

# TSH Testing at LabCorp

## *Methodology and Results Interpretation*

### **Background**

In August 2009, LabCorp converted instrumentation and methodology for thyroid hormone immunoassay testing from the Siemens Centaur to the Roche Elecsys system. Experts in thyroid disease testing have selected this technology as one of the most accurate and precise methods for this testing. It is successfully used by a number of regional and national laboratories, including ARUP Laboratory, Cleveland Clinic, and the Los Angeles County–University of Southern California Medical Center (Carole A. Spencer, PhD). Nevertheless, some clients have expressed concern regarding the comparability of the old and new methodologies and the possible increase in the number of elevated TSH results in their patient populations. The aim of this document is to address those concerns.

### **Assay Methodology**

Historically, immunoassays for the measurement of TSH have used different calibrations and are traceable to different reference standard preparations that may cause significant differences in results. Both Siemens and Roche methods are standardized to the same World Health Organization (WHO) Second International Standard for human TSH (IRP 80/558).<sup>1,2</sup> Published studies as well as internal LabCorp data show that the two methods agree reasonably well.<sup>3,4</sup> Human TSH has different glycoforms, however, and different immunoassays may recognize them differently. This may contribute to difficulties in assay standardization and lead to discordant results with individual patient samples.<sup>3</sup>

Prior to the introduction of any new methodology, LabCorp thoroughly evaluates the available peer-reviewed literature

and conducts its own in-house evaluation. Performance of the Roche Elecsys assay was determined to be one of the industry's best. Its precision is superior according to a number of national and international proficiency surveys, and its accuracy was confirmed by excellent recovery of WHO International Reference Preparation.<sup>4</sup>

In addition, overall recovery using the Siemens Centaur method was observed to be a few percentage points lower than that of the Roche Elecsys.<sup>4</sup> Consequently, TSH results obtained on the Centaur method are somewhat lower than those obtained by the Elecsys system.<sup>4</sup> Overall, there is strong scientific evidence that the Roche Elecsys methodology provides accurate and reliable TSH measurements. This method meets the performance requirements of The National Academy of Clinical Biochemistry as a third-generation assay for TSH<sup>5</sup> and has a functional sensitivity as low as 0.014  $\mu\text{IU}/\text{mL}$ .<sup>2</sup>

### **TSH Results Interpretation**

In 2008, LabCorp adopted the clinical decision limits for TSH (0.45 to 4.50  $\mu\text{IU}/\text{mL}$ ) as recommended by both the Endocrine Society and the American Medical Association.<sup>6</sup> Those guidelines employed a careful and conservative approach in their recommendations. The scientific panel admitted that the National Health and Nutrition Examination Survey (NHANES III), one of the largest national population studies, found that the reference interval for TSH concentration was 0.45  $\mu\text{IU}/\text{mL}$  to 4.12  $\mu\text{IU}/\text{mL}$ .<sup>6,7</sup>

Moreover, some investigators have suggested that the upper limit for serum TSH be set to 2.5  $\mu\text{IU}/\text{mL}$ .<sup>6</sup> Indeed, there is a higher rate of progression to overt hypothyroidism and

a higher prevalence of antithyroid antibodies in individuals with serum TSH levels higher than 2.5  $\mu\text{IU/mL}$ .<sup>6</sup>

The panel concluded, however, that despite the fact that serum TSH concentrations higher than 2.5  $\mu\text{IU/mL}$  but less than 4.5  $\mu\text{IU/mL}$  may identify some individuals with the earliest stage of hypothyroidism, there is no evidence for associated adverse consequences. Additionally, the consequences of subclinical hypothyroidism with serum TSH levels between 4.5  $\mu\text{IU/mL}$  and 10  $\mu\text{IU/mL}$  are minimal, and the panel recommends against routine treatment of patients with TSH levels in these ranges.<sup>6</sup>

**The American Association of Clinical Endocrinologists recommends that during patient treatment the TSH target level should be between 0.3  $\mu\text{IU/mL}$  and 3.0  $\mu\text{IU/mL}$ .**<sup>8</sup>

Another important complicating factor is that TSH concentration varies significantly within the same individual. Several studies report that serial TSH measurements from the same patient must vary by as much as 60% to 104% to be truly different and indicate clinically significant change with account to biological and analytical variations.<sup>9,10</sup>

A recent clinical review published by the Endocrine Society states that “. . . **it must be recognized that a normal range upper or lower limit, based on a reference population, does not of necessity mean that any person who falls outside that limit requires treatment or has illness. In the meantime, careful follow-up should be considered for asymptomatic patients with serum TSH levels between 3  $\mu\text{IU/mL}$  and 4.5  $\mu\text{IU/mL}$ , especially if they have positive anti-TPO antibodies.**”<sup>11</sup>

Guidelines from the American Thyroid Association warn that the prevalence of patients with subclinical hypothyroidism (that is defined as elevated TSH and normal  $\text{FT}_4$ ) may be as high as 17% in the adult population.<sup>6,12</sup>

## Conclusions

LabCorp's conversion to the Roche Elecsys methodology allows for early diagnosis of more patients with mild thyroid disorders, more precise monitoring of those patients, which can aid in early identification of patients who are progressing to overt disease and allow for the timely initiation of treatment.

## References

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