Total control of INR results: Certified plasmas with a web-based tool

- HemosIL® ISI Calibrate
- HemosIL INR Validate
- ISIweb™ Application
Local ISI Assignment and Validation

The World Health Organization (WHO) adopted the International Normalized Ratio (INR) in 1983 in an effort to reduce reagent variation and improve standardization. The International Sensitivity Index (ISI) is a measure of a reagent’s responsiveness to reduced levels of Vitamin K–dependent factors compared to a primary International Reference Preparation (IRP) of a like source.

\[ \text{INR} = \frac{\text{Plasma PT}}{\text{MNPT}} \]^\text{ISI}

While the INR system has significantly improved PT reporting, it is still associated with a high degree of variation and inconsistency among laboratories. Reliable INR determination depends upon accurate ISI and MNPT values.

Clinical and Laboratory Standards Institute (CLSI) and International Society on Thrombosis and Haemostasis (ISTH) (SSC) have published new guidelines to improve INR interlaboratory variability. Incorporating certified plasmas in the establishment of a local ISI has considerably reduced inter-laboratory imprecision. The following steps in the guidelines ensure optimal INR reporting:

- **Use of certified plasmas**
  - The certified plasmas may be composed of pooled, stable Anti–Vitamin K therapy (AVK) donors for likeness to fresh or artificially depleted plasma.
  - Certified plasmas, traceable to WHO International Reference Preparations, are used to assign species-specific values, corresponding to local laboratory thromboplastin.

- **Verification of INR results**
  - INR results obtained with the manufacturer’s ISI and the local MNPT are compared with the INR values of a set of at least three levels of certified plasma (INR 1.5 – 4.5).

- **Local system calibration**
  - A modified WHO procedure which determines and plots the local instrument/reagent PT values against the assigned values of certified plasmas on a log/log plot, using orthogonal regression analysis, is performed. The resulting analysis yields the new local ISI from the slope, and the new local MNPT from the intercept of this regression line.

- **Verification of INR results using new local system calibration parameters**
  - The new local ISI and MNPT are incorporated into the local laboratory instrument and verify that the new local ISI and MNPT can be implemented.

The CLSI and ISTH guidelines propose that each laboratory verify the use of the correct ISI when:

- changing the lot number of the thromboplastin reagent,
- a major instrument component is replaced,
- laboratory is not in compliance with an external quality assessment scheme.
Total Solution for Local ISI Assignment and Validation

This complete diagnostic solution features INR Validate, ISI Calibrate and the first self-guided, web-based tool, ISIweb. It offers total control over the local ISI assignment and validation process on IL Hemostasis systems, when monitoring patients undergoing oral anticoagulant therapy.

- Easy and intuitive system for reporting quality test results
- Increased efficiency in benchmarking standardized values
- Maximum performance of IL Hemostasis systems

### HEMOSIL INR VALIDATE

- Tri-level set of certified plasmas (made from stable human AVK donors) assess INR accuracy. Reference INR values are reagent-specific and range from 1.6 – 5.0.
- Test on a local instrument/reagent system using IL’s instrument/reagent-specific ISI and the laboratory’s established lot-specific MNPT.
- If the INR values are ±15% of the assigned reference values, as determined through ISIweb, the PT/INR system is verified.
- If the mean of any control level (INR) is > ±15% of their assigned reference values, as determined through ISIweb, a new local ISI calibration is recommended using HemosIL ISI Calibrate. INR Validate is used again to verify a newly established local ISI and MNPT.

### HEMOSIL ISI CALIBRATE

- Set of four certified plasmas (level A Normal and levels B–D Abnormal). The INR reference values have an INR range of 0.9 – 5.0. The normal plasmas are made from a pool of normal donors and the AVK plasmas are from stable human donors undergoing AVK therapy.
- Test on a local IL instrument/reagent system and enter the PT seconds into ISIweb, which compares them to reference values by plotting an orthogonal regression of the log/log plot. The new local ISI and new local MNPT are derived from the regression line.

### ISIWEB

- Web-based tool available to all IL customers using ACL Hemostasis systems and HemosIL PT reagents, in conjunction with INR Validate and ISI Calibrate kits, to verify local PT/INR systems and, if necessary, establish new local ISI and MNPT (CLSI and ISTH compliant).
- ISIweb electronically archives and reports all activities on local ISI assignment and validation—an essential tool for regulatory compliance and accreditation.
ISI Assignment and Validation Overview

Upon registration, each lab can perform the following functions:

1. INR Validation: To verify the accuracy of the INR
2. Local ISI Assignment: To establish a new local ISI
3. Validation of Local ISI: To verify new local ISI and new MNPT

Step 1
INR Validation

- Run INR Validate (in duplicate over three sessions)
- Enter INR results into ISIweb

The ISIweb algorithm will check that results are within expected values.

1. Pass: Continue using manufacturer’s ISI and local MNPT
2. Fail: Proceed to Step 2

Step 2
Local ISI Assignment

- Run ISI Calibrate (in duplicate over three sessions)
- Enter PT results (sec) into ISIweb

The ISIweb algorithm will check that results are within expected values and provide new local ISI and MNPT.

Step 3
Validation of Local ISI

- Run INR Validate with new local ISI and MNPT

The ISIweb algorithm will check that results are within expected values.

1. Pass: Use local ISI and MNPT
2. Fail: Call IL representative for assistance

With ISI Calibrate, INR Validate and ISIweb, total control of INR results is just a click away.
Efficiency and Compliance Through ISIweb

Accessible from www.ilww.com and www.ilus.com homepages, the ISIweb online registration screen allows users to register and log in instantaneously.

Following establishment of an ISIweb profile, all subsequent INR Validate and ISI Calibrate interactions will recall this data for maximum efficiency.

ISI Calibration Reports are generated online through ISIweb and can be stored electronically or printed, ensuring regulatory compliance.
Certified Plasmas for Local ISI Assignment and Validation

<table>
<thead>
<tr>
<th>PRODUCT</th>
<th>PART NUMBER</th>
<th>KIT CONFIGURATION</th>
<th>LEVELS OF AKV PLASMA</th>
<th>APPROXIMATE INR VALUES*</th>
</tr>
</thead>
<tbody>
<tr>
<td>INR Validate</td>
<td>0020010500</td>
<td>3 vials x 1 mL (lyo)</td>
<td>Level 1</td>
<td>1.6 – 2.4</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Level 2</td>
<td>2.5 – 3.5</td>
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<td></td>
<td></td>
<td></td>
<td>Level 3</td>
<td>3.8 – 5.0</td>
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<tr>
<td>ISI Calibrate</td>
<td>0020010600</td>
<td>4 vials x 1 mL (lyo)</td>
<td>Level A</td>
<td>0.9 – 1.1</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Level B</td>
<td>1.6 – 2.4</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Level C</td>
<td>2.5 – 3.5</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Level D</td>
<td>3.8 – 5.0</td>
</tr>
</tbody>
</table>

* INR values are kit-specific. Please refer to product package inserts.

For more information, visit www.ilww.com or contact your local IL sales representative/distributor.

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