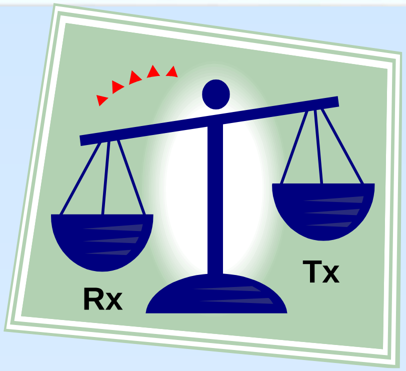

Chemistry in Dialysis Technology

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NANT 2017 Annual Symposium Feb. 20, 2017 Las Vegas, NV

The Starting Point

The role of the biomedical technician is to:

a) protect patients, through proper practice in the operation, repair and maintenance of the technology used in the clinic,

b) bring transparency to the technology, so clinical and medical professionals can deliver the best care possible.

For many in our industry, technical is a “black box”.

The Starting Point

If technical is a “black box”…..

then chemistry is a “black hole”.

The Starting Point

Chemistry is a branch of physical science that studies the composition, structure, properties, interaction and change of matter.

All the everyday objects that we can bump into, touch or squeeze are ultimately composed of matter, and therefore, chemicals.

The Starting Point

The matter around us is constantly moving, colliding, interacting and reacting with other matter.

In a tank of RO water, the molecules are moving continuously at fantastic speeds, and countless chemical reactions are occurring every instant. The water is in a state called "dynamic equilibrium".

Why Do I Need to Know Chemistry

- Patients are in “chemical imbalance”
- Chemical activity is fundamental to the dialysis treatment process.
- Many tasks and responsibilities in the clinic are “chemical” in nature

The good news is, you already use these chemical concepts everyday.

The bad news is, we're going to tell you about them anyway …

Using math, science and other evil arts.

How many think you know the answer to the following questions:

Why there are 2 parts to the concentrate?

Why do you put bleach through the machine?

Why do we have a 24 hr. limit on mixed bicarb?

Why is the dialysate pH so important?

Goals of this Workshop

Selected topics:

- Mixing concentrates from powder
- Dialysate chemistry
- Water quality and water purification systems
- Cleaning surfaces and equipment
- How Dialyzers and Machines Really Work

Part 1

Chemistry Principles and Mixing Concentrates

Terminology

- Chemical Element – an atom or atoms all with the same atomic number (Hydrogen, Carbon, Oxygen, Gold)
- Atomic number – the number of protons in the nucleus.
- Atomic weight – The total weight of the atom including all neutrons, protons, and electrons.
- Molecule – a group of atoms (same or different elements), bonded together.
- Ion – an element or molecule that has gained or lost one or more electrons giving it an electrical charge

Periodic Table of the Elements

Atomic Number Symbol Name Atomic Mass

1 IA 1A	2 IIA 2A	3 IIIB 3B	4 IVB 4B	5 VB 5B	6 VIB 6B	7 VIIB 7B	8	9 VIII 8	10	11 IB 1B	12 IIB 2B	13 IIIA 3A	14 IVA 4A	15 VA 5A	16 VIA 6A	17 VIIA 7A	18 VIIIA 8A
1 H Hydrogen 1.008																	2 He Helium 4.003
3 Li Lithium 6.941	4 Be Beryllium 9.012											5 B Boron 10.811	6 C Carbon 12.011	7 N Nitrogen 14.007	8 O Oxygen 15.999	9 F Fluorine 18.998	10 Ne Neon 20.180
11 Na Sodium 22.990	12 Mg Magnesium 24.305											13 Al Aluminum 26.982	14 Si Silicon 28.086	15 P Phosphorus 30.974	16 S Sulfur 32.066	17 Cl Chlorine 35.453	18 Ar Argon 39.948
19 K Potassium 39.098	20 Ca Calcium 40.078	21 Sc Scandium 44.956	22 Ti Titanium 47.867	23 V Vanadium 50.942	24 Cr Chromium 51.996	25 Mn Manganese 54.938	26 Fe Iron 55.845	27 Co Cobalt 58.933	28 Ni Nickel 58.693	29 Cu Copper 63.546	30 Zn Zinc 65.38	31 Ga Gallium 69.723	32 Ge Germanium 72.631	33 As Arsenic 74.922	34 Se Selenium 78.971	35 Br Bromine 79.904	36 Kr Krypton 84.798
37 Rb Rubidium 84.468	38 Sr Strontium 87.62	39 Y Yttrium 88.906	40 Zr Zirconium 91.224	41 Nb Niobium 92.906	42 Mo Molybdenum 95.95	43 Tc Technetium 98.907	44 Ru Ruthenium 101.07	45 Rh Rhodium 102.906	46 Pd Palladium 106.42	47 Ag Silver 107.868	48 Cd Cadmium 112.411	49 In Indium 114.818	50 Sn Tin 118.711	51 Sb Antimony 121.760	52 Te Tellurium 127.6	53 I Iodine 126.904	54 Xe Xenon 131.294
55 Cs Cesium 132.905	56 Ba Barium 137.328	57-71	72 Hf Hafnium 178.49	73 Ta Tantalum 180.948	74 W Tungsten 183.84	75 Re Rhenium 186.207	76 Os Osmium 190.23	77 Ir Iridium 192.217	78 Pt Platinum 195.085	79 Au Gold 196.967	80 Hg Mercury 200.592	81 Tl Thallium 204.383	82 Pb Lead 207.2	83 Bi Bismuth 208.980	84 Po Polonium [208.982]	85 At Astatine 209.987	86 Rn Radon 222.018
87 Fr Francium 223.020	88 Ra Radium 226.025	89-103	104 Rf Rutherfordium [261]	105 Db Dubnium [262]	106 Sg Seaborgium [266]	107 Bh Bohrium [264]	108 Hs Hassium [269]	109 Mt Meitnerium [268]	110 Ds Darmstadtium [269]	111 Rg Roentgenium [272]	112 Cn Copernicium [277]	113 Uut Ununtrium unknown	114 Fl Flerovium [289]	115 Uup Ununpentium unknown	116 Lv Livermorium [298]	117 Uus Ununseptium unknown	118 Uuo Ununoctium unknown

Lanthanide Series	57 La Lanthanum 138.905	58 Ce Cerium 140.116	59 Pr Praseodymium 140.908	60 Nd Neodymium 144.243	61 Pm Promethium 144.913	62 Sm Samarium 150.36	63 Eu Europium 151.964	64 Gd Gadolinium 157.25	65 Tb Terbium 158.925	66 Dy Dysprosium 162.500	67 Ho Holmium 164.930	68 Er Erbium 167.259	69 Tm Thulium 168.934	70 Yb Ytterbium 173.055	71 Lu Lutetium 174.967
Actinide Series	89 Ac Actinium 227.028	90 Th Thorium 232.038	91 Pa Protactinium 231.036	92 U Uranium 238.029	93 Np Neptunium 237.048	94 Pu Plutonium 244.064	95 Am Americium 243.061	96 Cm Curium 247.070	97 Bk Berkelium 247.070	98 Cf Californium 251.080	99 Es Einsteinium [254]	100 Fm Fermium 257.095	101 Md Mendelevium 258.1	102 No Nobelium 259.101	103 Lr Lawrencium [262]

Alkali Metal	Alkaline Earth	Transition Metal	Basic Metal	Semimetal	Nonmetal	Halogen	Noble Gas	Lanthanide	Actinide

Terminology

- Mole
  - International measure of quantity
  - 6.023 x 1023 (about 600 septillion)
  - Known as Avogadro's Number
  - Used to measure a quantity of atoms or molecules
  - Generally expressed in moles per liter for aqueous solutions

McGraw Hill Dictionary of Scientific and Technical Terms, 2nd edition, Editor - Daniel N. Lapedes, © 1978, McGraw Hill Book Company, ISBN 0-07-045258-X, p 1041, 132.

Terminology

- **Gram Atomic Weight**
  - The weight of one mole of a particular atom expressed in grams.
  - Gram Atomic Weights of dialysate atoms:

Sodium (Na) = 23.00	Chlorine (Cl) = 35.45
Potassium (K) = 39.10	Carbon (C) = 12.01
Hydrogen (H) = 1.008	Oxygen (O) = 16.00
Magnesium (Mg) = 24.31	Calcium (Ca) = 40.08

Handbook of Chemistry and Physics, 58th Edition, Editor - Robert C. West, Ph D, © 1977-78, CRC Press Inc., ISBN 0-8493-0458-X, p F-106

Terminology

- **Gram Molecular Weight**
  - The weight of one mole of a particular molecule expressed in grams.
  - Molecular weights are the sum of the atomic weights of the atoms in the molecule.
  - Sodium Chloride (NaCl) molecular weight =

    Na + Cl = 23.00 + 35.45 = 58.45 grams
  - Sodium Bicarbonate ($NaHCO_3$) =

    23.00 + 1.008 + 12.01 + 3(16.00) = 84.018 grams

Handbook of Chemistry and Physics, 58th Edition, Editor - Robert C. West, Ph D, © 1977-78, CRC Press Inc., ISBN 0-8493-0458-X, p F-106

Terminology

- **Equivalent (Eq):**
  - One mole of “activity” or charge (positive or negative).
  - Charges of the dialysate ions:

    Na^{+}, K^{+}, Mg^{++}, Ca^{++}, Cl^{-}, HCO_3^{-}, CH_3COO^{-}

  - One mole of Na^{+} ions = 1 Equivalent
  - One half mole of Ca^{++} ions = 1 Equivalent
  - 1/1000 Equivalent = 1 milliEquivalent = mEq
  - 1 milliEquivalent/liter = mEq/L
  - The number of positive charges in a solution always equals the number of negative charges

College Chemistry, Donald C. Gregg, © 1961, Allyn and Bacon Inc., p 220.

A Mixture vs. a Solution

- Mixture – a combination of components that are not in a fixed ratio. Different parts of the mixture may have different ratios of its components
  - These components can all be solids such as dirt or sand.
  - Liquid mixtures can contain solids that are insoluble but in suspension such a milk, beer, or some medications.
- Solution – a solid, liquid or gas where the components are distributed uniformly within the mixture
- Solution = Solvent + Solute
  - Solvent – larger component – the dissolver
  - Solute – smaller component – the disolvee

Dialysate Concentrate

- Created to simplify the preparation of dialysate.
- Solution made as concentrated as possible to reduce shipping costs and ease of handling.
- Sodium and Chlorides must be within +/-2% of the container label.
- All other compounds must be within +/- 5% of the container label or 0.1 mEq/L, (whichever is larger).

CSA Standards Z364.2.1 – 94, AAMI RD 52 : 2004

Albert Leslie Babb

- Univ. of British Columbia – 1948
  B.S. Chemical Engineering
- Univ. of Illinois – 1951
  PhD – Chemical Engineering
- Univ. of Washington – 1961-1981
  Head of Nuclear Engineering Dept.
- Created 1st Proportioning Dialysis Machine in 1963
- Created 1st Home Dialysis Machine in 1964
- Nominated for Noble Prize in 1977
- Professor Emeritus - 1992

Concentrate Proportioning Ratios

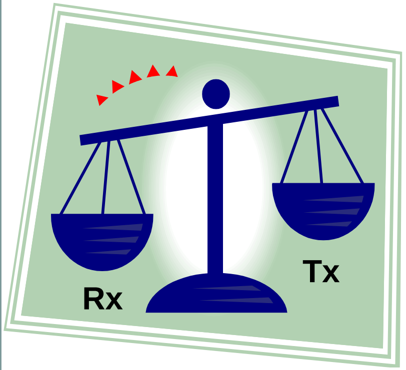
COMPANY	PARTS ACID	PARTS BICARB	PARTS WATER	PARTS DIALYSATE
Drake - Willock	1.00	1.83	34.00	36.83X
Cobe Laboratories	1.00	1.72	42.28	45X
Fresenius	1.00	1.225	32.775	35X
---------	1.00	1.10	34.00	36.1X

Concentrate Dilution Factors

COMPANY	ACID DILUTION	BICARB DILUTION	BICARB CALCULATION
Drake - Willock	36.83X 1:35.83	20.13X 1:19.13	36.83/1.83 = 20.13
Cobe Laboratories	45X 1:44	26.16X 1:25.13	45/1.72 = 26.16
Fresenius	35X 1:34	28.57X 1:27.57	35/1.225 = 28.57
---------	36.1X 1:35.1	32.81X 1:31.81	36.1/1.10 = 32.81

The first proportioning ratio (34:1) for acetate dialysate was established by a Canadian Engineer, Albert L Babb in 1963 at the University of Washington in Seattle.

Application Examples



Part 1

- **Making a solution**
- **Concentrate label information**
- **Calculations for concentrates**
- **3 - stream proportioning**

Application Lab

96 liters of water plus 7807 g. Sodium Bicarbonate

Does NOT equal

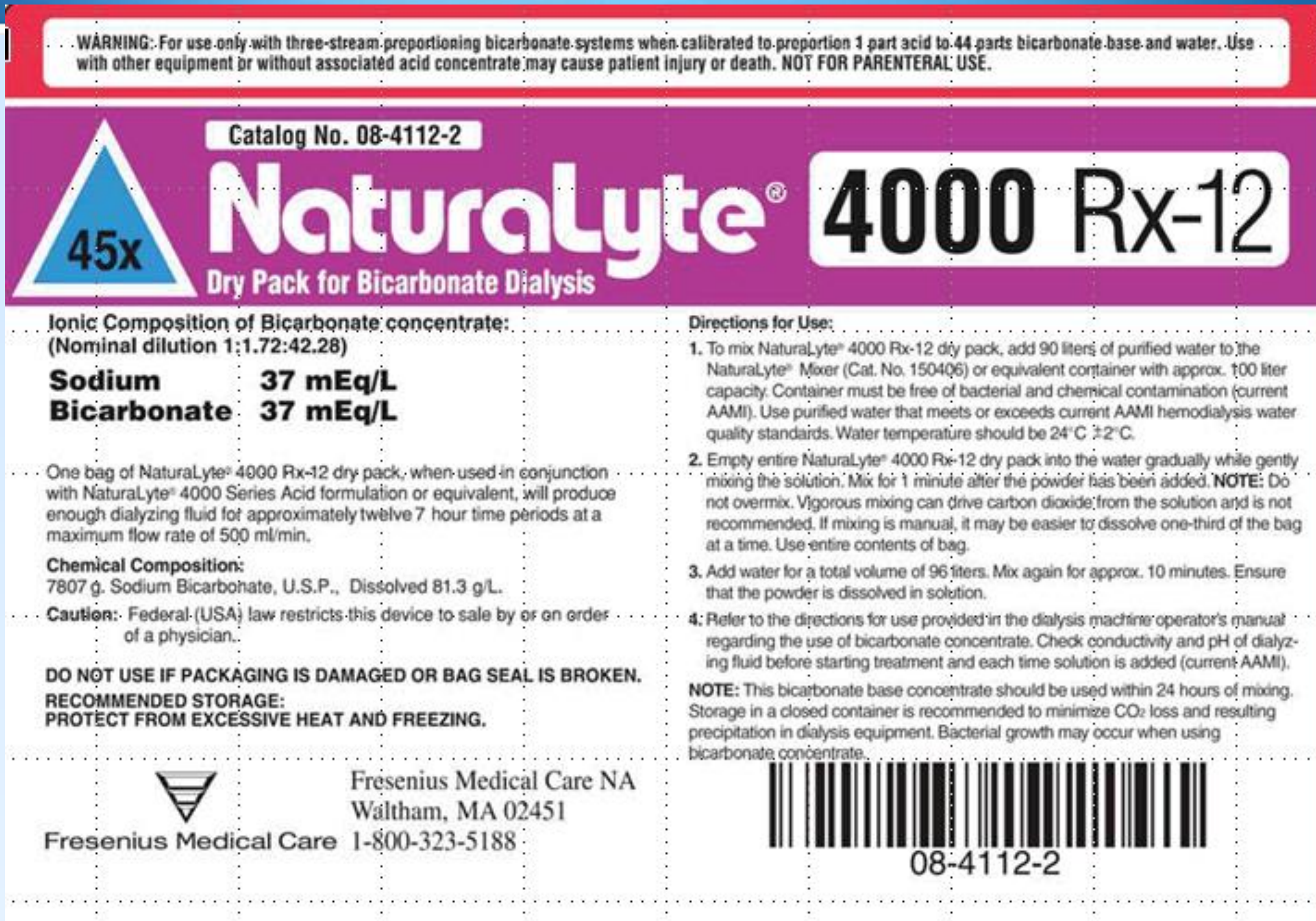
7807 g in 96 liter of solution

96 liters

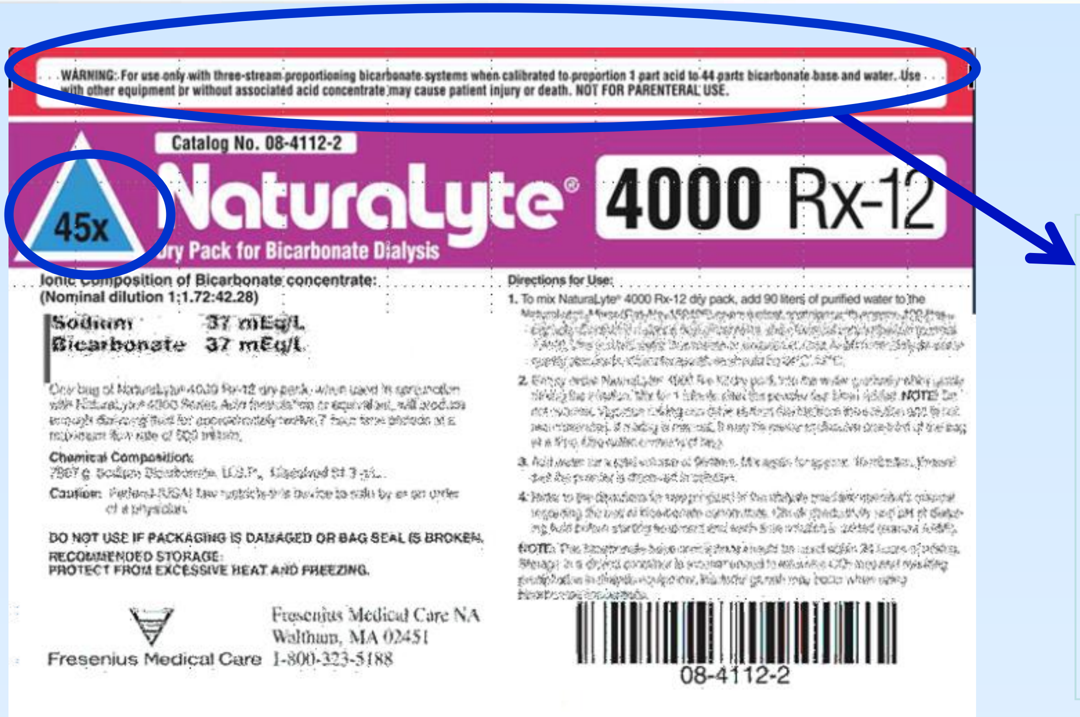
Does not equal

25 gallons

Bicarbonate Concentrate

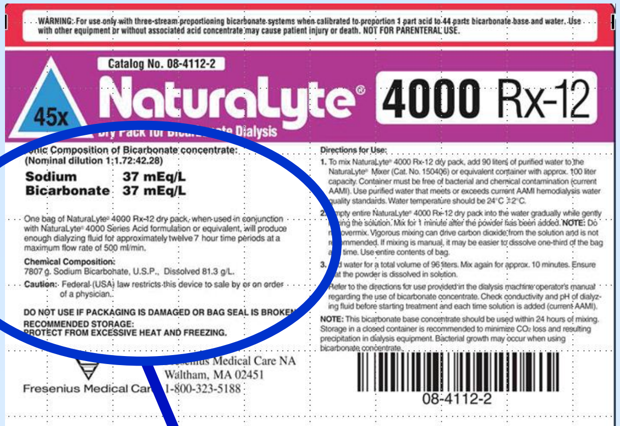


Bicarbonate Concentrate



Warning: For use with three-stream proportioning systems when calibrated to proportion 1 part acid to 44 parts bicarbonate base and water. Use with other equipment or without associated acid concentrate may cause patient injury or death. NOT FOR PARENTERAL USE.

Bicarbonate Concentrate



Ionic Composition of Bicarbonate concentrate:
(Nominal dilution 1 : 1.72 : 42.28)

Sodium 37 mEq/L
Bicarbonate 37 mEq/L
………………….
Chemical Composition:
7807 g. Sodium Bicarbonate U.S.P. Dissolved 81.3 g/L

Contribution to the preparation of dialysate

0.9677 M solution or 967.7 mEq

Application Lab

Chemical Composition:
7807 g. Sodium Bicarbonate U.S.P. Dissolved 81.3 g/L

7807 g in total of 96 liters = 7807/96 = 81.3229 g/L

Gram formula weight of $NaHCO_3$ = 84 grams per mole

81.3 g/L / 84 g/mole = .9677 moles / liter or 967.7 mmol / L

Bicarb has a charge (valance) of 1, so 967.7 mmol/L = 967.7 mEq/L

Application Lab

Ionic Composition of Bicarbonate concentrate:
(Nominal dilution 1 : 1.72 : 42.28) ➡ **note: the total is 45**

Sodium 37 mEq/L
Bicarbonate 37 mEq/L

Start with a bicarb concentrate properly made at = 967.7 mEq/L

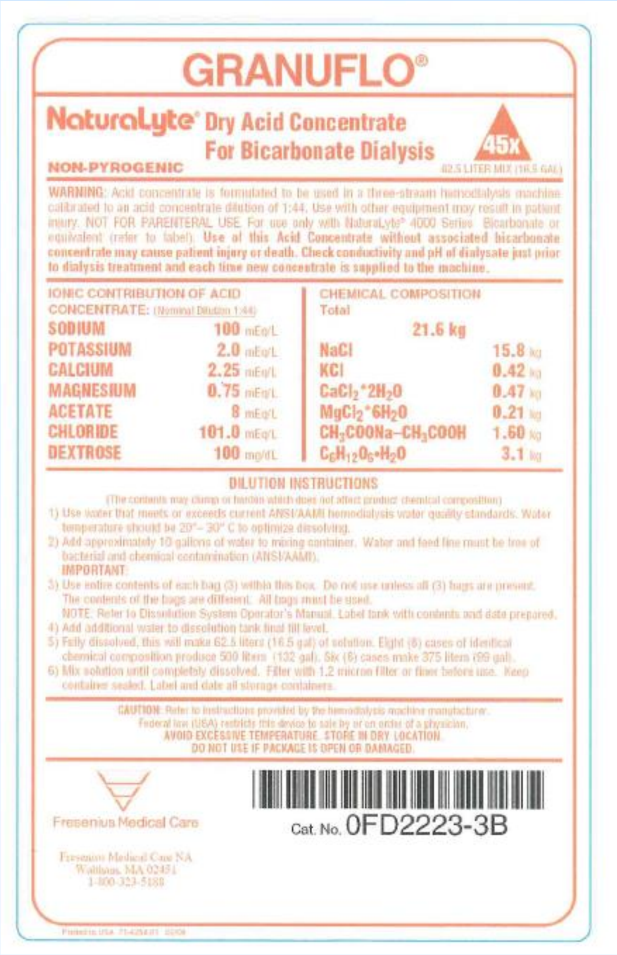
There are 1.72 parts bicarb concentrate in a total dilution of 45 parts

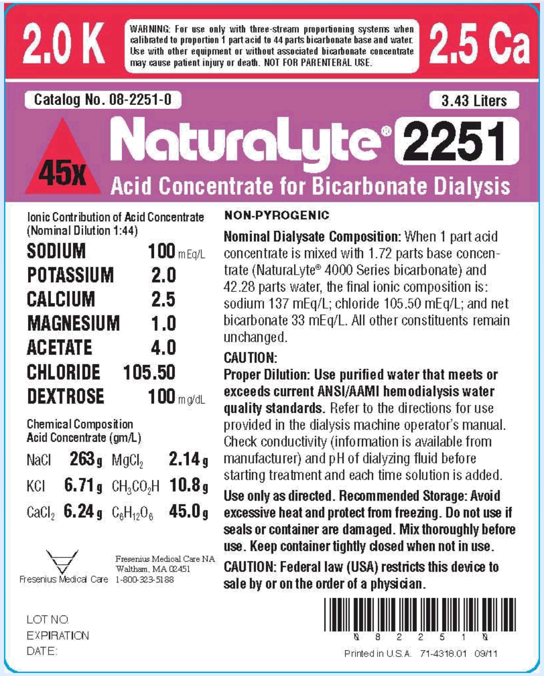
$$\frac{(967.7 \text{ mEq/L} * 1.72)}{45} = 36.987 \text{ mEq/L of Sodium Bicarbonate}$$

When dissolved,

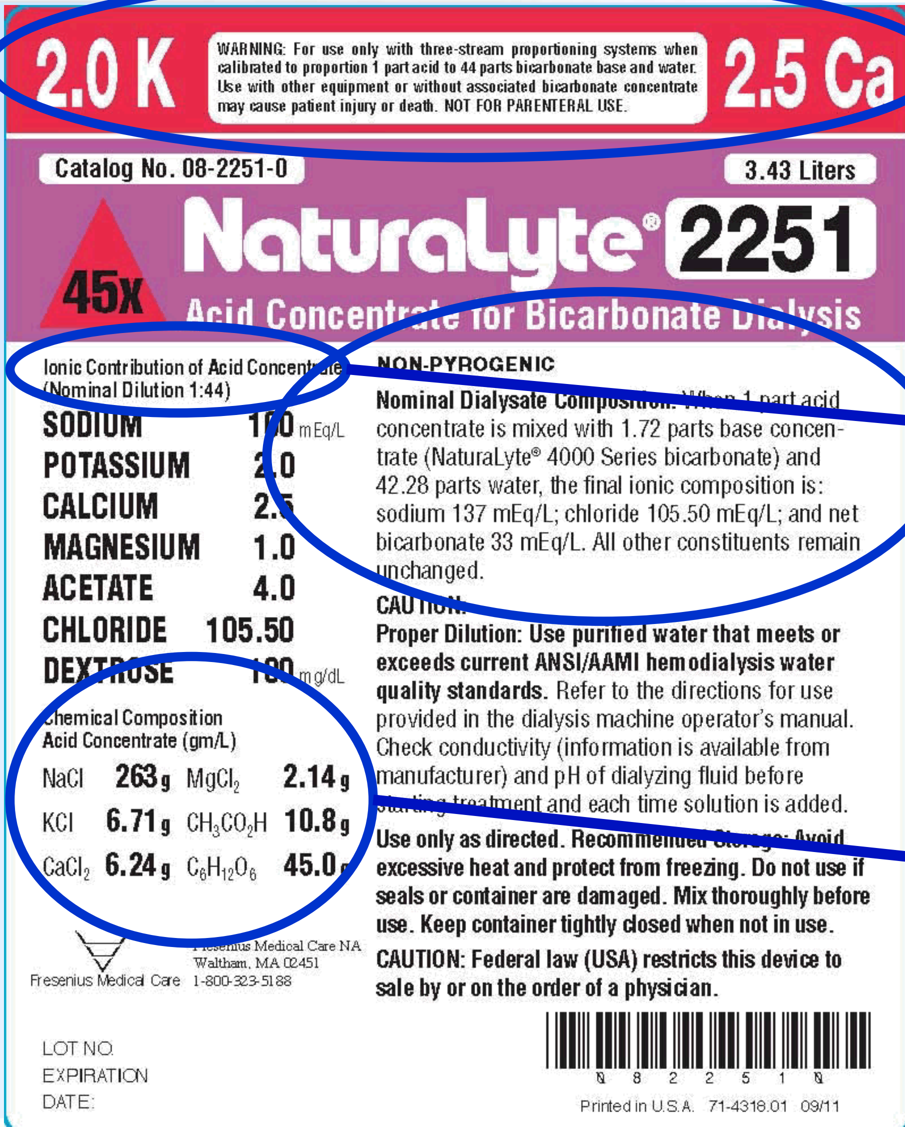
37 mEq/L <u>each</u> of sodium ion (Na^+) and bicarbonate ion (HCO_3^-)

Acid Concentrate





Acid Concentrate



3-stream proportioning with 1:45 (or 1+44) dilution

Ionic Contribution to dialysate

… final ionic composition … Na^+ 137 mEq/L … net bicarb 33 mEq/L

* see 3-stream propor. slide

…as a concentrate

Application Lab

Chemical Composition: (from the concentrate label) = 6.24 g/L Calcium Chloride

Gram formula weight of $CaCl_2$ = 111 grams per mole

6.24 g/L / 111 g/mole = ..056216 moles / liter or 56.216 mmol / L

Calcium has a charge (valance) of 2, so 56.216 mmol/L = 112.43 mEq/L

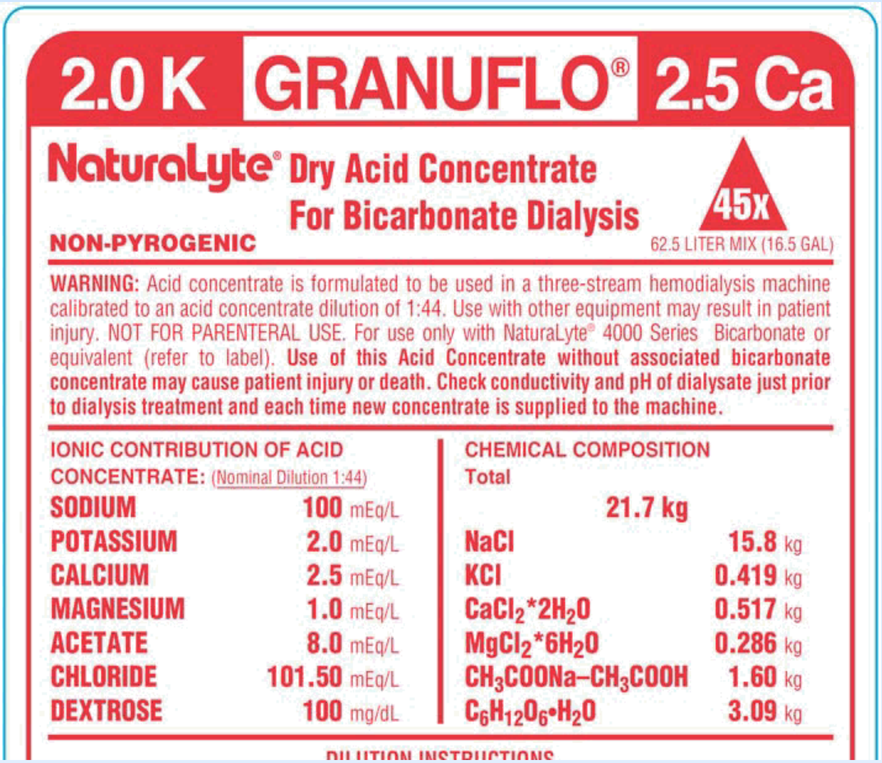
As dialysate:

Start with an acid concentrate at 112.43 mEq/L

There is 1 part acid concentrate in a total dilution of 45 parts

$$\frac{(112.43 \text{ mEq/L} * 1)}{45} = 2.4984 \text{ mEq/L of Calcium Chloride}$$

Acid Concentrate



Proportioning

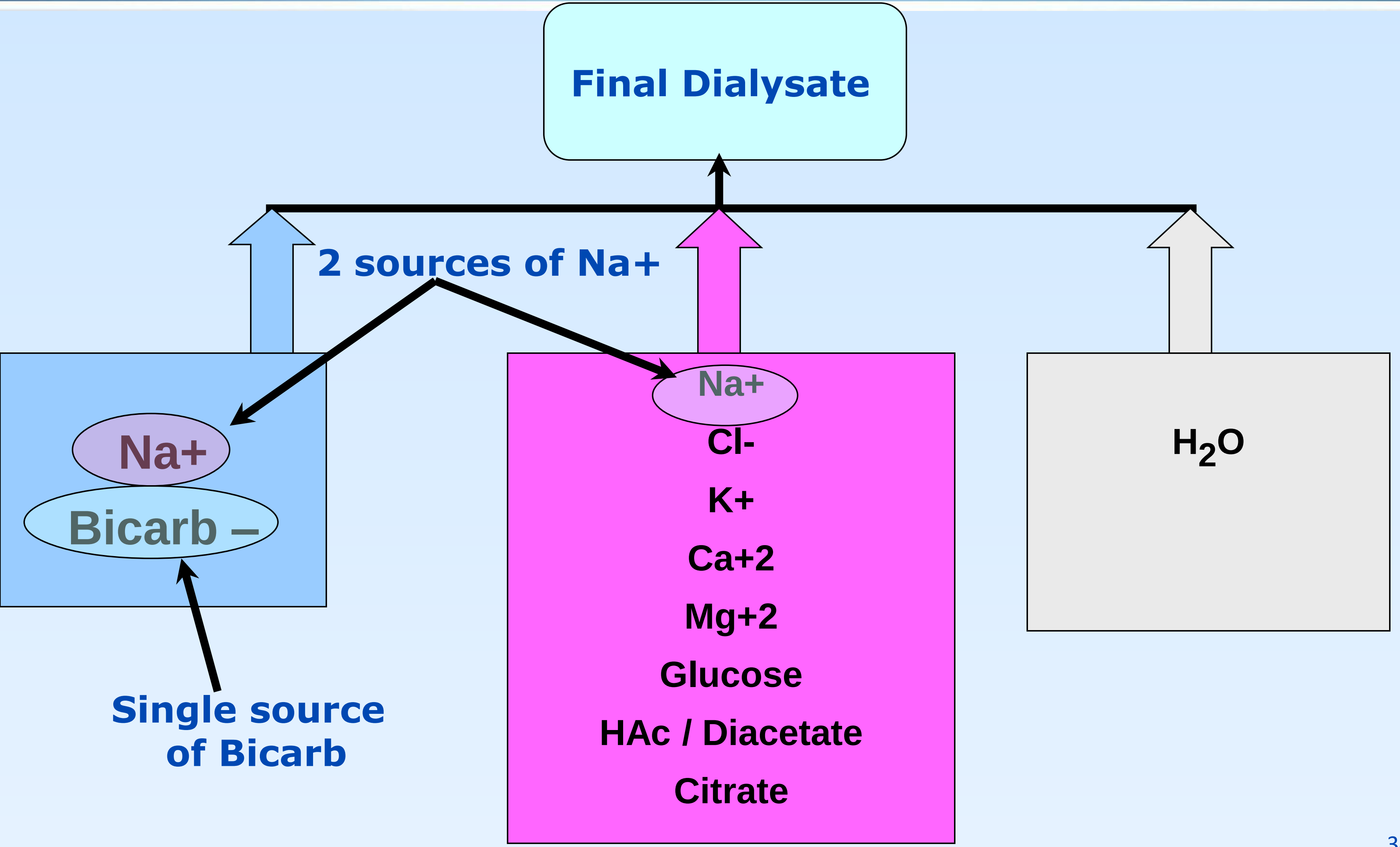
Type	Symbol	Mixing Ratio Acid : Bicarb : Water	Post Reaction Na^+ / Bicarb
Cobe	45x	1.00 : 1.72 : 42.28	[137] / [33]

Default proportioning – at 137/33, this is the relative amounts of each stream. If these Na^+ and bicarb settings are used, you will get the concentrations on the acid label in the final dialysate

Post reaction – with Fresenius machines, bicarb concentration is always given as the result post acid-base mixing

This 33 mEq/L came from adding 37 mEq/L bicarb, and 4 mEq/L were lost as CO_2 . The Na^+ doesn't go away.

Three stream proportioning



Concentrate Proportioning

3 stream proportioning

100 from acid, 37 from bicarb !

Setting		Actual	
Na^+	137 mEq/L	Na^+	137 mEq/L
K^+	2 mEq/L	K^+	2 mEq/L
Ca^{+2}	2.5 mEq/L	Ca^{+2}	2.5 mEq/L
Mg^{+2}	1.0 mEq/L	Mg^{+2}	1.0 mEq/L
Ac^-	4.0 mEq/L	Ac^-	4.0 mEq/L
Bic^-	33 mEq/L	Bic^-	33 mEq/L

For Fresenius machines, this is “post reaction bicarb”

Concentrate proportioning

3 stream proportioning

Setting/Label		Actual
Na^{+} 140 mEq/L	→	Na^{+} 140 mEq/L
K^{+} 2 mEq/L		K^{+} 2.06 mEq/L
Ca^{+2} 2.5 mEq/L		Ca^{+2} 2.57 mEq/L
Mg^{+2} 1.0 mEq/L		Mg^{+2} 1.03 mEq/L
Ac^{-} 4.0 mEq/L		Ac^{-} 4.12 mEq/L
Bic^{-} 33 mEq/L	→	Bic^{-} 33 mEq/L

Concentrate proportioning

3 stream proportioning

	Setting/Label			Actual
Na^{+}	137 mEq/L	→	Na^{+}	137 mEq/L
K^{+}	2 mEq/L		K^{+}	1.96 mEq/L
Ca^{+2}	2.5 mEq/L		Ca^{+2}	2.45 mEq/L
Mg^{+2}	1.0 mEq/L		Mg^{+2}	0.98 mEq/L
Ac^{-}	4.0 mEq/L		Ac^{-}	3.92 mEq/L
Bic^{-}	35 mEq/L	→	Bic^{-}	35 mEq/L

Part 2

More on Dialysate Chemistry

pH

- **Unit of measure that describes the degree of acidity or alkalinity of a solution**
- **Represented as the negative logarithm of the Hydrogen ion [hydronium ion] concentration or activity**

$$H_3O^+ + OH^- \rightleftharpoons 2H_2O$$

Hydronium Ion | **Hydroxyl Ion** | **Water**

- **When the Hydronium and Hydroxyl ion concentrations are equal, the solution is neutral and has a pH of 7.0 (0.0000001 mole/liter)**

The pH and Conductivity Handbook, © 1990/1991, Omega Engineering, Inc

pH

- **Acids have a pH below 7.0 (Higher H_3O^+)**
- **Bases have a pH above 7.0 (Lower H_3O^+)**
- **A pH increase of only 0.3 means the concentration of H_3O^+ has doubled**
- **The pH of various solutions:**
  - Blood = 7.35 – 7.45
  - Urine = 6.5 – 8.0
  - Baking Soda = 8.4
  - Vinegar = 2.9
  - Dialysate = 7.00 – 7.40
  - Bleach = 12.6 (more on this later)**
  - Sea Water = 8.0
- **Measurement of pH**
  - pH paper color indicators - limited accuracy
  - pH electrodes – AAMI recommended

The pH and Conductivity Handbook, © 1990/1991, Omega Engineering, Inc

Blood pH Relationships

Blood pH is directly related to the concentrations of bicarbonate and carbon dioxide in the blood. The relationship is defined by the Henderson-Hasselbalch Equation:

$$pH = pK + \log \frac{[HCO_3^-]}{0.03 \times pCO_2}$$

Where: pK = the blood pH from acids in the blood

HCO_3^- = bicarb concentration (mEq/L)

pCO_2 = carbon dioxide pressure (mmHg)

Burton, Richard B.; *Physiology by Numbers*; ©Cambridge University Press 1994; pp 127-130

Solving the equation

Blood normal values for pK, HCO_3^- , and pCO_2 are:

pK = 6.1, HCO_3^- = 24 mEq/L, and pCO_2 = 40 mmHg

Placing these values in the equation yields:

$$\text{Blood pH} = 6.1 + \log\left(\frac{24 \text{ mEq/L}}{0.03 \times 40 \text{ mmHg}}\right)$$

$$\text{Blood pH} = 6.1 + \log\left(\frac{24}{1.2}\right)$$

$$\text{Blood pH} = 6.1 + \log(20) = 6.1 + 1.3 = 7.4$$

Burton, Richard B.; *Physiology by Numbers*; ©Cambridge University Press 1994; pp 127-130

The Acid/Bicarbonate Reaction

When the Acetic Acid in the Acid concentrate mixes with the Bicarbonate ion in the Bicarb concentrate the following reaction occurs:

$$CH_3COOH + HCO_3^- \longrightarrow CO_2 + H_2O + CH_3COO^-$$

Acetic Acid	Bicarb Ion	Carbon Dioxide	Water	Acetate Ion
4 mM/L	4 mEq/L	4 mM/L	4 mM/L	4 mEq/L

(“classic” acid – base neutralization reaction)

**** **For 45X concentrates the 37 mEq/L concentrate becomes 33 mEq/L in the final dialysate solution.** ****

Why would a technician want to use bicarb dialysate?

- It requires two concentrates instead of one
- It adds more complexity to the machine making it harder to troubleshoot
- There is more testing necessary before you can start the treatment = more gadgets to calibrate
- It increases the chances of precipitation inside the fluid path = more vinegar/more bleach
- More concentrate storage means less workspace in the back room
- It makes the machine more costly which means less money for other technical instruments

Why? It's all about the patient!

- When acetate dialysate is used instead of bicarbonate dialysate, bicarbonate is dialyzed out of the patient and acetate is dialyzed in.
- As the bicarbonate is reduced, carbon dioxide combines with water to make more bicarbonate.
- The carbon dioxide reduction decreases the amount reaching the lungs.
- Low CO_2 in the lungs results in lower breathing rates.
- Less breathing lowers the oxygen levels in the lungs and blood.
- The patient may require oxygen and in extreme cases can go into cardiac arrest.
- At the end of the treatment the patient feels like an individual with a hangover and goes home to rest until the acetate is converted back to bicarbonate. (Krebs cycle)

Dialysate Chemistry vs. Blood Chemistry (mEq/Liter)

Constituent	Dialysate	Blood
Sodium	132 – 150	136 – 148
Potassium	0.0 – 4	3.5 – 5
Calcium	2.5 – 4.0	4.25 – 5.25
Magnesium	0.5 – 1.5	1.5 – 2.5
Chloride	100 - 110	95 - 103
Bicarbonate	25 - 40	22 - 26
Acetate	3.0 – 4.0	0.0
Dextrose	70 – 100 mg/dL	0.0 – 250 mg/dL
Carbon Dioxide	35 – 70 mmHg	40 mmHg

Dialysis Technology – A Manual for Dialysis Technicians, 3rd Edition, Jim Curtis & Philip Varughese, © 2003, National Association of Technicians/Technologists, p 191.

Conductivity

- Unit of Measure: milliSiemens/centimeter (mS/cm)
- Used to measure total ion concentration
- Factors that determine conductivity:
  - Total ions in solution (Total Ionic Strength = TIS)
  - Each ion's mobility (Conductance Factor)
  - Non ionic molecule concentration effect (Dextrose)
  - Dependent on Temperature (Reference 25^{o} C)
- Typical value for dialysate is 14.0 mS/cm at 25^{o} C
- For any electrolyte solution, the number of positive and negative ions are always equal

Conductance Factor

	Factor for TIS/2 = 137	Factor for TIS/2 = 160	Factor per mmol/L
Sodium Chloride	104.51	103.40	0.04826
Potassium Chloride	126.49	125.47	0.04435
Calcium Chloride	103.36	101.52	0.08000
Magnesium Chloride	106.29	105.23	0.04609
Sodium Acetate	70.17	69.03	0.04957
Sodium Bicarbonate	73.97	72.28	0.07348

Factors from the Drake-Willock Conductance Tables

Conductivity Calculation

Electrolyte	(#1) Conductance Factor	(#2) Charge mEq/L	(#3) Multiply #1 x #2	Divide #3 by 1000 Conductivity mS/cm
NaCl	104.178	100.00	10,418	10.418
KCl	126.185	2.00	252.4	0.252
$CaCl_2$	102.810	2.50	257.0	0.257
$MgCl_2$	105.973	0.75	79.5	0.080
$NaC_2H_3O_2$	69.829	4.00	279.3	0.279
$NaHCO_3$	73.464	33.00	2,424.3	2.424
Total Dialysate Conductivity without Dextrose				13.710

The Case of the Increasing Bicarbonate

Bath fixed components: Ca^{++} (1.5 mmol/L), K^{+} (2 mmol/L), Mg^{++} (0.5 mmol/L), CH_3COO^- (3.0 mmol/L), $C_6H_{12}O_6$ (8.33 mmol/L)

Conductance factors: NaCl = 104.51, $NaHCO_3$ = 73.97

Bicarb (mmol/L)	30.0	31.0	32.0	33.0	34.0	35.0	36.0
Chloride (mmol/L)	110.0	109.0	108.0	107.0	106.0	105.0	104.0
Conductivity (mS/cm)	13.87	13.84	13.81	13.78	13.74	13.71	13.68

Acid Concentrate Modification

Potassium – 30 mL raises 4.5 liter of acid concentrate by 0.5 mmol/L

All values in mmol/L

	No Spike	1 Spike	2 Spikes	3 Spikes	4 Spikes	5 Spikes	6 Spikes
Na	100	99.34	98.68	98.04	97.40	96.77	96.15
K	1	1.49	1.99	2.48	2.97	3.47	3.96
Ca	1.5	1.49	1.48	1.47	1.46	1.45	1.44
Mg	0.5	0.497	0.493	0.490	0.487	0.484	0.481
Cl	105	104.80	104.62	104.44	104.27	104.11	103.96
$C_2H_3O_2$	3	2.98	2.96	2.94	2.92	2.90	2.88
Cond (mS/cm)	13.665	13.657	13.650	13.644	13.639	13.635	13.631

Conductivity Temperature Compensation

- The conductivity of an electrolyte solution, such as dialysate, varies with temperature
- For dialysate, this change is about 1.80 – 2.20% per degree Centigrade
- For the conductivity values to reflect total ion concentration, all values must be corrected to the same temperature, which is 25^o C
- All dialysate machines utilize a temperature measuring device (normally a thermistor) to measure the dialysate temperature and correct the conductivity reading for the difference between the actual conductivity at the dialysate temperature and 25^o C

Conductivity Temperature Compensation

Table for 14.00 mS/cm @ 25°C

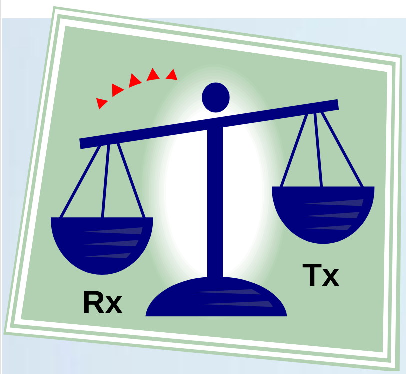
Temperature (degrees Celsius)	Uncompensated Cond. (mS/cm)	% Change from 25.0°C	Compensated by Thermistor
34.0	16.83	20.2	14.00
35.0	17.18	22.7	14.00
36.0	17.54	25.3	14.00
37.0	17.90	27.8	14.00
38.0	18.27	30.5	14.00
39.0	18.65	33.2	14.00
40.0	19.03	36.0	14.00

Compensation @ 2.07%/^{0}C

Density vs. Specific Gravity

- Density – the mass of a particular substance per unit volume. In dialysis density is generally measured in grams/cc.
- Specific Gravity (sp gr.) – The ration of the density of a substance compared to the density of a standard substance
- In dialysis the standard substance is usually water at 4^0 C. The density at this temperature is 0.999975 gm/cc.

Application Examples

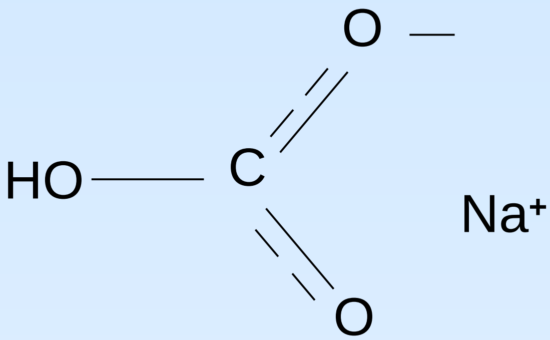


Part 2

- Bicarb chemistry made easy
- Taking good measurements
- Limitations of conductivity and total chlorine measurements

The Bicarbonate Reaction

Bicarbonate reacts with water !



Sodium Bicarbonate

$$NaHCO_3 + H_2O \rightleftharpoons H_2CO_3 + Na^+ + OH^- + (Na^+ + HCO_3^-)$$

Sodium Bicarbonate

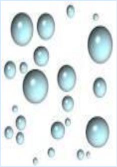
Carbonic Acid

Bicarbonate

$$NaHCO_3 + H_2O \rightleftharpoons H_2CO_3 + Na^+ + OH^-$$

Sodium Bicarbonate

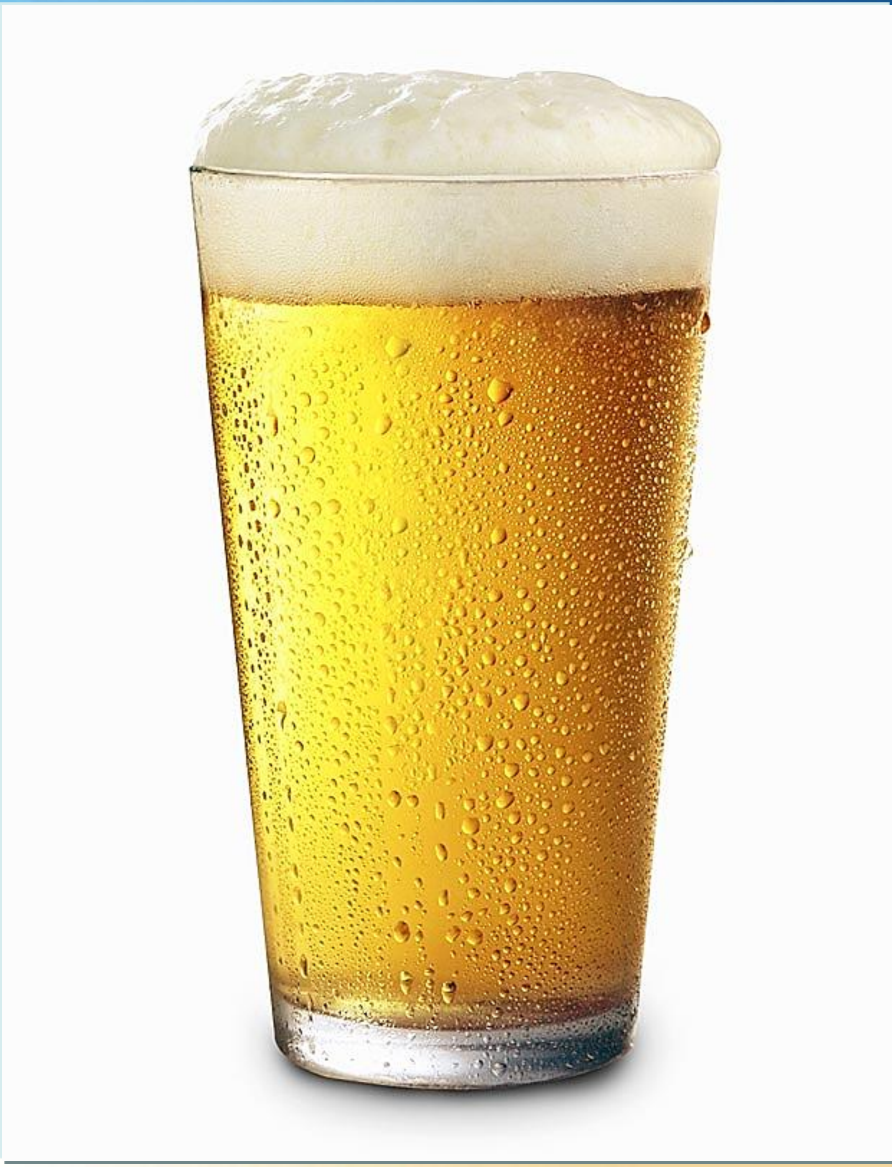
Carbonic Acid



$$CO_{2\ (g)} + H_2O$$

Can you give a familiar example of CO_2 dissolved in water?

(I'll give you a couple hints)



(here's another)

Bicarbonate

When mixing bicarb, think soda pop !

Chemicals in solution are in a state of dynamic equilibrium

$$Na^+ + HCO_3^- + H_2O \rightleftharpoons H_2CO_3 + Na^+ + OH^-$$

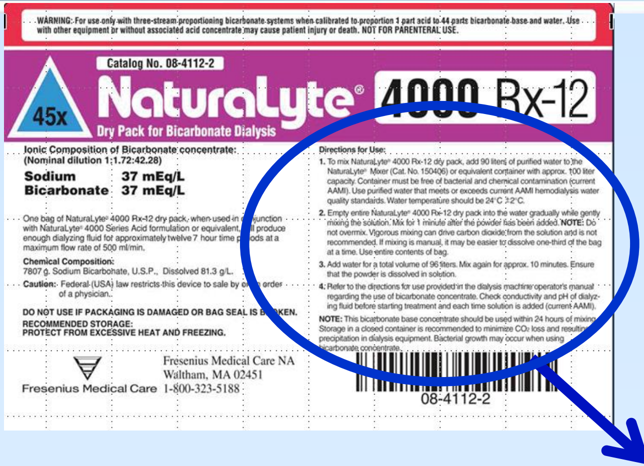
Sodium Bicarbonate

Carbonic Acid

$$CO_{2\,(g)} + H_2O$$

As CO_2 leaves solution (time, temp, agitation), more and more bicarbonate is lost (it goes flat)!

Bicarbonate Concentrate



Directions for Use:

1. To mix NaturaLyte® 4000 Rx-12 dry pack, add 90 liters of purified water to the NaturaLyte® Mixer (Cat. No. 150406) or equivalent container with approx.. 100 liter capacity. Container must be free of bacterial and chemical contamination (current AAMI). Use purified water that meets or exceeds current AAMI hemodialysis water quality standards. Water temperature should be 24°C ± 2°C
2. Empty entire NaturaLyte® 4000 Rx-12 dry pack into the water gradually while gently mixing the solution. Mix for 1 minute after the powder has been added. **NOTE:** Do not overmix. Vigorous mixing can drive carbon dioxide from the solution and is not recommended. If mixing is manual, it may be easier to dissolve one-third of the bag at a time. Use entire contents of bag.
3. Add water for a total volume of 96 liters. Mix again for approx. 10 minutes. Ensure that the powder is dissolved in solution.
4. Refer to the directions for use provided in the dialysis machine operator's manual regarding the use of bicarbonate concentrate. Check conductivity and pH of dialyzing fluid before starting treatment and each time solution is added (current AAMI).

NOTE: This bicarbonate base concentrate should be used within 24 hours of mixing. Storage in a closed container is recommended to minimize CO_2 loss and resulting precipitation in dialysis equipment. Bacterial growth may occur when using bicarbonate concentrate.

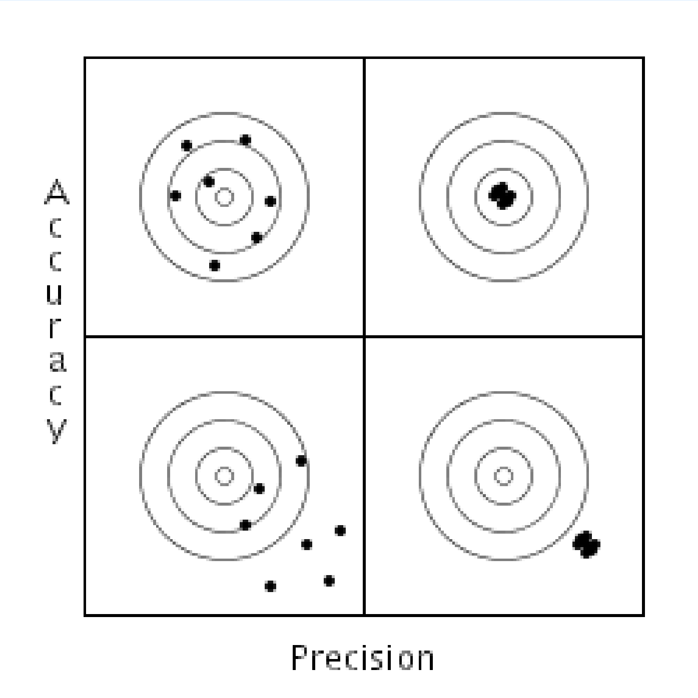
Taking good measurements

How do you know your meter is working properly ?

Metrology – the study of measurement

- Accuracy refers to the closeness of a measured value to a standard or known value.

- Precision refers to the closeness of two or more measurements to each other.



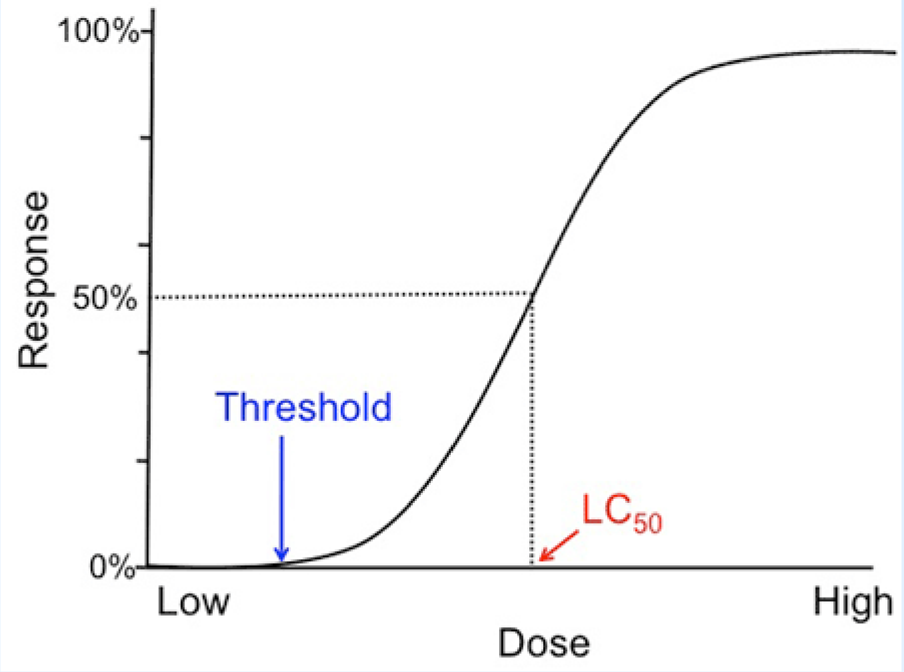
Application Lab

Meter – device that measures

- Conductivity meter
- pH meter
- Graduated cylinder
- Hydrometer
- Volt – Amp meter
- Pressure transducer

Each has a response curve:

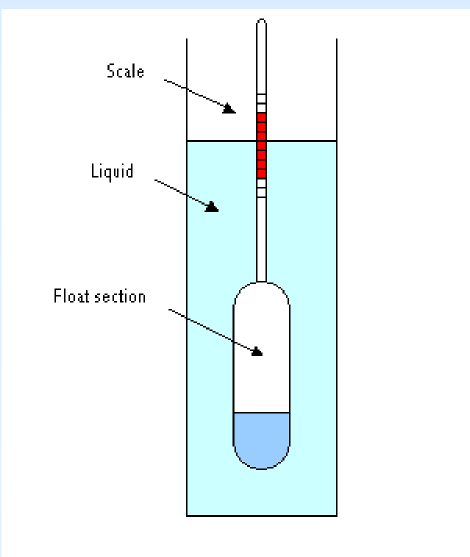
- Slope (discrimination)
- Threshold (sensitivity)
- Operating Range

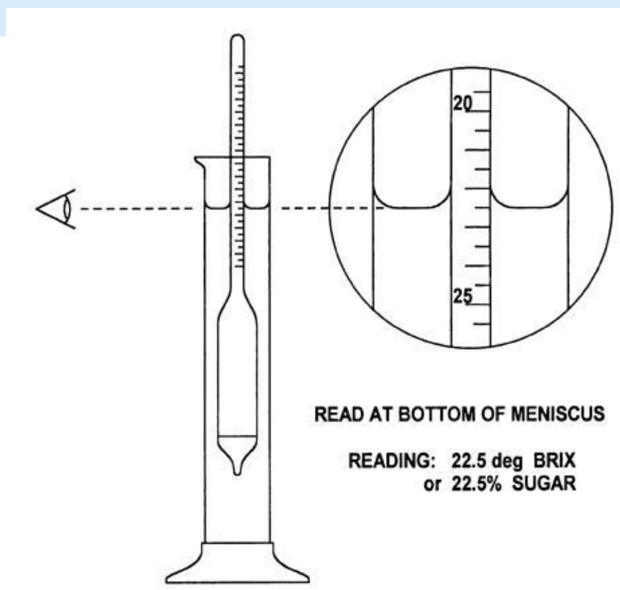


Specific Gravity

- Used in determining if Granuflo is mixed properly (all bags in the mixer).

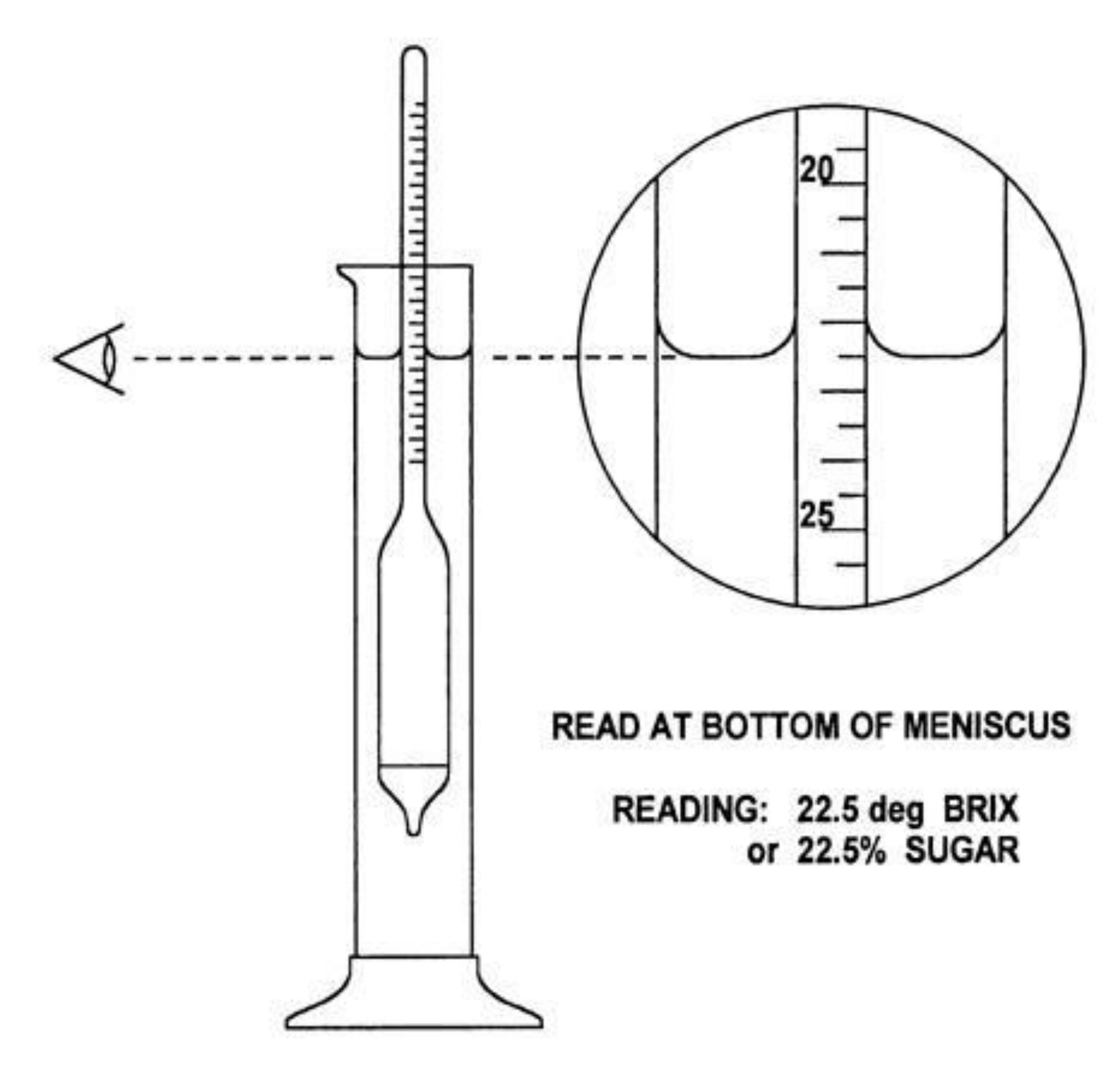
- The measurement device is a hydrometer





Hydrometer

- Read the meniscus
- Effect of bubbles
- Effect of temperature



Conductivity

Cations (mEq/L)		Anions (mEq/L)	
Na^{+}	137	Cl^{-}	105.5
K^{+}	2	Ac^{-}	4.0
Ca^{+2}	2.5	Bic^{-}	33
Mg^{+2}	1.0		
Total	142.5	Total	142.5

Far more Na^{+} and Cl^{-} than anything else (85.5%)

Conductivity

Conductivity is:

- A very important safety tool to use before and during the Tx.

It is NOT:

- A sodium or bicarbonate detector.
- It is not the "goal" (Rx are not written for mS/cm).
- A guarantee of dialysate safety.

Conductivity

- GIGO – meeting a conductivity range is not a substitute for proper concentrate preparation and handling.
- Each 0.1 mS/cm = about 1 mEq/L ionic strength, IF you have good control
- AAMI water Na^+ specification

Conductivity

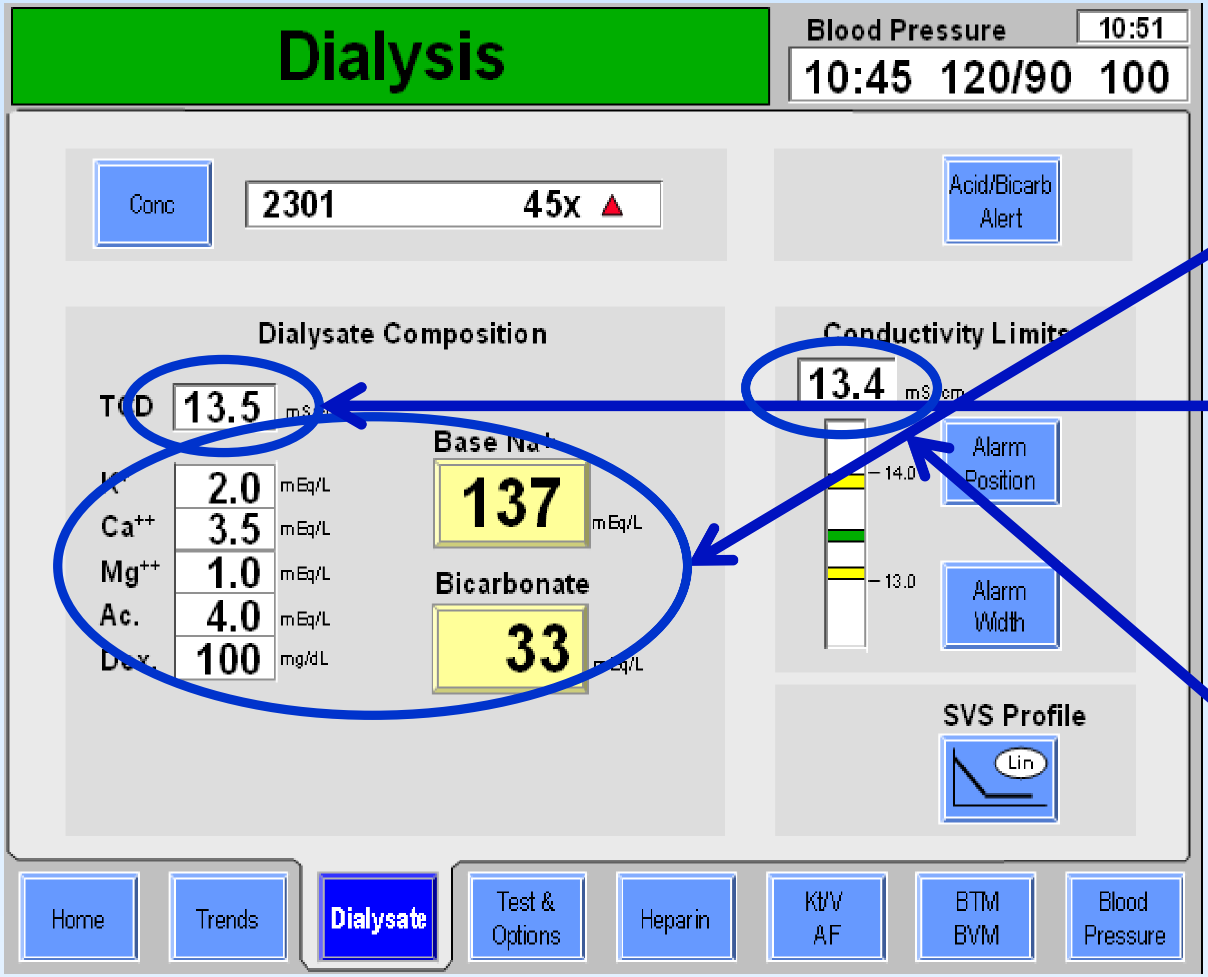
What is "theoretical conductivity":

- A value calculated by the machine. It is the conductivity of the exact prescribed dialysate under ideal conditions.
- It is the "expected" conductivity, which if not met, may indicate a problem in the dialysate.

It is NOT:

- A "target" to which the machine (or other equipment) should be adjusted or calibrated.

Conductivity



For this exact formulation / Rx

This is the theoretical or expected conductivity

This is the actual conductivity of the dialysate

Using Chlorine Test Strips

- Collect a fresh **100 ml** sample of RO water from a sample valve located after the first carbon filter or bank of carbon filters

- While dipping the strip, move it back and forth at a constant gentle rate of approximately two, **1"-2" wide strokes** (one forward – one backward) per second for **60 seconds**

Testing Total Chlorine

Failure to follow procedures can lead to the under-estimation of total chlorine present in the water.

Part 3

Chemistry of "Cleaning"

Oxidation and Reduction

- Oxidation – A chemical reaction where an element or radical loses an electron. The charge (valance) will increase.
  - $Na \rightarrow Na^{+}$ (Sodium is oxidized)
- Reduction – A chemical reaction where an element or radical gains an electron. The charge will decrease.
  - $HCO_3^{-} \rightarrow CO_3^{--} + H^{+}$ (Bicarbonate becomes carbonate)
- Oxidation-reduction reactions - Any chemical reaction where one component looses an electron, there will be another that gains an electron. Noted simply as a redox reaction.

Bleach

- Bleach - Sodium Hypochlorite ($NaOCl$) dissolved in water, with $NaOH$ as a stabilizer.   The household strength is 6% or 60,000 ppm. Bleach is a strong oxidizer.
- Bleach whitens materials by destroying chromophores which create the color in fabrics and liquids.
- It's use in dialysis is as a surface disinfectant. One part bleach to 9 parts water yields a concentration of 6,000 parts per million
- For drinking water, one tablespoon per gallon will purify water yielding a concentration of 234 ppm of $NaOCl$ = 111 ppm free chlorine.
- Never mix a strong acid (like HCl) with bleach, and be very careful with weak acids (like vinegar). It can produce chlorine gas, which can be deadly.
- Never mix ammonia and bleach. It will produce chloramine gas which is highly toxic.

Why is precipitation a problem in dialysis machines?

- The problem is Calcium Carbonate ($CaCO_3$) has a high degree of insolubility in water.
- The same is true for Magnesium Carbonate.
- Calcium ions (Ca^{++}) and Carbonate ions (CO_3^{--}) just love to get together.
- The dialysate must have Calcium ions to regulate the Calcium level in the patient’s blood
- Sodium bicarbonate is a major component of dialysate to regulate blood pH
- The bicarbonate ion reacts to create carbonate ions
- White stuff upstream from the dialyzer? Think precipitation and use vinegar
- White stuff downstream of the dialyzer? Think protein and use bleach

Solubility Product Constant (K_{sp})

- Ksp is a number generated for a molecule that determines its maximum solubility at a particular temperature (normally 25ºC).
- The number is the product of the solubility of the individual ions that make up the molecule measured in moles/liter

$$A_cB_d \leftrightarrow cA + dB = Al(OH)_3 \leftrightarrow Al^{+++} + 3\ OH^-$$

$$K_{sp} = [A]^c \times [B]^d \quad Ksp = [Al^{+++}] \times [3xOH^-]^3 = 5 \times 10^{-33}$$

$$[X] \times [3X]^3 = 27X^4 = 5 \times 10^{-33}$$

- $X = 3.7 \times 10^{-9}$ moles/liter and $Al(OH)_3$ molecular weight = 78.004

The solubility of Aluminum hydroxide is only 78.004 x 3.7 x 10^{-9} = 2.9 x 10^{-7} grams/liter = 0.29 micrograms/L

K_{SP} - Calcium Carbonate

- K_{SP} of $CaCO_3 = 8.7 \times 10^{-9}$

$$[Ca^{++}] \times [CO_3^{--}] = 8.7 \times 10^{-9}$$

$$[\ X\ ] \times [\ X\ ] = 8.7 \times 10^{-9} \text{ so } [\ X^2\ ] = 8.7 \times 10^{-9}$$

$$[\ X\ ] = \text{square root of } 8.7 \times 10^{-9} = 9.3 \times 10^{-5} \text{ moles/liter}$$

1 mole of $CaCO_3$ weighs = 100.09 grams

100.09 grams x 9.3×10^{-5} = 9.3 milligrams/L

Calcium and Magnesium Compounds

Molecule	G.M.W.	Ksp	mol/L	Dissolved
$CaCO_3$	100.087	8.70×10^{-9}	9.3×10^{-5}	9.3 mg/L
$Ca(OH)_2$	74.093	5.02×10^{-6}	1.08×10^{-2}	800 mg/L
$MgCO_3$	84.314	6.82×10^{-6}	2.6×10^{-3}	220 mg/L
$Mg(OH)_2$	58.320	5.61×10^{-12}	1.12×10^{-4}	6.5 mg/L

$CaCO_3$ in dialysate

For dialysate, the Calcium and Carbonate concentrations are:

- Calcium ion = 3.25 mEq/L = 1.63×10^{-3} mol/L
- Carbonate ion = 4×10^{-5} mol/L

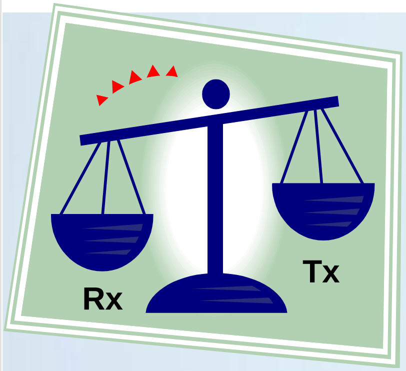
$$[Ca^{++}] \times [CO_3^{--}] = [1.63 \times 10^{-3}] \times [4.0 \times 10^{-5}] = 6.5 \times 10^{-8}$$

$$K_{SP} \text{ of } CaCO_3 = 8.7 \times 10^{-9}$$

The dialysate concentration is higher than the K_{SP} of $CaCO_3$, so precipitation will form.

At low levels the reaction is metastable, hence, precipitation forms slowly.

Application Examples



Part 3

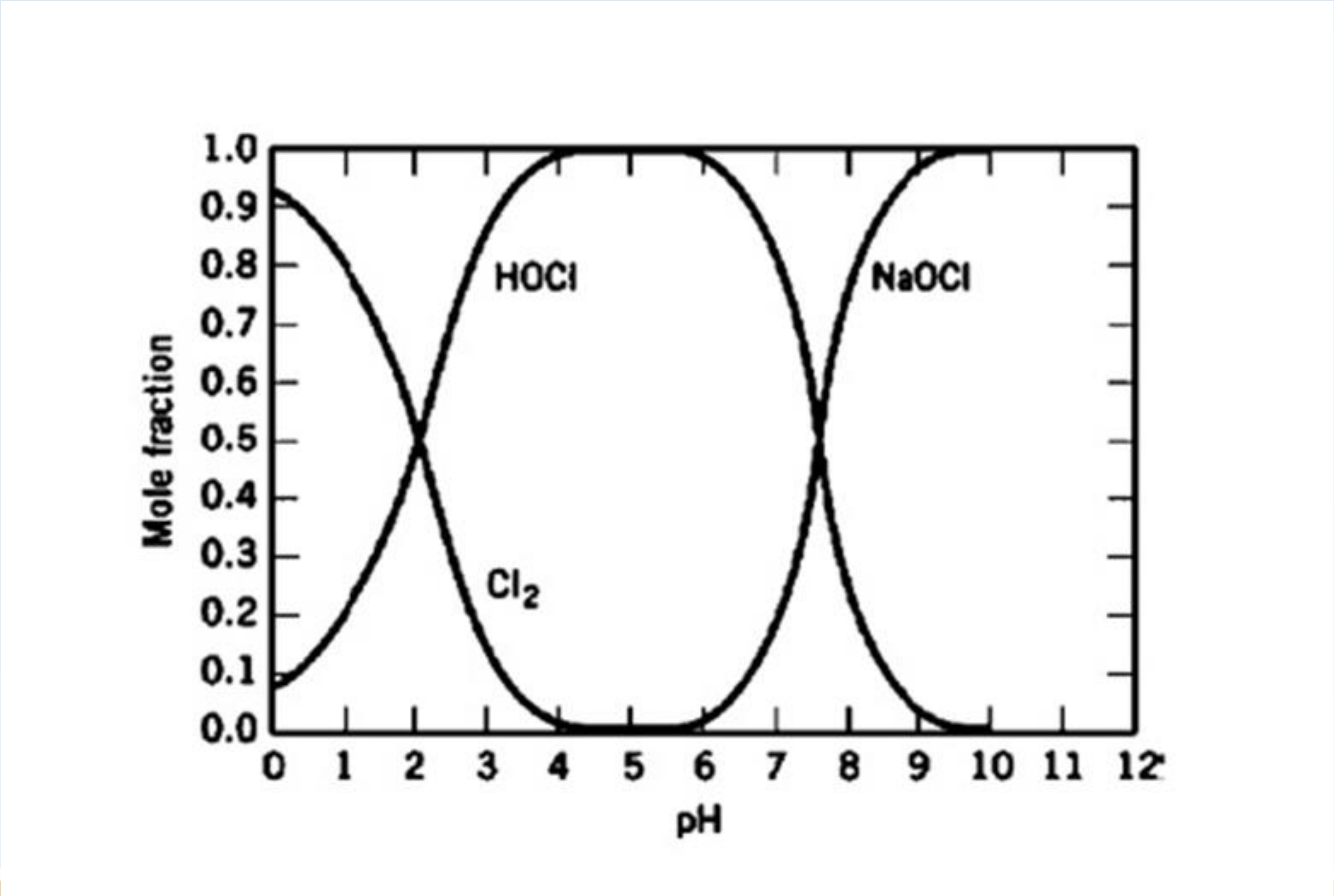
- Disinfection
  - Bleach and pH
- Descaling

Application Lab

- Hypochlorous acid reacts with a wide variety of biomolecules, including DNA, RNA, lipids and fatty acid groups, and proteins.
- Disinfection is due to widespread oxidation of many biomolecules
- Like all chemical reactions, disinfection needs <u>time</u> to occur.
- Rate of reaction is increased by higher <u>concentrations</u> of reactants, and higher temperature.

Application Lab

- Note the pH where Cl_2 is zero
- At pH 6, you have nearly all hypochlorous acid, with no Cl_2 or hypochlorite.



Solubility Product Constant (K_{sp})

What if I add an excess amount of acid?

$$HCl + Al(OH)_3 \leftrightarrow Al^{+3} + 3\,OH^- + H^+ + Cl^-$$

$$OH^- + H^+ = \text{[any guesses?]}$$

The acid is effectively removing the hydroxide from solution, "driving equilibrium" to the soluble Al^{+3} form.

K_{SP} - Calcium Carbonate

What if I add an excess amount of acid?

$$HCl + CaCO_3 \rightleftarrows Ca^{+2} + CO_3^{--} + H^{+} + Cl^{-}$$

Carbonate (CO_3^{--}) and acid make bicarbonate HCO_3^{-}

Bicarbonate and acid make Carbonic acid H_2CO_3

The acid is effectively removing the carbonate through CO_2, and “driving equilibrium” to the soluble Ca^{+2} form

Part 4

Water Purification

What is Water?

- A liquid consisting of 11% Hydrogen and 89% Oxygen by weight.
- 4.3 billion gallons falls in the USA each day.
- Reference for 0^{O} C and 100^{O} C.
- Defines Specific Heat:
  - calorie = energy to raise one cc by 1^{O} C
  - BTU = energy to raise one pound by 1^{O} F
- Defines Specific Gravity:
  - 1 cc at 4^{O} C weighs 1 gram.
- Is 55% to 78% of the human body

What's in Water?...Everything!

- Dissolved Solids:
  - Minerals, Salts, Some organics
- Undissolved Solids:
  - Silica Compounds, Heavy Metal Oxides, Complex Organics
- Gases:
  - Nitrogen, Oxygen, Chlorine, Chloramines, Fluorine
- Micro Organisms:
  - Algae, Bacteria, Fungi

Pure Water

- Water that has been processed for a particular use
- Water that has been treated to neutralize but not necessarily removed contaminants that may be harmful to humans or animals
- Levels of various ions may be safely ingested by humans but not diffused into a patient’s blood stream across a dialyzer membrane

Federal Interim Primary Drinking Water Regulations

CONTAMINANTS	STANDARD
CALCIUM, MAGNESIUM, SODIUM, POTASSIUM, ALUMINUM, CHLORAMINES	T.D.S. <500 mg/l*
CHLORIDE, SULFATE	250 mgL
NITRATE	10.0 mg/L
ZINC	5.0 mg/L
FLUORIDE	1.6 mg/L**
COPPER, BARIUM	1.0 mg/L
ARSENIC, LEAD, SILVER, CHROMIUM	0.05 mg/L
CADMIUM, SELENIUM	0.01 mg/L
MERCURY	0.002 mg/L
MICROBIAL COUNT	1 COLONY/100ml

* 1 mg/L = 1 P.P.M.

** AT 70.7 - 79.2 DEG. F. Higher temperature requires lower concentrations and visa versa

AAMI Standard Water

CONTAMINANT	SUGGESTED MAXIMUM LEVEL mg/L
CALCIUM	2 (0.1 mEq/L)
MAGNESIUM	4 (0.3 mEq/L)
SODIUM**	70 (3 mEq/L)
POTASSIUM	8 (0.2 mEq/L)
FLUORIDE	0.2
CHLORINE	0.5
CHLORAMINES	0.1
NITRATE (N)	2
SULFATE	100
COPPER, BARIUM, ZINC	each 0.1
ALUMINUM	0.01
ARSENIC, LEAD, SILVER	each 0.005
CADMIUM	0.001
CHROMIUM	0.014
SELENIUM	0.09
MERCURY	0.0002

230 mg/L (10 mEq/L) where sodium concentration of the concentrate has been reduced to compensate for excess sodium in the water, as long as conductivity of the water is being continuously monitored.

FIPDWR vs. AAMI

Contaminant	FIPDWR/AAMI Ratio	RO % Rejection Requirement
Zinc, Copper Barium, Arsenic	50 : 1	98%
Lead, Silver Cadmium, Mercury	10 : 1	90%
Fluoride	8 : 1	87.5%
Nitrate	5 : 1	80%
Chromium	3.5 : 1	71%
Sulfate	2.5 : 1	60%
Selenium	1 : 9	
Microbial Count	1 : 20,000	

Bacteria and Endotoxin Restrictions for Water

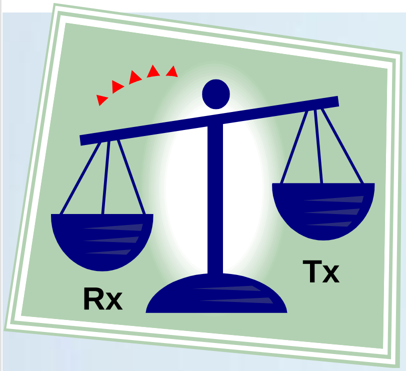
	Bacteria cfu/mL	Endotoxin EU/mL
AAMI RD5:1981	200	Not Specified
AAMI RD52: 2004	200 Action Level = 50	2 Action Level = 1
European Pharmacopeia	100	0.25
Swedish Pharmacopeia	100	0.25
Ultrapure	0.1	0.03

Ultrapure Dialysate, Richard Ward, Seminars in Dialysis, Vol 17, No 6, Nov/Dec 2004, pp 489-497

How tough are bacteria?

- Bacteria were the first life forms on earth and have been around for about 3.5 billion years
- The number of bacteria in or on your body out number the number of human cells 10 to 1
- Time between bacteria (Pseudomonas aeruginosa) entering a pipe and attaching to the pipe wall: 30 seconds
- 99.9% of bacteria in water systems are on the pipe walls
- In theory, 1 ppb of organic matter in water is enough to produce 9,500 bacteria/mL
- Biofilms can be 100 layers thick. Bacteria at the surface are different than bacteria in the lower layers
- A level of one endotoxin unit/mL in water can represent a level of 430K bacteria/mL

Application Examples

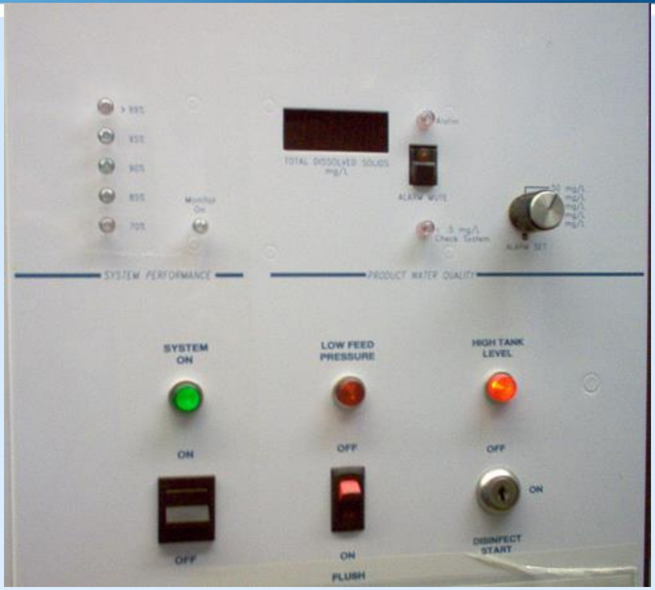


Part 4

- Disinfection
  - Bleach and pH
- Descaling

Chemical Quality and “TDS”

- RO machines are capable of removing 90 to 99% molecules and ionic elements such as Na+, Ca+, Cl-, etc.
- The contaminants in the water are measured by conductivity.
- The RO continuously monitors for contaminants by using either:
  - Conductivity or TDS
  - Percent Rejection
  - Same, exact thing expressed in 2 different ways.



TDS and % rejection

- TDS [Total Dissolved Solids] or “permeate conductivity” – conductivity of the RO water. Smaller numbers are “better”.

- TDS is expressed as ppm
- Permeate conductivity is in uS (microsiemens)

- % rejection = the ratio of the water conductivity before and after the RO. The % of contaminants rejected. Bigger numbers are “better”.

- TDS is an “absolute” metric of water purity, while % rejection is relative to the input.

- Focus on TDS or permeate conductivity
- – especially the trends!

TDS and % rejection

- If the incoming conductivity = 558 uS
- The outgoing conductivity = 6 uS
- What is the % rejection?

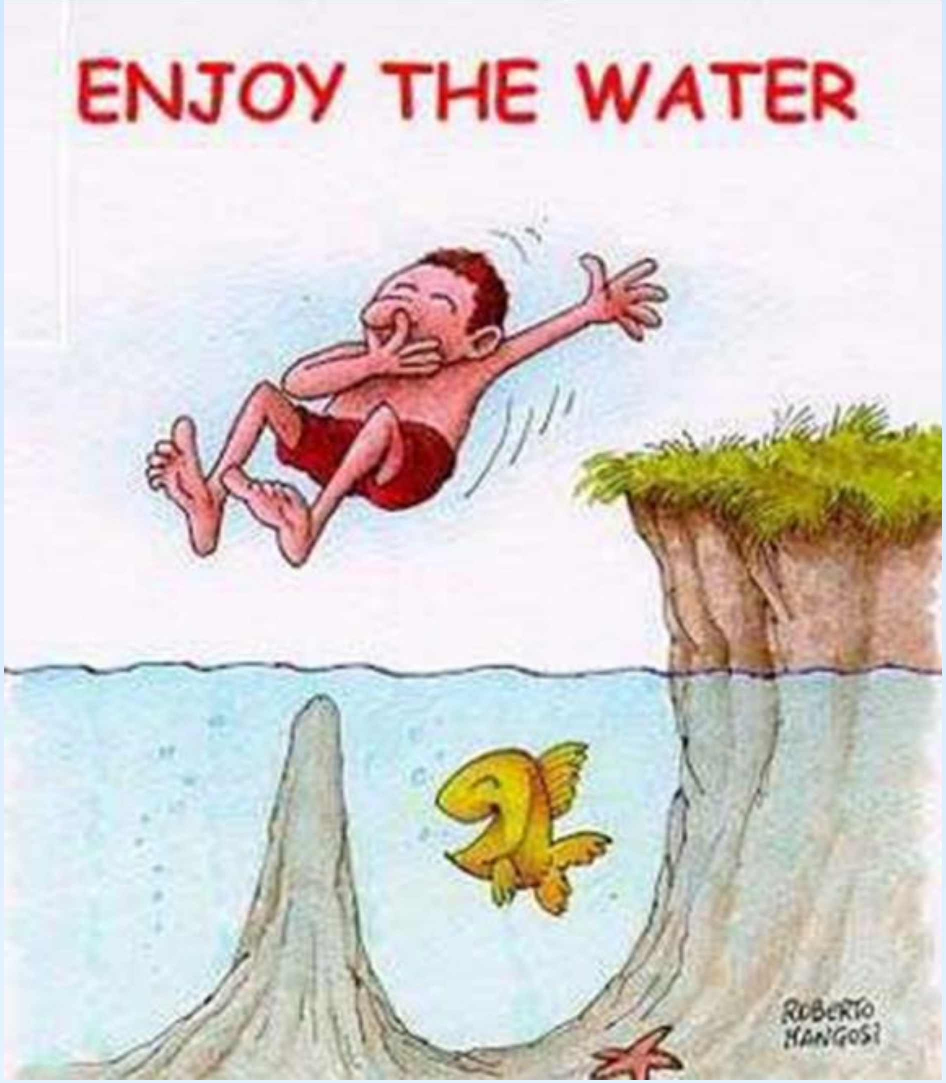
- (558-6)/558 = 99%

- If the incoming conductivity = 258 uS
- The outgoing conductivity = 4 uS
- What is the % rejection?

- (258-4)/258 = 98%

- Which RO is giving better water?

Water Quality


ENJOY THE WATER
ROBERTO MANGOSI