The Advantage of Direct Clot Detection Technology

- Based on Gold Standard mechanical methods
- “Purest” approach to clot detection
- Affords a reliable low cost device and test strip

Simple direct optical clot detection system - light path passing through test strip

Test Strip with blood clot at top of micro wheel. Offers visual confirmation of clot formation (endpoint).

Close-up of micro wheel removed from a test strip.
## POC PT/INR Meter Comparison

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Coag-Sense</th>
<th>CoaguChek XS</th>
<th>INRatio 2</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Tests Performed</strong></td>
<td>PT/INR</td>
<td>PT/INR</td>
<td>PT/INR</td>
</tr>
<tr>
<td><strong>Intended Use</strong></td>
<td>Professionals/patients</td>
<td>Professionals/patients</td>
<td>Professionals/patients</td>
</tr>
<tr>
<td><strong>Core Technology</strong></td>
<td>Direct micro mechanical detection of clot. Clot interrupts light path.</td>
<td>Electrochemical. Thrombin generation converts a substrate into an electrochemically active product.</td>
<td>ElectroChemical. Coagulation process is detected by impedance. An algorithm picks kinetic point of inflection.</td>
</tr>
<tr>
<td><strong>In Simple Terms</strong></td>
<td>A clot is “seen” and reported immediately without any secondary conversions. Testing time is actual prothrombin time (PT).</td>
<td>First chemical reaction, then electric signal which is “converted” into INR using an algorithm.</td>
<td>As clot is getting formed resistance to flow of current is measured and “converted” to give INR using an algorithm.</td>
</tr>
<tr>
<td><strong>Calibration</strong></td>
<td>Bar code on strip</td>
<td>Code chip/Bar code</td>
<td>Code chip</td>
</tr>
<tr>
<td><strong>Quality Control</strong></td>
<td>Two control strips</td>
<td>Integrated Procedural¹</td>
<td>Integrated Procedural¹</td>
</tr>
<tr>
<td><strong>Sample Volume</strong></td>
<td>10 µl (&lt;1 drop) min.</td>
<td>10 µl (&lt;1 drop) min.</td>
<td>15 µl (1 drop)</td>
</tr>
<tr>
<td><strong>Sample Type</strong></td>
<td>Whole blood or plasma</td>
<td>Whole blood</td>
<td>Whole blood</td>
</tr>
<tr>
<td><strong>Measuring Range</strong></td>
<td>0.8 - 8.0 INR</td>
<td>0.8 – 8.0 INR</td>
<td>0.7 – 7.5 INR</td>
</tr>
<tr>
<td><strong>Hematocrit Range</strong></td>
<td>15%-60%</td>
<td>25%-55%</td>
<td>30%-55%</td>
</tr>
<tr>
<td><strong>Hematocrit Range Limitation</strong></td>
<td>Wide range removes hematocrit level risk in addition to providing tight correlation with reference lab. Red blood cells are not required as system can run plasma controls.</td>
<td>Published paper concludes that 10% variance can be expected from reference due to hematocrit differences when comparing with reference plasma analyzer.²</td>
<td>The impedance to flow of current will depend upon how the red blood cells stack up in the channels, and this is directly influenced by the “number” of cells.</td>
</tr>
<tr>
<td><strong>Testing time</strong></td>
<td>&lt;1 minute (Actual PT)</td>
<td>~1 minute</td>
<td>~1 minute</td>
</tr>
</tbody>
</table>

¹ Not a true functional control test, only checks strip for temperature damage from shipping. Does not test thromboplastin reagent in test channel.
Importance of Hematocrit Values and Detection Methods

Hematocrit values and differences in clot detection mechanisms are cited as top potential sources of inaccuracy between whole blood (WB) and plasma assays

**Hematocrit**

Hematocrit is the percentage of blood volume that is occupied by red blood cells. It is normally about 45% for men and 40% for women. Hematocrit error applies to all WB assays and is, therefore, an important variable to understand. The impact of hematocrit values remains significant, especially in samples with high INRs. Hence, the sickest patients with high (patients with polycythemia) or low hematocrit values (eg, patients with anemia, substantial blood loss, or dehydration) are most at risk for a clinically significant error, particularly if they have INRs more than 3.0. A study done with CoaguCheck S concluded that INR differences between CoaguChek S and plasma PT may be explained in part by the hematocrit. The magnitude of the effect of hematocrit on the INR difference was not greater than approximately 10%. However this 10% variance at critical INR values can make a difference in how a patient will be managed.

CoaguSense with its industry widest hematocrit range of 15 to 60% overcomes this limitation and allows reporting an INR, thus offering the advantage of enhanced decision making and immediate dose adjustments to a full segment of population.

**Detection technology** also plays a role in system accuracy. A system's comparison to reference laboratory plasma based analyzer can be dependent upon its allowed hematocrit range and clot detection mechanism. To enhance the accuracy or "trueness" all analyzers have to be calibrated ultimately to the conventional WHO calibration tilt-tube method. Since Coag-Sense uses direct clot detection technology similar to the WHO method, it can generate INR results that closely correlate with plasma based reference analyzers.

3. Timothy K. Amuokele, MD, PhD, Chris Ferrell, MT(ASCP) and Wayne L. Chandler, MD Comparison of plasma with whole blood prothrombin time and fibrinogen on the same instrument. *American Journal of Clinical Pathology*, 133, 550-556.
Importance of Proper Sampling to Produce Accurate Results

- Proper lancing and sample application is key to accurate POC PT/INR testing in general
  - This is a timing assay that requires sufficient blood volume and timely application.
  - We are measuring a process not a molecule.

- POC PT/INR sampling requirements:
  - Use 21g lancet (diabetes lancets not recommended)
  - Good coagulation results require good blood flow. Squeeze finger from side to open up wound produce pea sized bead of blood.

- Advantage of direct clot detection: if sampling not correct will not give a result (clot)
  - Coag-Sense system either finds a clot or it doesn’t (error preferred over erroneous result)
  - Competing systems try to estimate when a clot has formed based on secondary events
    - More likely to give erroneous result if sampling incorrect as does not require a definitive clot formation, only an inflection point in the curve fitting algorithm
    - Users often continue to add sample to get meter to allow testing to advance
    - Susceptible to low hemoglobin and hematocrit levels in sample
Coag-Sense Prothrombin Time System - Competitive Advantage

- First POC system to directly detect clot formation
- Testing time is actual Prothrombin Time
- Excellent accuracy and precision (CV 2.5%)
- Complexity of entire device is reduced as only a simple binary detection system is required
- Run whole blood samples or plasma controls
- No interference from blood components
- Not affected by low hemoglobin & hematocrit levels
- Results comparable to gold standard WHO tilt-tube method