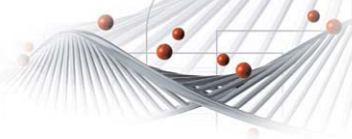




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# BACK TO BASICS: LAB TRAINING

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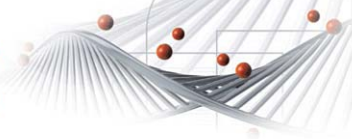
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## Objectives

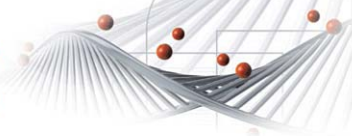
- Define Lab Normal/Reference Range
- Identify the problem/challenge:
  - Local vs. Central labs
  - US vs. SI lab units
- Discuss success strategies for optimum efficiency with lab data management





## Lab Normal/Reference Range

- Depends on:
  - Equipment
  - Reagents
  - Methods
- Affected by:
  - Age
  - Gender
  - Infection
  - Trauma
  - Food



## Abnormal lab value

- What does “abnormal” mean?
  - Out of the reference range/flagged: hi or low
- This does not mean the value is clinically significant (CS):
  - An abnormal value (hi or low) may be “normal” for a particular individual, or it may be “expected” due to disease or treatment for disease



## Lab Normal Range: Units

- US system
- SI system (the System International):
  - Global studies
  - Central labs



## Units Terminology

- **gram**: common measurement for weight (WT)
  - **mg** (milligrams), **g** (grams) per liter
- **mole**: “gram molecular weight”
  - quantity based on atomic WT of substance
  - many tests in SI system expressed as number of moles per liter (in US system, measurements usually in g per liter)
  - **mmol** (millimoles), **μmol** (micromoles) per liter



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### Lab Units Abbreviations

- **dL** - Deciliter
- **IU** - International Unit
- **kat** - Katal
- **L** - Liter
- **mEq** - Milliequivalent
- **mm<sup>3</sup>** - Cubic millimeter\*
- **µL** – Microliter

\* mm<sup>3</sup> = µL



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### Fractions & Multipliers

- **mega (M):** 10<sup>9</sup> or x 1,000,000
- **kilo (k):** 10<sup>3</sup> or x 1,000
- **deca or deka:** 10<sup>1</sup> or x 10
- **deci (d):** 10<sup>-1</sup> or 1/10
- **milli (m):** 10<sup>-3</sup> or 1/1,000
- **micro (µ):** 10<sup>-6</sup> or 1/1,000,000
- **nano (n):** 10<sup>-9</sup> or 1/1,000,000,000
- **pico (p):** 10<sup>-12</sup> or 1/1,000,000,000,000





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### Some Local Lab examples

- '/CMM' = '10E6/L'
- '10<sup>3</sup>/UL' = '10E9/L'
- 'K/UL' = '10E9/L'
- 'MILL/CMM' = '10E12/L'
- '/MM<sup>3</sup>' = '10E6/L'



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### The Basics: Hematology lab panel

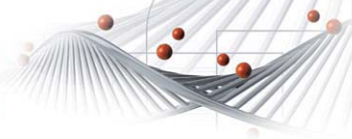
- Hemoglobin (**Hb**) & Hematocrit (**Hct**)
- Complete Blood Count (**CBC**)/hemogram:
  - White Blood Cells (**WBC**) or Leukocyte (**Le**) Count w/Differential
  - Red Blood Cells (**RBC**) or Erythrocyte Count
  - RBC Indices: Mean Corpuscular Volume (**MCV**), Mean Corpuscular Hemoglobin (**MCH**), Mean Corpuscular Hemoglobin Concentration (**MCHC**)
  - Reticulocyte Count
  - Platelet or Thrombocyte Count





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### Hematology

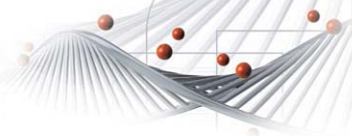
Lab Test	US Normal	SI Normal
<b>Hb</b>	12 – 16 g/dl (W) 14 – 18 g/dl (M)	7.4-9.9 mmol/L(W) 8.7-11.2mmol/L(M)
<b>Hct</b>	37 - 47 % (W) 42 - 52 % (M)	0.37-0.47 <b>volume fraction</b> (W) 0.42-0.52 volume fraction (M)

W = women; M = men



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### Hematology (cont.)

Lab Test	US Normal	SI Normal
<b>RBC</b>	4.2-5.4x10 <sup>6</sup> /mm <sup>3</sup> (W) 4.7-6.1x10 <sup>6</sup> /mm <sup>3</sup> (M)	4.2 - 5.4 x 10 <sup>12</sup> /L (W) 4.7 - 6.1 x 10 <sup>12</sup> /L (M)
<b>Platelets</b>	150,000 -400,000/mm <sup>3</sup>	150 - 400 x 10 <sup>9</sup> /L

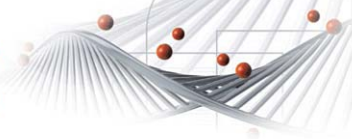
\* mm<sup>3</sup> = μL; μ = 10<sup>-6</sup>





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### Hematology panel

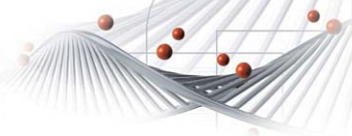
WBCs w/Differential:

- Granulocytes [polymorphonuclear (PMN) Le or “polys”]:
  - Neutrophils (**Ne**) or segmented Ne/”segs”
  - Eosinophils (**Eo**)
  - Basophils (**Ba**)
- Lymphocytes (**Ly**)
- Monocytes (**Mo**)



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### Hematology

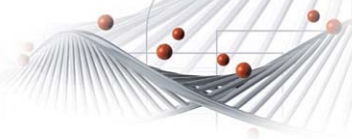
Lab Test	US Normal	SI Normal
<b>WBC</b>	5000-10.000/mm <sup>3</sup>	5 - 10 x 10 <sup>9</sup> /L
<b>Ne</b>	55 - 70 %	0.55 - 0.7 fraction of WBC
<b>Ly</b>	25 - 40 %	0.25 - 0.4 fraction of WBC





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### Hematology (cont.)

Lab Test	US Normal (%)	SI Normal (fraction of WBC)
Mo	2 – 8	0.02 - 0.08
Eo	1 - 4	0.01 - 0.04
Ba	0 - 1	0 - 0.01



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### Hematology: Differential Count

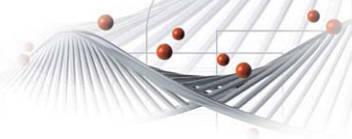
Lab Test	%	Absolute (per mm <sup>3</sup> )
Ne	55 -70	2500 - 8000
Ly	25 – 40	1000 – 4000
Mo	2 – 8	100 – 700
Eo	1 – 4	50 – 500
Ba	0 - 1	25 - 100





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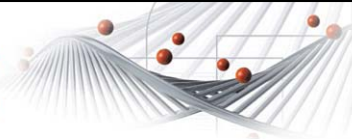
### The Basics: Chemistry lab panel

- Comprehensive Metabolic Panel (CMP)
- 14 specific tests:
  - Glucose
  - Calcium (**Ca**)
  - Albumin
  - Total Protein
- Electrolytes:
  - Sodium (**Na**)
  - Potassium (**K**)
  - Bicarbonate (**CO<sub>2</sub>**)
  - Chloride (**Cl**)



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### Chemistry panel

- Kidney function tests:
  - Blood Urea Nitrogen (**BUN**)
  - Creatinine
- Liver function tests (LFT):
  - Alkaline Phosphatase (**ALP**)
  - Alanine Aminotransferase (**ALT**) or Serum Glutamic-Pyruvic Transaminase (**SGPT**)
  - Aspartate Aminotransferase (**AST**) or Serum Glutamic-Oxaloacetic Transaminase (**SGOT**)
  - Bilirubin





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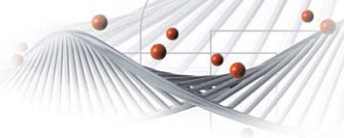
### Chemistry

Lab Test	US Normal	SI Normal
Glucose	70 - 110 mg/dl	3.9 - 6.1 mmol/L
Ca	9.0 - 10.5 mg/dl	2.25 - 2.75 mmol/L
Albumin	3.5 - 5.0 g/dl	35 - 50 g/L
Total Protein	6.4 - 8.3 g/dl	64 - 83 g/L



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### Chemistry (cont.)

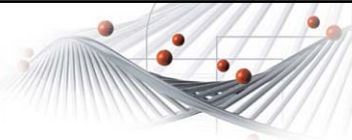
Lab Test	US Normal mEq/L	SI Normal mmol/L
Na	136 - 145	136 - 145
K	3.5 - 5.0	3.5 - 5.0
Bicarbonate	23 - 30	23 - 30
Cl	98 - 106	98 - 106





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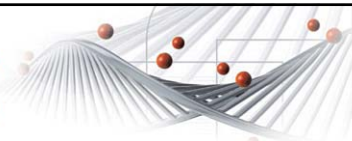
### Chemistry (cont.)

Lab Test	US Normal	SI Normal
<b>BUN</b>	10 - 20 mg/dl	3.6 - 7.1 mmol/L
<b>Creatinine</b>	0.5 - 1.1 mg/dl (W) 0.6 - 1.2 mg/dl (M)	44 - 97 $\mu$ mol/L (W) 53 - 106 $\mu$ mol/L (M)



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### Chemistry (cont.)

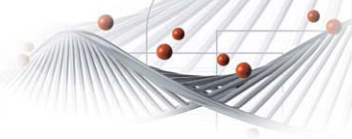
Lab Test	US Normal	SI Normal
<b>ALP</b>	30 - 120 units/L	0.5 - 2.0 $\mu$ kat/L
<b>ALT</b>	4 - 36 units/L	4 - 36 units/L
<b>AST</b>	0 - 35 units/L	0 - 0.58 $\mu$ kat/L
<b>Bilirubin</b>	0.3 - 1.0 mg/dl	5.1 - 17.0 $\mu$ mol/L





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### Lab Units Conversion Tools

- Jay Clinical Services Clinical Laboratory Software and Consulting
- Clinical Analyte Unit Conversion:
  - Select Analyte
  - Select Units
  - Enter number to be converted in Value box
  - Click Calculate



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### Example

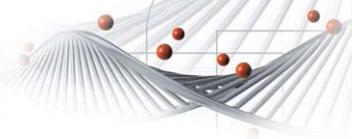
<b>Convert from</b>	<b>Analyte</b>	<b>Convert to</b>
mg/dl	Cholesterol	mmol/L
<b>Value</b>		<b>Answer</b>
199	<b>Factor</b>	5.51
	0.002586	
	Calculate	
	Reset	





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## Lab Units Conversion Tools

- LabQuest Unit Conversion

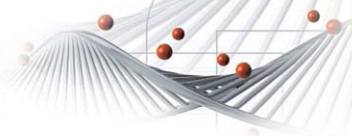
### Conversion Table – US Units to SI Units:

<i>Chemistry</i>	<i>US Units</i>	<i>Multiply by</i>	<i>SI Units</i>
BUN	mg/dl	0.357	mmol/L
Ca	mg/dl	0.25	mmol/L
K	mEq/L	1	mmol/L



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## Study Team Responsibilities

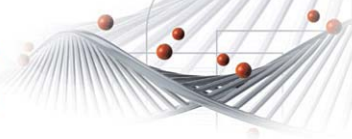
- Each team member has a role in good laboratory management:
  - Clinical Trials Coordinator (CTC)
  - Clinical Research Associate (CRA)
  - Project Manager (PM)
  - Data Manager (DM)
  - Medical Monitor (MM)





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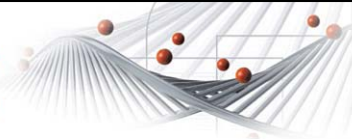
### Clinical Trials Coordinator

- Check FDA form 1572 for Local Labs
- Ensure Reference ranges collected
  - dated w/Lab name
- Throughout the trial collect updated ranges



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### Clinical Research Associate

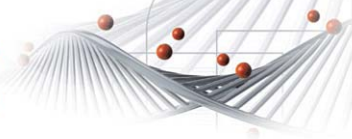
- Review Reg. binder for local Lab ranges/up-to-date
  - Collect updated reference ranges/dated & submit to CTC/TMF
- Understand the significance of the lab tests
- Train the site at SIV
- Check CRF values/units (pre-printed) against local Lab reference ranges
- Site staff will check “normal” or “abnormal” lab values as per the local Lab reference ranges





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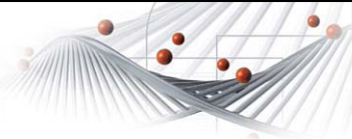
### CRA (cont.)

- Site staff will check “normal” or “abnormal” lab values as per the local Lab reference ranges
- Investigator will consider flagged/abnormal (hi/low) values
  - Clinically significant (CS) or
  - Not clinically significant (NCS)
- Collect copy of lab report along with the CRF page



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### Project Manager

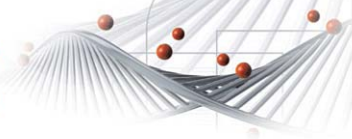
- Ensure a process is followed for collecting the updated local Lab reference ranges
  - Monitoring Plan provide specific direction to the team
- Train team on what labs are required for the trial
- Check CRFs against Protocol
- Develop worksheets in conjunction with DM
- Check lab listings regularly





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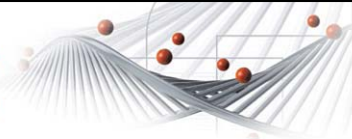
### Data Manager

- Collect local Lab reference ranges:
  - For the period of time any subject had labs drawn per the protocol.
- Check CRF against protocol
- Develop process/worksheets with PM
  - Maintain spreadsheet with the Normal values units for each local Lab
- Send lab listings to PM regularly



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### Medical Monitor

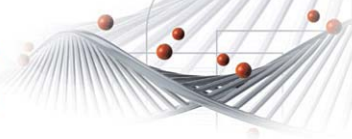
- Train team on significance of the lab tests required for the trial
- Train team on what is “expected” for the particular indication
- What to look for: i.e.. If a particular analyte goes hi/low it could mean this...





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### Summary

- Collecting lab results as data points is an important part of the clinical research process
- Keeping Lab Reference Range up-to-date ensures collected lab values are being compared to correct reference
- Knowledgeable clinical research staff has lab training with tools available to assist them in lab data review and collection
- Clinical research team teamwork excels
- Good quality of lab data submitted to the FDA accelerates the drug approval process



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### References

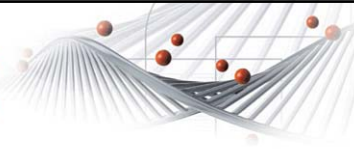
- ✓ Pagana, T: Mosby's Manual of Diagnostic and Laboratory Tests, 2006
- ✓ Fischbach, F: Common Laboratory and Diagnostic Tests, 2006
- ✓ Hopkins, T: Lab Notes, Guide to Lab and Diagnostic Tests, 2005
- ✓ Fischbach, F: A Manual of Laboratory and Diagnostic Tests, 2004
- ✓ Jay Clinical Services Clinical Laboratory Software and Consulting website
- ✓ LabQuest Unit Conversion website
- ✓ US National Library of Medicine website



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# Thank You !

