

Clinical Expectation For PT/INR Comparisons

The following references from **CLSI** (Clinical and Laboratory Standards Institute), formerly known as **NCCLS** (National Committee for Clinical Laboratory Standards), the **WHO** (World Health Organization), and the **ISO** (International Organization for Standardization), aid in understanding the underlying issues associated with correlations and comparisons between two PT/INR systems. They validate that system accuracy, which is affected by systematic bias and random effects (and is inversely related to measurement uncertainty), impacts the degree to which the individual results produced by an oral-anticoagulation monitoring system agree with INR values when the system is used as intended.

The **CLSI** is an international, standards developing organization that promotes the development and use of voluntary consensus standards and guidelines within the healthcare industry. The CLSI-approved guideline, "Point of Care monitoring of anticoagulation therapy" states that:

"INR standardization considerably improves comparability of results obtained with different test systems. However, it does not correct for all potential variables, and that is true for both laboratory based and POC-PT (Point Of Care- Prothrombin Time) test systems. Moreover, poor correlation of the INRs obtained with highly sensitive (low-ISI) thromboplastins and less sensitive (high-ISI) thromboplastins may be observed. Results exceeding an INR of 5.0 generally have reduced trueness, precision and linearity, both in POC and laboratory based PT testing. These results should be interpreted accordingly."

The World Health Organization Expert Committee on biological standardization in its Technical Report Series No. 889 states that:

"For the calibration procedure blood samples from healthy subjects and patients who have been on oral anticoagulants for at least 6 weeks should be selected. Samples from patients treated with heparin should not be used. It is recommended that patients' samples with INR values in the range 1.5 to 4.5 should be selected."

In another section of the same Technical Report the use of calibrated thromboplastins in clinical practices is discussed:

"All medical staff and health auxiliaries involved in controlling oral anticoagulant treatment should be encouraged to use the INR system. It should be appreciated, however, that this system can be accurate only in the INR range explored by the calibration procedure, i.e. 1.5 to 4.5."

ISO is a worldwide federation of national standards bodies (ISO member bodies). In the ISO Draft of 2004, titled "Clinical laboratory testing and in vitro diagnostic test systems-in vitro monitoring systems for anticoagulant therapy self testing", guidelines are provided for oral anticoagulation monitoring systems users.

The primary objectives are to establish requirements for oral-anticoagulation monitoring systems that will enable lay users to achieve acceptable performance.

The following minimum acceptable accuracy criteria apply to system accuracy verification studies performed by **Professional Operators**:

- In the INR range **below 2.0**, 90% of the allowable differences between results from the POC system and reference system shall be ± 0.5 .
- In the INR range of **2.0 to 4.5**, 90% of the allowable differences between results from the POC system and reference system shall be $\pm 30\%$.
- In the INR range of **4.6 to 6.0**, no performance criteria are listed for INR values.
- In the INR range of **2.0 to 4.5** the allowable bias (**Average Difference**) shall be ± 0.3 INR.

Note: In order to have confidence that these criteria have been met, it is important to include the appropriate number and range of both normal and anti-coagulated samples.

The following acceptance criteria apply to **Lay User** performance evaluation:

- In the INR range 2.0 to 4.5, 95% of all results obtained by the Lay User and the trained Health Care Professional (HCP) shall be within ± 0.5 INR when the test is performed by both, on the same device.
- The average difference between the Lay User's results and the HCP's results shall be $< 10\%$ for a population of users.

By following manufacturer's recommended testing instructions, most patients in the therapeutic range will have test results comparable to the trained professional's result when tested side by side on the user's device.

References

1. The NCCLS Point of Care monitoring of anticoagulation therapy; approved guideline, NCCLS document H49-A Vol. 24 No. 23 (TSBN 1-56238-540-2), NCCLS, 940 West Valley Road, Suite 1400, Wayne, PA, 19087-1898 USA, 2004.
Section 8.3.1.3 Test Result Interpretation and Limitations.
2. WHO Technical Report Series 889, WHO Expert Committee on Biological Standardization, Forty-eighth report.
Section 6.1.1 The Calibration procedure, Calibration of a secondary standard, Blood Samples.
Section 7 The use of calibrated thromboplastins in clinical practice.
3. (ISO/DIS 17593) ISO Draft of 2004, titled "Clinical Laboratory Testing and In Vitro Diagnostic Test Systems-In Vitro Monitoring Systems for Anticoagulant Therapy Self Testing".