

## Standardization of PT/INR Testing

### Background

Prothrombin time (PT) is the test of choice for monitoring patients on oral anticoagulants. PT was reported for many years as the clotting time in seconds. To standardize results, a ratio of the patient's PT result and the mean of the normal range was calculated.

It is now widely accepted that the anti-coagulation level and the appropriate drug regimen are best determined on the basis of the International Normalized Ratio (INR). The INR value depends on the sensitivity of the thromboplastin reagent used relative to the International Reference Preparation (IRP), a thromboplastin prepared from human brain.<sup>1,2</sup>

This standardization system was introduced by the World Health Organization (WHO) in 1983 to provide a common basis for the interpretation of the PT results independent of the sensitivity of the thromboplastin reagent which tends to vary from one manufacturer to another.<sup>1,3</sup>

### Importance of INR

To resolve the problem of PTs, varying widely between methods, the use of the INR system has been recommended for monitoring patients on oral anticoagulant therapy. This recommendation is supported by the **American College of Chest Physicians, the National Heart, Lung and Blood Institute and the British Society for Hematology**.<sup>11</sup>

This reporting system provides a reliable, standardized means of reporting the state of anticoagulation with minimal variability between different laboratories, reagents, and instrumentation used to perform testing.<sup>12,13</sup>

In 1985, the International Committee on Thrombosis and Hemostasis/International Committee for Standardization in Hematology recommended adoption of the INR system to facilitate international agreement on therapeutic ranges and allow direct comparison of clinical trials.<sup>5</sup>

### Standardization

Since thromboplastins are produced using different methods and from different sources. The comparative sensitivity of an individual thromboplastin can vary greatly. The more sensitive the thromboplastin reagent, the longer will be the resulting PT and conversely, the less sensitive the reagent the shorter the resulting PT.<sup>4</sup>

Variance can even occur within a single batch depending on shelf life. This variability in sensitivity and its effect on PT outcomes can have a detrimental effect on the management of warfarin therapy in patients requiring anti-coagulation. This variability has also caused great international debate and concern for several decades.<sup>5,14</sup> Today, thromboplastins are calibrated against the standard thromboplastins with sensitivities comparable to the first International Reference Preparation (IRP) and are assigned an International Sensitivity Index (ISI).<sup>6</sup>

$$\text{INR} = (\text{Patient PT} / \text{Mean of normal patient range})^{\text{ISI}}$$

### Performance Criteria

\* Standardization should be accompanied by educational efforts in order to optimize the proper use and interpretation of test results.

\* The ISI value is critical for calculation of the INR, because the ISI value is the exponent in the formula. Consequently, small errors in the ISI assignment may affect the calculated INR substantially.<sup>14</sup>

\* It should be remembered that the INR only has meaning for patients on a stable dose of oral anticoagulants. The INR should not be used to evaluate the coagulation status of patients who have not been anti-coagulated for at least one week or in those with an abnormal PT for other reasons, e.g., liver disease.<sup>8</sup>

\* Thromboplastins from recombinant sources have been introduced with ISI values close to 1.0, yielding precise results.<sup>9,10</sup>

## INR Reporting Format

While the INR reporting format may improve the management of anti-coagulated patients, the INR is inappropriate in three subsets of patients. First it is designated for patients who are stabilized on oral anticoagulant therapy and is not appropriate for those patients who have recently begun their treatment. Second, patients with liver disease should not be monitored by the INR since they frequently lack circulating factors. Lastly, patients who are being routinely screened for clotting factor deficiencies should not be evaluated with the INR.

## Resources Available for Standardization

HemoSense INRatio meter is traceable to the World Health Organization. There is a network of laboratories that perform the INR testing and are similarly standardized. A partial list of participating network laboratories include the following:

### Haemostasis

Reference Laboratory Henderson  
Research Center 711 Concession Street  
Hamilton, ON L8V 1C3, Canada

### Heamost. And Thr Research

C2-R Leiden  
University Medical Center  
Albinusdreef 2 2333 ZA  
Leiden, Netherlands

**For further information please call  
HemoSense Technical Support  
1-877-436-6444**

## References

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HemoSense, Inc.  
651 River Oaks Parkway  
San Jose, CA 95134  
1-877-436-6444 toll free  
408-719-1393 tel  
408-719-1184 fax  
[www.hemosense.com](http://www.hemosense.com)

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