#1

# Handling of Samples with Elevated Total Proteins

Prepared by: S.Smeal/AS/DN
Revised 12/4/13 Dr. David Morris PhD_____

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3/13/19

**Annual Review**

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Revisions:

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| Added Chloride 3/2019 DN | | |
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Lifespan AMC-Department of Pathology

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## Policy

Although the manufacturer does not note any particular interference with the performance of electrolytes on samples containing high levels of Total Protein, our internal studies and the literature have clearly shown that there is a negative bias on electrolyte results (sometimes classified as pseudohyponatremia) if the Total Protein exceeds or is equal to 10.0 g/dL, with some methods. The effect is a result of the methodology employed on the Beckman-AU, an Indirect ISE. It employs a sample dilution prior to analysis with the calculated assumption of body water per ml of patient sample.
To circumvent this issue, we have employed the use of the I-Stat to measure the Sodium and Potassium on these samples which contain high levels of Total Protein. The I-Stat utilizes a Direct ISE methodology where the sample is measured without sample dilution.

One of the challenges has been to identify these patients that have high levels of Total Protein. **If in any of the following scenarios, a Total Protein of ≥ 10.0 g/dL is obtained, the specified procedure which follows should be performed. Some of the steps we have taken include**:

- If the Total Protein is ordered, we have set the autoverification process on Remisol to "hold" any sample where the Total Protein concentration is greater than or equal to 10.0 g/dL. Remisol will also generate a comment to the Tech to notify them to perform IStat.
- If the Anion Gap is < 2, a Total Protein will be performed via a reflex rule in Remisol. (no charge to patient)
- If a patient has been identified either through prior analysis or by diagnosis to be a Multiple Myeloma patient, a Total Protein should be performed, if not already ordered. If the result is ≥ 10.0 g/dL, the sample should be performed on the I-Stat.

## Procedure

Once a sample has been determined to have a Total Protein concentration of ≥ 10.0 g/dL, the following actions should be taken.

- The sample should be analyzed on the I-Stat, following that procedure for Chloride, Sodium and Potassium.
- The I-Stat results obtained should then be manually entered as the reportable results in place of the results obtained on the AU, and the canned comment (@ISTA) added to the Sodium result. The phrase states, "Sodium, Potassium and Chloride results reported at this time/date were performed on the I Stat analyzer. Presence of high serum protein concentrations may interfere with accurate measurements of electrolytes on the Beckman Analyzer, which is the lab's routine method."
- If critical, the result should be called to the ordering physician as per protocol.

#2

# I-STAT Testing

## Chloride/Sodium/Potassium / BF pH

Copy 3/13/19

Adopted: 3/3/16 Syed Latif PhD _____

Prepared/Revised by: D.Lee/D.Smeal/D. Napert

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**MANUFACTURER**: I-STAT Corp/Abbott Diagnostics

## PRINCIPLE:

The I-STAT System delivers quantitative results for a panel of tests on a small sample of whole blood in less than two minutes. Portability and simplicity of operation permit its use by qualified health care professionals at the point of patient care.

To perform a test, the operator fills a cartridge with sample, seals the cartridge with its snap closure, and inserts the cartridge into the analyzer. Insertion of a cartridge activates the analyzer. The single-use cartridge contains the calibrating solution, a sample handling system and all sensors for a panel of tests. The analyzer automatically controls all functions of the system including fluid movement within the cartridge, calibration, and continuous quality monitoring. This degree of automation, along with the ability to test fresh whole blood, eliminates many sources of error.

During the testing cycle, the operator must enter an operator and a patient identification number. When the testing cycle is completed, results are displayed and a complete test record is stored. These test results can be retrieved and viewed on the analyzer. The test record is transmitted to the Central Data Station where it can be printed and/or transmitted to the Laboratory Information System.

### ANALYZER FUNCTIONS

The I-STAT analyzer is a microprocessor-controlled electromechanical instrument which:

1. Identifies the cartridge type
2. Controls the flow of fluids within the cartridges
3. Applies required electrical signals to certain types of sensors within the cartridges
4. Measures electrical signals generated at the sensors
5. Calculates concentrations of analytes using the generated electrical signals
6. Displays the results in numerical values and on bar graphs
7. Communicates the results to a printer and computer via infrared link
8. Senses and communicates operational errors
9. Maintains an internal clock/calendar
10. Stores all test records and electronic Simulator QC results

### MICROPROCESSOR

The microprocessor control system manages all functions of the analyzer. It accesses three types of memory storage devices. The replaceable EPROM plug-in module stores the software program. The RAM, which is backed up by an internal lithium battery, is used for temporary storage of sensor signals measured during operation and for storage of test records. The EEPROM stores factory calibration information, the instrument serial number and a cumulative count of uses. The EEPROM does not rely on the lithium battery for maintaining this information.

### SENSOR INTERFACE

Electrical signals from the sensors are conducted from the contact pads on the cartridge, through the internal connector in the analyzer, to the sensor interface circuit board. These circuits amplify the signals from the sensors so that they can be further processed by the main electronic circuit board.

Four signals are relayed to the main electronic circuit board from the sensor interface circuit board:

1. A multiplexed potentiometric signal line
2. A multiplexed amperometric signal line
3. An AC fluid conductivity signal
4. A digital identification code to identify insertion of a cartridge or the Electronic Simulator

MECHANICAL SYSTEM

A single DC gear motor drives four mechanical system components

1. A latching mechanism for locking the cartridge in place
2. An electrical interconnecting system which brings the analyzer's electrical internal connector into contact with the contact pads on the cartridge
3. A calibrant delivery system
4. A sample delivery system

The rotational motion of the gear motor is translated to the mechanical system via a nut traveling along the length of a lead screw attached to the motor's shaft.

ANALOG-to-DIGITAL CONVERSION

An analog-to-digital converter converts all analog signals into digital form so that the microprocessor can perform mathematical calculations on the signals. An analog signal multiplexer makes it possible for the microprocessor to measure six different analog signals:

1. The potentiometric signals from the sensor interface circuit
2. The amperometric signals from the sensor interface circuit
3. A DC conductivity signal
4. The battery voltage
5. A thermistor signal representing the internal temperature of the analyzer
6. A motor feedback signal used to control the speed of the mechanical motion

ANALOG CONTROL SIGNALS

The analyzer creates and applies two types of signals to the sensors: a digital-to-analog converter generates a voltage which is applied to amperometric sensors, and the AC conductivity circuit generates an AC excitation signal which is applied to the conductivity sensors. The digital-to-analog converter also provides voltage to the motor driver circuit.

OPERATOR INTERFACE:

The microprocessor control system coordinates the reading of information from the keypad, the writing of information onto the display, and the communication of results via an IR link.

## CLINICAL SIGNIFICANCE:

Serum/plasma/ is used for the determination of sodium, chloride and potassium for those patient's whose total protein is greater than 10 g/dl.

- Potassium measurements are used in the diagnosis and treatment of hypokalemia (metabolic alkalosis, metabolic acidosis or the absence of acid-base disturbances), hyperkalemia (over-administration of potassium, acidosis, or crush injuries), renal failure, Addison's disease or other diseases involving electrolyte imbalance.
- Sodium measurements are used in the diagnosis and treatment of aldosteronism (excessive secretion of hormone aldosterone), diabetes insipidus, adrenal hypertension, Addison's disease, dehydration, inappropriate antidiuretic hormone secretion, or other diseases involving electrolyte imbalance.

Body fluid pH performed on serous fluids such as peritoneal, pleural (thoracic) and pericardial (chest) is useful in the diagnosis of tuberculosis, malignancy, inflammation or infection.

TMH-Whole blood potassium can be performed on CLL (Chronic Lymphocytic Leukemia) patients and others that have an extremely high white count may have what is known as Pseudohyperkalemia. The potassium result can be artificially high on venipuncture serum and plasma.

**Acceptable Specimens:**

1. Serum or heparinized plasma, free from hemolysis, is the recommended specimen.
2. Serum/plasma should be separated from the cells within two hours after collection.
3. All body fluids should be collected in a heparinized syringe and sent to the lab for pH determinations.
4. Pleural and thoracentesis fluid require a heparinized syringe for pH determinations.
5. Whole blood (K+) or Sodium (7/24/18DN) collected in a Blood Gas syringe – Room Temp, No Ice. Refer to *Appendix WBK1* (TMH).

**Unacceptable Specimens**

1. Pleural/thoracentesis fluids not received in heparinized syringe will be cancelled.

   Cancel as ".NOT_PERFORMED" and add comment: **@NOPH**
   *Specimen not received in heparinized syringe.*
   *Called to:*

   If physician persists and wants pH performed, result as "See Note", report the value, add the result comment **@NHEP** and document requesting physician.
   *Specimen not collected in heparinized syringe. Interpret with caution.*
   *Physician requested testing be performed and reported.*
   *Called to:*

2. The sample must be properly labeled with the minimum of the patient's name and date of birth. For more information on the acceptability of samples, see Specimen Rejection Policy in Administrative Manual.

**Specimen Handling / Sample Volume**

1. The optimum amount of serum/plasma or body fluid is 65uL.
2. For optimum results, samples should be analyzed as soon as possible after collection.
3. All blood and fluid samples should be handled as if they were capable of transmitting disease. Universal precautions should be observed.

**Collection**

1. Expel any bubbles that occurred during the sample collection.
2. Samples should be capped if not analyzed immediately so as to avoid room air contamination.
3. The optimum amount of sample is 65uL.

## INSTRUMENTATION:

I-STAT Analyzer
Electronic Simulator
Central Data Station
(Optional) Printer

## REAGENTS and SUPPLIES:

Every cartridge includes a sealed foil pack that contains a calibrant solution with a known concentration of each analyte. During the first part of the testing cycle the calibrant solution is automatically forced out of the foil pack and over the sensors. The signals produced by the sensors in response to the calibrant solution are stored. Once this sequence is completed, the analyzer automatically moves the sample over the sensors. By comparing the sensors' responses to the sample with that of the calibrant, the concentration of each analyte in the sample is calculated.

- Lab will store cartridges at 2-8$^0$C (35 – 46$^0$F). Cartridges cannot be used after the expiration date and must be discarded.

  Cartridges must be acclimated to room temperature as follows:
  - An entire box of 25 for one hour
  - A single cartridge for 5 minutes

  **Once acclimated to room temperature, the cartridges are good for the time defined on the cartridge box and pouch. New expiration dates must be noted on the box or pouch once it is moved to room temperature. Do not use cartridges if the room temperature has exceeds 30.0 C (86.0 F)**

- Upon receipt of a new shipment of cartridges, Biochemistry will verify that the transit temperatures were satisfactory using the four window temperature indicator strip affixed to the cartridge boxes. If the temperature exceeds the recommended tolerance limits during transport, notify I-STAT immediately for replacement.

## I-STAT SYSTEM CHECKS:

**On-Board Monitoring System**

- The portable Clinical Analyzer continuously monitors its electronic and mechanical components, battery voltage, temperature, and the flow of calibrant solution and sample within the cartridge. If at any point during the test cycle a problem is detected, the analyzer stops, resets, and displays a message describing the problem and the next step to be taken. Sensor signals are also monitored.
- It is important for data retrieval that the date and time be correct. The current date, time, battery voltage, and temperature may be checked on the status page.

## QUALITY CONTROL:

## DAILY

**Internal and External Electronic Simulator**

The analyzer performs an internal electronic check and calibration during each testing cycle as well as an internal electronic simulator test every eight hours of use. The internal simulator performs a temperature and humidity check before each use.

- The External Electronic Simulator is a quality control device. This reusable device simulates the electronic signals generated by the cartridges, but stresses the analyzer's signal detection functions more than a control solution. The Electronic Simulator provides an independent check on the ability of the analyzer to take accurate and sensitive measurements of voltage and current from the cartridge.

- **The External Electronic Simulator is performed twice yearly for temperature verification and on an as needed basis. The I-STATs are programmed to internally perform the Simulation. The "SIM" will prompt the operator if a manual check is needed.**

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**PASS** If the analyzer is operating within specifications, PASS will be displayed. Proceed to use the analyzer.

**FAIL** If the analyzer is not operating within specification limits, FAIL will display along with one or more letters.
Repeat Electronic Simulator check again.
If the analyzer fails again, DO NOT USE the analyzer. Return it to the lab for troubleshooting.

**REMOVE**

Wait until the LOCKED prompt disappears from the screen before removing the Simulator.

## Monthly Liquid QC

- Quality Control (at least 2 levels) is performed by the Biochemistry Lab on each lot of cartridges before they are released to the unit.
- Quality Control (at least 2 levels) is performed monthly on each instrument on each cartridge type used in the testing location.
- The control solutions are aqueous and require no preparation.
- QC materials are stored between 2 – $8^0$C and should be used before their expiration date.
- Quality control values must be within the established range based on CLEW and lot number.
- Patient testing will not be performed if Liquid QC fails.
- QC will be performed whenever there is a question of instrument performance.

## Instrument Performance Checks

**AMR Validation:** Twice yearly the Analytical Measurement Range (AMR) is confirmed with Abbott I-Stat TriControls Calibration Verification Material.

**Comparability:** Twice yearly, results are compared between methods and/or instruments as appropriate with same sample types and/or QC material. Acceptable limits are posted on the worksheets.

## PROCEDURE:

1. **VERIFY that the analyzer has been checked using the Electronic Simulator prior to use.** The "SIM" will prompt the operator if a manual check is needed.
2. The I-STAT analyzer is always "off". The device has a 45-second delay that automatically turns the unit off if no one is using it. Press the display key. Test Menu opens, Chose number"2" I STAT cartridge
3. The I-STAT analyzer is a thermal unit as signified by the "37°" symbol located on the bottom. A thermal unit allows for other types of cartridges to be used in the analyzer. The I-STAT analyzer will be kept at room temperature on the unit
4. Remove the cartridge from the pouch after it reaches room temperature
5. While the cartridge is not fragile it should be handled as follows to avoid difficulty in filling or rejection by the analyzer.

    - Do not remove a cartridge from its protective pouch until the pouch is at the room temperature of the room where it is to be used; condensation on the cartridge pads may prevent proper contact with the analyzer. Use the cartridge immediately after removing it from its protective pouch.
    - Do not contaminate the contact pads with fingerprints or talc from gloves, as the analyzer may not be able to make proper contact with the cartridge.
    - Do not exert excessive pressure over the central area of the label as the calibrant pack underneath could burst prematurely.
    - Do not cover the air vent as the sample will not be able to flow to the FILL TO mark.

6. Do not use a cartridge on which blood or any other fluid has spilled as the analyzer may become contaminated.
7. Place the cartridge on a flat surface or hold horizontally.
8. Direct needle, pipette tip, or capillary tube into the sample well.
9. The cartridge will be filled SLOWLY AND STEADILY until the blood reaches the blue triangular "FILL TO" mark. NOTE: Hold the cartridge by its sides or lay it on a flat surface. Holding your thumb on top of the cartridge may prevent blood from entering as the cartridge contains an air pocket.
10. Immediately close the cover over the fill hole (press on the rounded end, NOT DIRECTLY over the well, of the closure until it snaps into place) and insert the cartridge into the analyzer.
11. The I STAT prompts to scan or enter the operator ID(10 digits). The lab will use 3333333333 as the universal user ID.
12. Manually enter the patient's ID. The ID is the accession number preceded with zeros for a nine digit patient ID number. Confirm this entry by entering twice.
13. Scan the Cartridge Barcode
14. Push the cartridge slowly and smoothly through the cartridge door until it will go no further.
15. The analyzer will turn itself on and indicate "**LCK**" on the screen. This indicates that the cartridge is locked in place. **DO NOT REMOVE THE CARTRIDGE WHEN "LCK" IS ON THE SCREEN. YOU WILL DAMAGE THE CONTACTS.**
16. When the results come up on the screen, remove the cartridge and dispose of it in the appropriate infectious waste container. **DO NOT REMOVE THE CARTRIDGE WHEN "LCK" IS ON THE SCREEN. YOU WILL RUIN THE CONTACTS.**
17. Dock the Instrument to keep the battery charged.

## Operation Precautions and Limitations

1. If **** is displayed in place of one or more results, fill and test another cartridge using a freshly collected sample. This indicates that the individual sensor has been compromised.
2. If **** is displayed again, perform pH reading on the pH Meter.
3. Results outside the reportable ranges are flagged with a <, >, or <> sign indicating the result is below or above the limits of the analyzer.
4. No result will be displayed if a problem is detected during the testing cycle. The analyzer will stop the testing cycle and display a message describing the problem.

## Reporting Results

1. If the pH is above or below the reportable range, the result should be confirmed by ph meter.

2. If the ph meter results agree, then the results can be reported as <6.50 or >8.20. If the results don't agree, report out pH meter results.

3. When results for analytes exceed CRITICAL RANGES, the critical value call policy should be followed to ensure results are communicated in a timely manner.

4. For plasma where high protein interference is suspected, report I-STAT results for Cl, Na, and K using manual entry in LIS.

   Add result comment @ISTA:

   *Chloride, Sodium and Potassium results reported at this time and date were performed on the I-STAT analyzer. The presence of high serum protein concentrations may interfere with accurate measurements of electrolytes on the Beckman analyzer which is the lab's routine method.*

**Reportable Ranges**

| Assay | Units | Reportable Range |
|---|---|---|
| Cl | mEq/L | 65-140 |
| Na | mEQ/l | 100-180 |
| K | mEQ/l | 2.0-9.0 |
| pH | | 6.5 - 8.20 |

**Critical Values:**

| | |
|---|---|
| I Sodium | <125 or >150 mEq/L |
| I Potassium | <3.0 or >6.0 mEq/L |
| I Chloride | <85 or >120 mEq/L |

## REFERENCE VALUES:

| | | |
|---|---|---|
| Sodium | 131-143 mEQ/L | 0-1 month |
| | 131-145 mEQ/L | 1 mon-1 yr. |
| | 132-143 mEQ/L | 1yr-5yrs. |
| | 135-143 mEQ/L | 5 yrs.-10yrs |
| | 133-143 mEQ/L | 10 yrs-15 yrs. |
| | 135-143 mEQ/L | 15 yrs.-150yrs. |
| Potassium | | |
| | 3.7-5.9 mEq/L | 0-1 month |
| | 4.1-5.3 mEq/L | 1 month-1 yr. |
| | 3.4-4.7 mEq/L | 1-12 yrs |
| | 3.6-5.1 mEq/L | 12-150 yrs. |
| Chloride | 99-116 mEq/L | 0 mins-1 month |
| | 98-118 mEq/L | 1 mos-12 mos |
| | 98-116 mEq/L | 1 yr-5 yrs |
| | 99-114 mEq/L | 5 yrs-10 yrs |
| | 98-115 mEq/L | 10 yrs-15 yrs |
| | 98-110 mEq/L | 15 yrs-150 yrs |

**LIMITATIONS of the PROCEDURE: Known Interfering Substances**

| Analyte | Interferant | Effect |
|---|---|---|
| Potassium | Hemolysis | Potassium results will increase as the degree of Hemolysis increases. |

For more information on limitations and Interfering substances, refer to the I-STAT procedure manual, Cartridge and Test information section.

## Instrument Status and Stored Results

There are two kinds of information that can be retrieved from the I-STAT portable clinical analyzer by way of the **MENU**. We have the capability of viewing the "Status" of the analyzer and looking at "Stored Results".

**STATUS:**

1. Press the display key to turn the unit on.
2. Once the unit turns on the **Test MENU** opens. Toggle **Menu** a second time, for the **Administration Menu**
3. Choose "1 – Analyzer Status" , "2 – Data Review" or "5-Clock Set
4. Press the number 1 on the keypad for Analyzer Status
5. The following information is now available to view
    - Amount of volts left in the battery. Note: the analyzer utilizes two 9-volt batteries; however, fully charged batteries will probably not read more than 8.4 – 8.6 volts. Rechargeable Lithium batteries are recommended for long term use.
    - Barometric pressure
    - Room temperature
    - Several lines of codes concerning the current version of the software.
    - Serial number of the handheld
    - Total number of records stored and number of records unsent.
6. Choose #5 for Clock Set to adjust date or time (*Enter* through password prompt)
7. Choose #2 to review / recall data for Quality controls, Simulator Results of Patient testing

**STORED RESULTS**

1. Turn the unit on.
2. Once the unit has come on, press the word **MENU**. Option #1 allows for the last result performed to be viewed
3. Press Menu a second time for the Administration Menu to see more archived data
4. Press the number "1 "on the keypad for Patient Results, "2" for Controls, or "3" for Simulator
5. Once the Patient result key has been chosen, a patient ID is requested.
    - Date, Time and Patient Identifier is displayed with results
    - Toggle the right arrow to see more results from that event.
    - Toggle the "2" to move to the next set of results on that patient.

6. When you are finished looking at the results you can either print them or press the word ENT and then Menu. This will return you to the Menu Screen. If you want to look up another patient, start with step #3 above.
7. If you are finished, leave the analyzer alone and it will turn itself off.

## PROCEDURAL NOTES:

1. Refer to the I-STAT System Manual for troubleshooting
2. Refer to the I-STAT System Manual for cleaning and decontamination.
3. Biochemistry will perform periodic (as needed) electrode cleaning using the Ceramic Cartridge.

## ATTACHMENTS:

1. Appendix WBK1-(TMH) *Whole Blood Potassium on I-STAT Pseudohyperkalemia and CLL patients.*

## REFERENCES:

I-STAT System Manual, October 2012

Kohn, GL, Hardie, WD: *Measuring Pleural Fluid pH High Correlation of a Handheld Unit to a Traditional Tabletop Blood Gas Analyzer*, CHEST 2000:118:1626-1629

Body Fluid pH Correlation , Lifespan AMC-Biochemistry Laboratory, Syed Latif PhD. February 2016.

AU vs i-STAT Plasma Correlation, Lifespan AMC- Biochemistry Laboratory, Syed Latif PhD. February 2016.