References


Elecys® Anti-TSHR
The first fully automated assay for detection of autoantibodies to the TSH receptor

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**Indications of TSH receptor autoantibody measurements:**

- Detection or exclusion of Graves’ autoimmune hyperthyroidism and differentiation from disseminated autonomy of the thyroid gland
- Monitoring the therapy of Graves’ disease and prediction of relapse
- Assessing the risk of development of fetal hyperthyroidism in the last trimester of pregnancy

**Test components**
The Elecsys Anti-TSHR assay uses soluble immuno-complexes of native porcine TSH receptor and a biotinylated mouse monoclonal capture antibody directed against the C-terminal end of the porcine TSH receptor and a ruthenium labeled human monoclonal thyroid-stimulating autoantibody (M22).

**Elecsys® Anti-TSHR**
The first fully automated TRAb assay with testing time of 27 minutes
In accordance with current manual TRAb assays, Elecsys Anti-TSHR cannot distinguish between stimulating and blocking antibodies due to the close proximity of the epitopes of both antibody subtypes.\(^2,3\) Labeled M22 binding will always compete with binding of both TRAb subtypes.

Test principle of Elecsys Anti-TSHR

1. Step (9 minutes):
   TSH receptor autoantibodies (TRAb) in the patient sample - if present - bind to the TSH binding pocket of a complex of porcine TSH receptor and biotinylated capture antibody (monoclonal mouse antibody to the C-terminal end of the porcine TSH receptor).

2. Step (9 minutes):
   Further binding of autoantibodies from the sample to the TSH receptor/biotinylated capture antibody complex.

3. Step (9 minutes):
   Streptavidin coated microparticles and a human monoclonal detection antibody (M22) labeled with a ruthenium complex are added. Bound TRAb are detected by their ability to inhibit the binding of labeled M22 to the TSH binding pocket on the TSH receptor complex. Transfer of the reaction mixture into the measuring cell and measurement of the signal.

Commercially available radioimmunoassay with recombinant human TSH receptor vs. Elecsys Anti-TSHR (MODULAR ANALYTICS E170).

Samples which were positive or borderline in the routine assay were measured.

\[
Y = 1.045 - 0.249x \\
N = 216 \\
r = 0.9790
\]

Radioimmunoassay with recombinant human TSH receptor (IU/L) vs. Elecsys Anti-TSHR (IU/L)

A commercially available radioimmunoassay (with recombinant human TSH receptor and iodine-125-labeled bovine TSH as tracer) vs. Elecsys Anti-TSHR (with native porcine TSH receptor and ruthenium labeled, human monoclonal autoantibody M22 as tracer) leads to diagnostically comparable results.

Good comparability between porcine and human TSH receptor

The good comparability between Elecsys Anti-TSHR (native porcine TSH receptor) and a conventional radioimmunoassay using recombinant human TSH receptor was demonstrated in external studies of 2nd generation assay systems.\(^10,11,12\)

\[^{10,11,12}\text{Results are in agreement with recently published studies which found no difference between the use of recombinant TSH receptor of human origin and native TSH receptor of porcine origin in terms of sensitivity and predictive value in the treatment of Graves’ disease when using comparable 2nd generation assay systems.}\]
Clinical evaluation of Elecsys Anti-TSHR

“In spite of the short measuring time of only 27 minutes, the assay showed the same or better results with the existing commercial products. The short measuring time would contribute to speedy, preconsultation diagnosis of thyroid disease, especially of Graves’ disease”.7

Distribution of serum TSH receptor autoantibodies (TRAb) measurements in different patient groups using Elecsys Anti-TSHR. The points less than 0.2 IU/L and more than 40 IU/L stand out of the measuring range.*

* Elecsys Anti-TSHR recommended measuring range 0.3 - 40 IU/L
In an external study using the Elecsys Anti-TSHR assay on samples from 436 apparently healthy individuals, 210 patients with thyroid diseases* without diagnosis of Graves’ disease, and 102 patients with untreated Graves’ disease an optimal cut-off of 1.75 IU/L was determined. At this cut-off the sensitivity was calculated at 96% and the specificity at 99%.

The calculated receiver operating characteristic (ROC) curve had an area under the curve (AUC) of 0.99. The upper limits of Anti-TSHR values in the cohorts of healthy individuals and in patients with thyroid disease without diagnosis of Graves’ disease were 1.22 IU/L and 1.58 IU/L, respectively (97.5 percentile).

* 91 subacute thyroiditis, 45 adenomatous goiter, 27 Hashimoto’s disease, 32 painless thyroiditis, 7 autonomously functioning thyroid nodules, 1 toxic multinodular goiter, 7 others.

Reference range

Comparison of sensitivity, specificity and positive rate between Elecsys Anti-TSHR and three commercial TRAb assays in patients with Graves’ disease, painless thyroiditis and subacute thyroiditis.

<table>
<thead>
<tr>
<th>Cut-off</th>
<th>Elecsys Anti-TSHR</th>
<th>TRAb CT</th>
<th>TRAb 2nd</th>
<th>TRAK human</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cut-off</td>
<td>1.86 IU/L*</td>
<td>15 % Inhibition</td>
<td>15 % Inhibition</td>
<td>1 IU/L</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>97.0 %</td>
<td>91.6 %</td>
<td>100 %</td>
<td>98.7 %</td>
</tr>
<tr>
<td>Specificity</td>
<td>99.1 %</td>
<td>97.7 %</td>
<td>96.4 %</td>
<td>98.5 %</td>
</tr>
<tr>
<td>Positive rate</td>
<td></td>
<td>91.6 % (57/63)</td>
<td>100 % (25/25)</td>
<td>98.7 % (38/39)</td>
</tr>
<tr>
<td>Graves’ disease</td>
<td>0.2 % (0/50)</td>
<td>0 % (0/36)</td>
<td>0 % (0/33)</td>
<td>3.0 % (1/33)</td>
</tr>
<tr>
<td>Painless thyroiditis</td>
<td>1.5 % (2/135)</td>
<td>3.2 % (3/94)</td>
<td>7.7 % (2/26)</td>
<td>17.2 % (5/29)</td>
</tr>
<tr>
<td>Subacute thyroiditis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive rate</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Graves’ disease</td>
<td>0.7 % (7/105)</td>
<td>0.7 % (7/99)</td>
<td>0.7 % (7/99)</td>
<td>0.7 % (7/99)</td>
</tr>
<tr>
<td>Painless thyroiditis</td>
<td>0.4 % (4/90)</td>
<td>0.4 % (4/90)</td>
<td>0.4 % (4/90)</td>
<td>0.4 % (4/90)</td>
</tr>
<tr>
<td>Subacute thyroiditis</td>
<td>1.5 % (2/135)</td>
<td>3.2 % (3/94)</td>
<td>7.7 % (2/26)</td>
<td>17.2 % (5/29)</td>
</tr>
</tbody>
</table>

a) Using the manufacturers’ cut-offs

b) Using the optimal cutoff by ROC analysis

Anti-TSHR: TSH receptor autoantibody, ROC: receiver operating characteristics.

* Elecsys Anti-TSHR recommended cut-off is >1.75 IU/L.
Elecsys® Anti-TSHR

High complexity testing simplified and automated

Elecsys® Anti-TSHR test characteristics

| Testing time | 27 minutes |
| Test principle | Competition principle |
| Calibration | 2-point calibration |
| Sample material | Serum |
| Sample volume | 50 µL |
| Analytic sensitivity | 0.3 IU/L |
| Functional sensitivity | 0.9 IU/L |
| Measurement range | 0.3–40 IU/L |
| Traceability | NIBSC 90/672 |
| Total precision (EPS - A2) | E2010: 1.8–9.7% (25.5–1.73 IU/L) \nE170: 1.9–11.4% (24.6–1.71 IU/L) |

Expected values:

- Anti-TSHR negative ≤ 1.75 IU/L
- Anti-TSHR positive > 1.75 IU/L

First fully automated TRAb assay

allows full consolidation of thyroid testing on Elecsys 2010 cobas® modular platform and MODULAR ANALYTICS

Rapid availability of results with testing time of 27 minutes helps optimize internal and external processes. Current manual TRAb assay results are available after approx. 3 hours at the earliest.

Automated testing can be integrated into the workflow on a routine laboratory analyzer without splitting of patient samples. No necessity of collecting a certain number of patient samples as advisable for manual assays.

Proven clinical and technical performance through validation in a multicenter study and an independent single site as demonstrated in peer reviewed publications.7,8,9

Order number

Elecsys® Anti-TSHR
100 tests 04 388 780 190

PreciControl ThyroAB
for 1×2 mL each of PreciControl Thyro 1 and 2 05 042 666 190