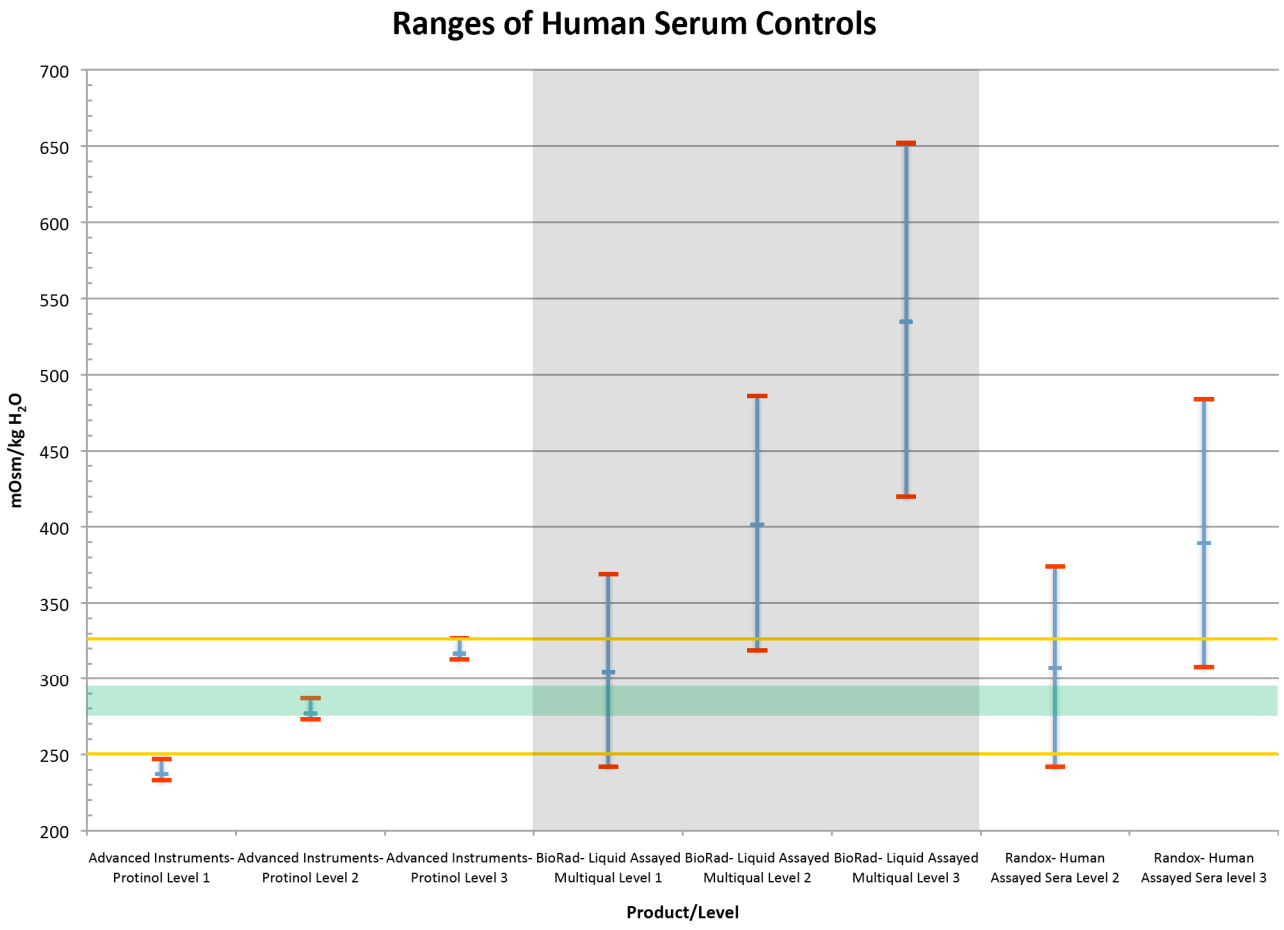
Freezing point osmometers can take measurements over an extremely broad range, so testing controls at decision levels ensures the accuracy of the instrument in the desired range.

Other important parameters to evaluate for a good osmometer control solution are the vial-to-vial and lot-to-lot variability. Under this parameter, liquid controls offer a clear advantage over lyophilized controls. Lyophilized controls must be reconstituted in the laboratory which is a difficult process to repeat with precision. This increases the likelihood of vial-to-vial variability because it opens a window for operator error. Liquid controls remove this error as they eliminate the reconstitution process. Low lot-to-lot variability also decreases the chances for operator error. In establishing control values for a new lot, it is more likely that the operator will notice a shift in the instrument if each lot of control is always in a reliably tight range.

Serum Osmometer Controls

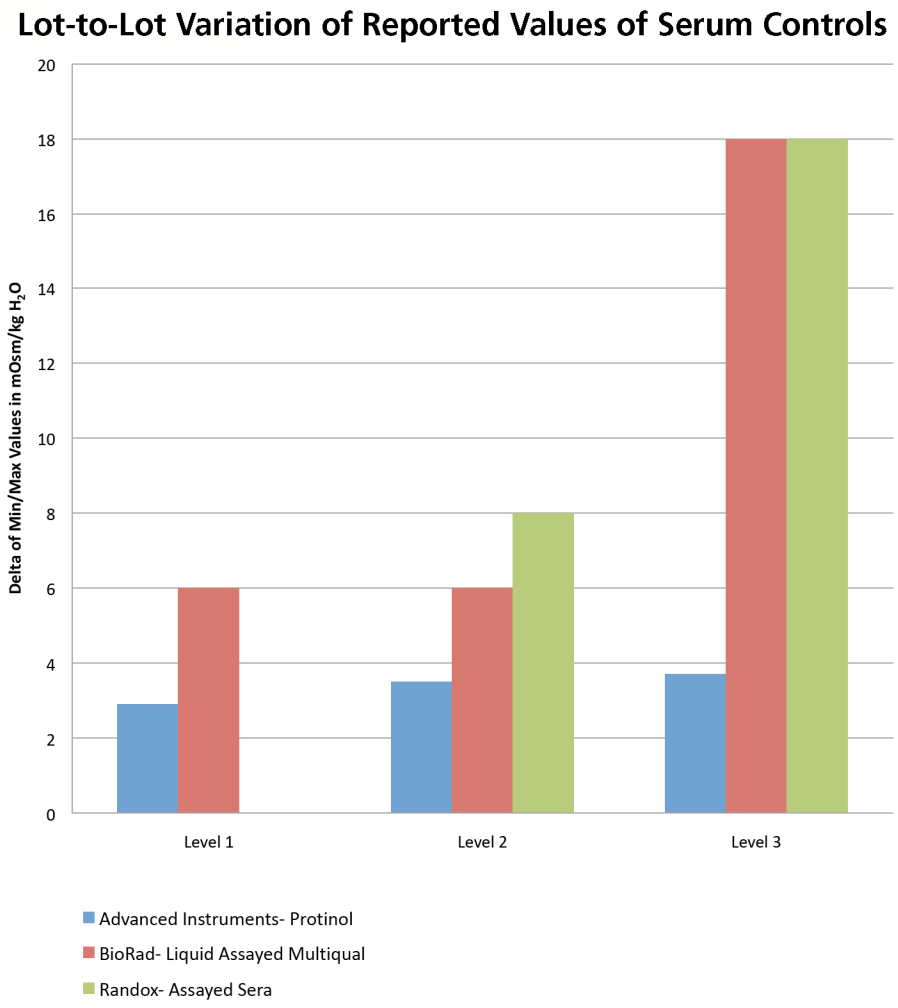
For most healthy adults, the osmolality of human serum will fall between 275-295 mOsm/kg H_20[1]. The mean extreme values of human serum are, at the low end, 250 mOsm/kg H_20 and, at the high end, 326 mOsm/kg H_20[2]. Following the regulations and guidelines already outlined, an ideal control solution should provide values near these levels. Figure 1 shows the mean values and the acceptable performance ranges of three leading human serum control manufacturers: Advanced Instruments, Bio-Rad, and Randox. Figure 2 (next page) shows the lot-to-lot variation of the actual mean values as labeled on the products by the manufacturers.[3]

Figure 1. Displays the acceptable performance range and average values as stated by the manufacturers of serum controls offered by three manufacturers, the normal human serum range is highlighted in green and the mean extreme values are highlighted in orange.



Serum Osmometer Controls (cont.)

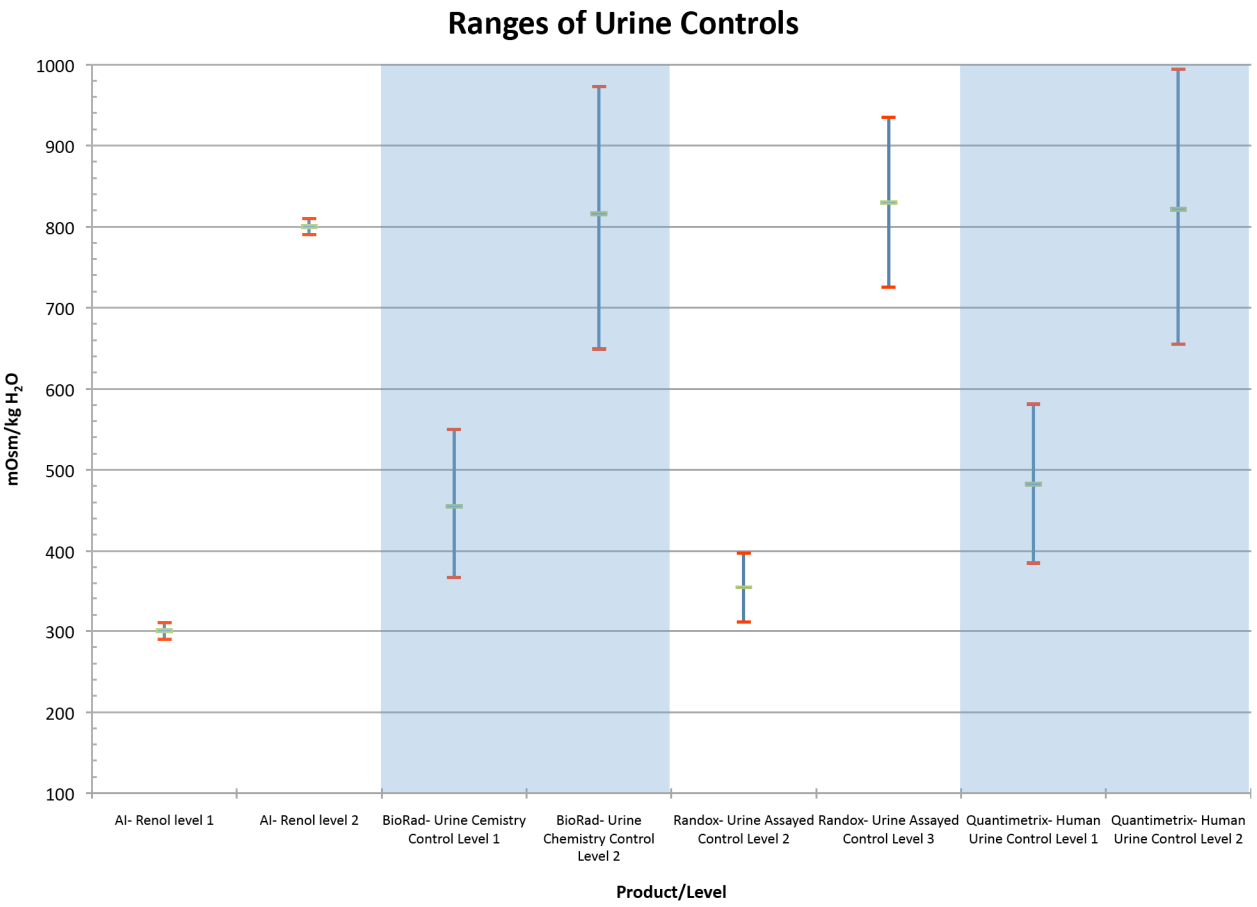
Figure 2. Shows the difference between the minimum reported value and the maximum reported value of all the observed lots of serum controls (Randox only ofers Levels 2 and 3)



Urine Osmometer Controls

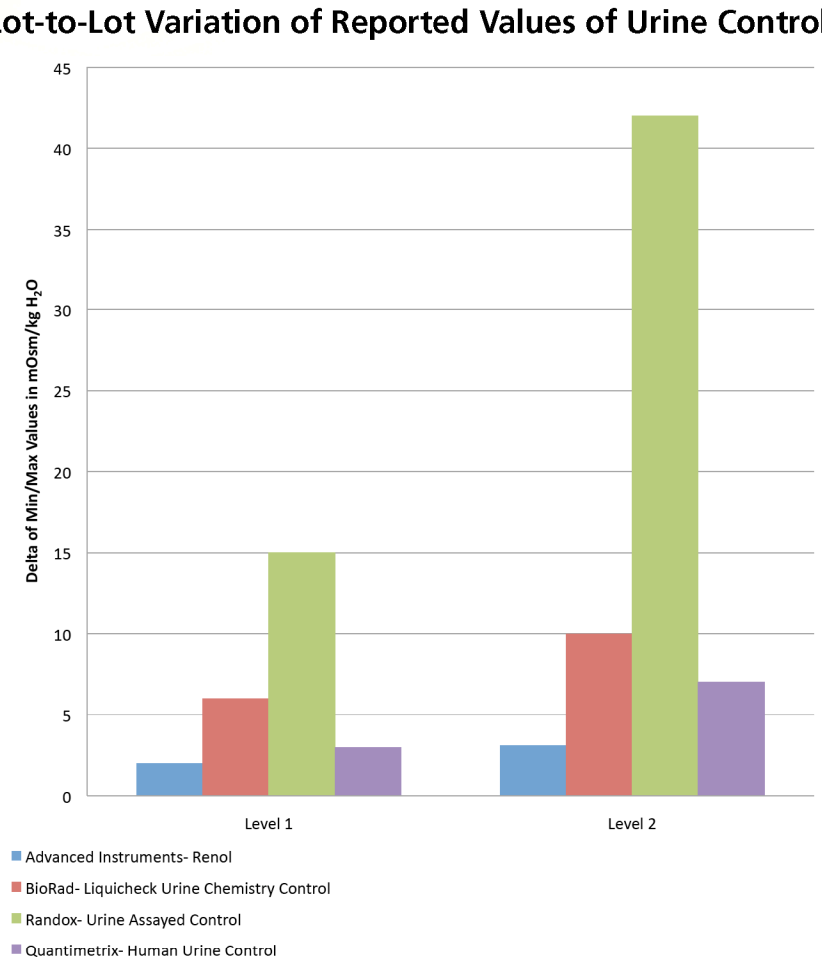
For healthy adults, the osmolality of urine can range widely depending on many fluctuating variables. Therefore normal values and critical limits cannot be universally applied as they can be with human serum. A healthy adult could have urine osmolality values that read between 50 and 1200 mOsm/kg H_20 depending on the subject's fluid intake[1]. Decision levels must be established on a patient to patient basis, making the CAP guideline to have both concentrations of control be at relevant decision points inapplicable for these controls. A tight acceptability range and low vial-to-vial and lot-to-lot variability remain important in helping the operator detect drifts in the measuring instrument more effectively. Figure 3 displays the acceptable performance ranges and averages of four leading human urine control manufacturers: Advanced Instruments, Bio-Rad, Randox, and Quantimetrix. Figure 4 (next page) shows the lot-to-lot variation of actual mean values of controls for these four manufacturers.

Figure 3. Displays the acceptable performance range and average values as stated by the manufacturers of four different human serum control manufacturers



Urine Osmometer Controls (cont.)

Figure 4. Shows the difference between the minimum reported value and the maximum reported value of all the observed lots of urine control



ANALYSIS

While all three manufacturers meet the CLIA requirement of providing two concentrations of serum control, both Advanced Instruments and Bio-Rad provide three levels for added flexibility. However, the CAP stipulation that these controls be near relevant decision points is not uniformly met. The extreme levels and the normal human range have been mentioned previously and the CAP guidelines indicate that the levels should be near these important decision points. Protinol achieves this. The 240 mOsm/kg H_20 level is near the minimum extreme value, the 280 mOsm/kg H_20 level is within the normal range, and the 320 mOsm/kg H_20 level is near the high extreme value.

Bio-Rad has only one concentration that is a possible measurement of human serum. This level, which averages 305 mOsm/kg H_20, is above the range of normal human serum, though it could be considered near the extreme high value. The other two concentrations, 402 and 535 mOsm/kg H_20, are not possible patient values, meaning Bio-Rad only offers one level that is near a relevant decision point. It does not offer a concentration near the low extreme nor does it offer a concentration with the normal human serum range.

ANALYSIS (cont.)

Randox has one concentration, 304 mOsm/kg H_20, that is a feasible value for human serum. The higher level, which averages 384 mOsm/kg H_20 is, again, well above a relevant decision point, and falls short of the CAP guidelines.

Westguard rules also prefer low vial-to-vial and lot-to-lot variability because it decreases the likelihood of an operator overlooking a shift or bias in the instrument. After reviewing the lot-to-lot variation of actual mean values for the serum controls it is clear that Protinol® has the least variability. The operator can be sure that each vial and each lot of Protinol will be very nearly the same value every time. This makes an inaccurate instrument very easy to spot. Bio-Rad and Randox offer products with greater variability, as well as a very wide range of performance acceptability.

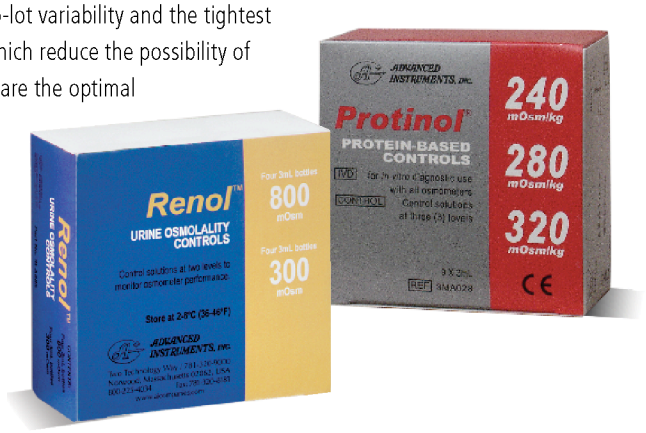
Therefore the instrument could have a vast shift, however the control would still technically be within specification. Randox also offers their products in lyophilized form which creates more potential for error in the rehydration process.

The same trend in lot variability resurfaces in analyzing urine controls. Renol™, the Advanced Instruments offering, shows a clear advantage in least variation from lot-to-lot. This will signal a shift in instrument performance far sooner than will the products from Bio-Rad, Randox, and Quantimetrix. With those products, a user could hypothetically have an accurate reading of 800 mOsm/kg H_20 one day, then the next get a reading from the same vial of 900 mOsm/kg H_20 and the product would not be out of specification.

"For serum controls, only Advanced Instruments' Protinol meets CAP guidelines by offering multiple levels near relevant decision points."

CONCLUSION

Though all the products analyzed meet the CLIA regulation of providing two control concentrations, not all of them sufficiently support good QC practices. For serum controls, only Advanced Instruments' Protinol meets CAP guidelines by offering multiple levels near relevant decision points. Additionally, both Protinol and Renol have the smallest lot-to-lot variability and the tightest acceptable performance ranges which reduce the possibility of operator error. Protinol and Renol are the optimal matrix based control solutions to ensure the accuracy of an osmometer when testing human serum and urine samples.



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