



September 18, 2018

Roche Diagnostics  
Reanna Toney  
Principal, Regulatory Affairs  
9115 Hague Road  
Indianapolis, IN 46250

Re: K181233

Trade/Device Name: Elecsys FT4 III  
Regulation Number: 21 CFR 862.1695  
Regulation Name: Free thyroxine test system  
Regulatory Class: Class II  
Product Code: CEC  
Dated: August 2, 2018  
Received: August 3, 2018

Dear Reanna Toney:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at <https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm> identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part

801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see <https://www.fda.gov/CombinationProducts/GuidanceRegulatoryInformation/ucm597488.htm>); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to <http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm>.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (<https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/>) and CDRH Learn (<http://www.fda.gov/Training/CDRHLearn>). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (<http://www.fda.gov/DICE>) for more information or contact DICE by email ([DICE@fda.hhs.gov](mailto:DICE@fda.hhs.gov)) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

  
**Kellie B. Kelm -S**

for Courtney H. Lias, Ph.D.

Director

Division of Chemistry and Toxicology Devices

Office of In Vitro Diagnostics

and Radiological Health

Center for Devices and Radiological Health

Enclosure

## Indications for Use

510(k) Number (if known)

k181233

Device Name

Elecsys FT4 III

Indications for Use (Describe)

Assay for the in vitro quantitative determination of free thyroxine in human serum and plasma. Measurements obtained by this device are used in the diagnosis and treatment of thyroid disease.

The electrochemiluminescence immunoassay "ECLIA" is intended for use on the cobas e 411 immunoassay analyzer.

Type of Use (Select one or both, as applicable)

☒ Prescription Use (Part 21 CFR 801 Subpart D)

☐ Over-The-Counter Use (21 CFR 801 Subpart C)

### CONTINUE ON A SEPARATE PAGE IF NEEDED.

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k181233  
Elecsys FT4 III  
510(k) Summary

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of 21 CFR 807.92.

In accordance with 21 CFR 807.87, Roche Diagnostics hereby submits official notification as required by Section 510(k) of the Federal Food, Drug and Cosmetics Act of our intention to market the device described in this Premarket Notification 510(k).

The purpose of this Traditional 510(k) Premarket Notification is to obtain FDA review and clearance for the Elecsys FT4 III.

|                                              |                                                                                                                                                                                                                                                             |
|----------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Submitter Name</b>                        | Roche Diagnostics                                                                                                                                                                                                                                           |
| <b>Address</b>                               | 9115 Hague Road<br>P.O. Box 50416<br>Indianapolis, IN 46250-0457                                                                                                                                                                                            |
| <b>Contact</b>                               | Reanna Toney<br>Phone: (317) 521-4516<br>FAX: (317) 521-2324<br>Email: reanna.toney@roche.com<br><br>Secondary Contact Name<br>Michael Leuther<br>Phone: (317) 521-3930<br>FAX: (317) 521-2324<br>Email: Michael.leuther@roche.com                          |
| <b>Date Prepared</b>                         | September 18, 2018                                                                                                                                                                                                                                          |
| <b>Proprietary Name</b>                      | Elecsys FT4 III                                                                                                                                                                                                                                             |
| <b>Common Name</b>                           | Free thyroxine                                                                                                                                                                                                                                              |
| <b>Classification Name</b>                   | Radioimmunoassay, Free thyroxine test system                                                                                                                                                                                                                |
| <b>Product Codes,<br/>Regulation Numbers</b> | CEC, 21CFR862.1695                                                                                                                                                                                                                                          |
| <b>Predicate Devices</b>                     | Elecsys FT4 II (K131244)                                                                                                                                                                                                                                    |
| <b>Establishment Registration</b>            | For the Elecsys FT4 III, the establishment registration number for Roche Diagnostics GmbH in Mannheim, Germany is 9610126, and for Penzberg, Germany, 9610529. The establishment registration number for Roche Diagnostics in the United States is 1823260. |

## 1. DEVICE DESCRIPTION

The Elecsys FT4 III immunoassay is used for the in vitro quantitative determination of free thyroxine in human serum and plasma. It is intended for use on the **cobas e** 411 immunoassay analyzer. The **cobas e** family of analyzers uses electrochemiluminescence immunoassay “ECLIA” technology.

### 1.1. Reagents

The reagent working solutions include:

Rackpack (kit placed on analyzer)

- M: Streptavidin-coated microparticles
- R1: Anti-T4-Ab~biotin
- R2: Anti-T4-Ab~Ru(bpy)<sub>3</sub><sup>2+</sup>

## 2. INDICATIONS FOR USE

Assay for the in vitro quantitative determination of free thyroxine in human serum and plasma. Measurements obtained by this device are used in the diagnosis and treatment of thyroid disease.

The electrochemiluminescence immunoassay “ECLIA” is intended for use on the **cobas e** 411 immunoassay analyzer.

## 3. TECHNOLOGICAL CHARACTERISTICS

The following tables compare the Elecsys FT4 III with its predicate device, Elecsys FT4 II assay (k131244).

**Table 1: Assay Comparison**

| <b>Feature</b>                          | <b>Predicate Device:<br/>Elecsys FT4 II (k131244)</b>                                                                                                                                                                                                                                                                                                                                                                                                    | <b>Candidate Device:<br/>Elecsys FT4 III</b>                                                                                                                                                                                                                                                                                                                                                                                                                                    |
|-----------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Intended Use/<br>Indications for<br>Use | Assay for the in vitro quantitative determination of free thyroxine in human serum and plasma. Measurements obtained by this device are used in the diagnosis and treatment of thyroid disease.<br><br>The electrochemiluminescence immunoassay “ECLIA” is intended for use on Elecsys and cobas e immunoassay analyzers.                                                                                                                                | Assay for the in vitro quantitative determination of free thyroxine in human serum and plasma. Measurements obtained by this device are used in the diagnosis and treatment of thyroid disease.<br><br>The electrochemiluminescence immunoassay “ECLIA” is intended for use on the <b>cobas e 411</b> immunoassay analyzer.                                                                                                                                                     |
| Detection Method                        | Electrochemiluminescent Assay                                                                                                                                                                                                                                                                                                                                                                                                                            | same                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| Applications/Test Time                  | 18 minute application                                                                                                                                                                                                                                                                                                                                                                                                                                    | same                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| Instrument Platform                     | Elecsys and <b>cobas e</b>                                                                                                                                                                                                                                                                                                                                                                                                                               | <b>cobas e 411</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| Sample/Reagent Ratio                    | 15 µL                                                                                                                                                                                                                                                                                                                                                                                                                                                    | same                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| Sample Type/Matrix                      | Serum and plasma (Li-heparin, K <sub>2</sub> -EDTA, K <sub>3</sub> -EDTA                                                                                                                                                                                                                                                                                                                                                                                 | same                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| Reagents                                | M: Streptavidin-coated microparticles (transparent cap), 1 bottle, 12 mL: Streptavidin-coated microparticles 0.72 mg/mL; preservative<br>R1: Anti T4-Ab~Ru(bpy) (gray cap), 1 bottle, 18 mL: Polyclonal anti-T4-antibody (sheep) labeled with ruthenium complex 75 ng/mL; phosphate buffer 100 mmol/L, pH 7.0; preservative<br>R2: T4~biotin (black cap), 1 bottle, 18 mL: Biotinylated T4 2.5 ng/mL; phosphate buffer 100 mmol/L, pH 7.0; preservative. | M: Streptavidin-coated microparticles (transparent cap), 1 bottle, 12 mL: Streptavidin-coated microparticles 0.72 mg/mL; preservative<br>R1: Anti T4-Ab~Ru(bpy) (gray cap), 1 bottle, 18 mL: Polyclonal anti-T4-antibody (sheep) labeled with ruthenium complex 75 ng/mL; phosphate buffer 100 mmol/L, pH 7.0; preservative<br>R2: T4~biotin (black cap), 1 bottle, 18 mL: Biotinylated T4 2.5 ng/mL; free D-biotin 8 ng/mL; phosphate buffer 100 mmol/L, pH 7.0; preservative. |
| Biotin                                  | D-Biotin concentration in the R2 reagent buffer: 50 ng/mL                                                                                                                                                                                                                                                                                                                                                                                                | D-Biotin concentration in the R2 reagent buffer: 8 ng/mL                                                                                                                                                                                                                                                                                                                                                                                                                        |
| Calibrator                              | FT4 II CalSet                                                                                                                                                                                                                                                                                                                                                                                                                                            | CalSet FT4 III                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| Calibration Method                      | 2-point calibration                                                                                                                                                                                                                                                                                                                                                                                                                                      | same                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |

| Feature                          | Predicate Device:<br>Elecsys FT4 II (k131244)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Candidate Device:<br>Elecsys FT4 III                                                                                                                                             |
|----------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Calibration Interval             | <p>Calibration must be performed once per reagent lot using fresh reagent (i.e. not more than 24 hours since the reagent kit was registered on the analyzer).</p> <p>Calibration interval may be extended based on acceptable verification of calibration by the laboratory.</p> <p>Renewed calibration is recommended as follows:</p> <ul style="list-style-type: none"> <li>▪ after 1 month (28 days) when using the same reagent lot</li> <li>▪ after 7 days (when using the same reagent kit on the analyzer)</li> <li>▪ as required: e.g. quality control findings outside the defined limits</li> </ul> | same                                                                                                                                                                             |
| Controls                         | PreciControl Universal                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | same                                                                                                                                                                             |
| Traceability/<br>Standardization | This method has been standardized against the Elecsys FT4 method. The Elecsys FT4 assay is traceable to the Enzymun-Test which was standardized using equilibrium dialysis.                                                                                                                                                                                                                                                                                                                                                                                                                                   | This method has been standardized against the Elecsys FT4 II method. The Elecsys FT4 II assay is traceable to the Enzymun Test which was standardized using equilibrium dialysis |
| Reagent Stability                | <p>Store at 2-8 °C.</p> <p>Do not freeze.</p> <p>Store the Elecsys reagent kit upright in order to ensure complete availability of the microparticles during automatic mixing prior to use.</p> <p>Unopened at 2-8 °C. up to stated expiration date</p> <p>After opening at 2-8 °C. 84 days (12 weeks)</p> <p>On the analyzers. 28 days (4 weeks) onboard or 56 days (8 weeks) when stored alternatively in the refrigerator and on the analyzer, with the total time onboard on the analyzer not exceeding 120 hours</p>                                                                                     | same                                                                                                                                                                             |
| Measuring Range                  | 0.101-7.77 ng/dL<br>(1.3-100 pmol/L)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | same                                                                                                                                                                             |
| LoB                              | 0.03 ng/dL (0.4 pmol/L)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 0.02 ng/dL (0.3 pmol/L)                                                                                                                                                          |
| LoD                              | 0.05 ng/dL (0.6 pmol/L)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 0.04 ng/dL (0.5 pmol/L)                                                                                                                                                          |
| LoQ                              | 0.101 ng/dL (1.3 pmol/L)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | same                                                                                                                                                                             |

| Feature                             | Predicate Device:<br>Elecsys FT4 II (k131244)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | Candidate Device:<br>Elecsys FT4 III                                                                                                            |                            |                    |      |       |       |      |       |       |     |        |       |                   |          |       |                       |          |       |                                |        |       |                                     |        |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                |                            |                    |      |       |       |      |       |       |     |        |       |                   |          |       |                       |          |       |                                |        |       |                                     |        |       |
|-------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------|--------------------|------|-------|-------|------|-------|-------|-----|--------|-------|-------------------|----------|-------|-----------------------|----------|-------|--------------------------------|--------|-------|-------------------------------------|--------|-------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------|----------------------------|--------------------|------|-------|-------|------|-------|-------|-----|--------|-------|-------------------|----------|-------|-----------------------|----------|-------|--------------------------------|--------|-------|-------------------------------------|--------|-------|
| Analytical<br>Specificity           | The following cross-reactivities were found, tested with fT4 concentrations of approximately 0.974 ng/dL (12.5 pmol/L) and 2.66 ng/dL (34.2 pmol/L):                                                                                                                                                                                                                                                                                                                                                                                                                       | The following cross-reactivities were found, tested with fT4 concentrations of approximately 1.01 ng/dL (13 pmol/L) and 3.03 ng/dL (39 pmol/L): |                            |                    |      |       |       |      |       |       |     |        |       |                   |          |       |                       |          |       |                                |        |       |                                     |        |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                |                            |                    |      |       |       |      |       |       |     |        |       |                   |          |       |                       |          |       |                                |        |       |                                     |        |       |
|                                     | <table><tr><td>Cross-reactant</td><td>Concentration tested ng/dL</td><td>Cross-reactivity %</td></tr><tr><td>L-T3</td><td>50000</td><td>0.005</td></tr><tr><td>D-T3</td><td>50000</td><td>0.002</td></tr><tr><td>rT3</td><td>190000</td><td>0.007</td></tr><tr><td>3-iodo-L-tyrosine</td><td>10000000</td><td>0.000</td></tr><tr><td>3,5-diiodo-L-tyrosine</td><td>10000000</td><td>0.000</td></tr><tr><td>3,3',5-triiodothyroacetic acid</td><td>100000</td><td>0.000</td></tr><tr><td>3,3',5,5'-tetraiodothyroacetic acid</td><td>100000</td><td>0.001</td></tr></table> | Cross-reactant                                                                                                                                  | Concentration tested ng/dL | Cross-reactivity % | L-T3 | 50000 | 0.005 | D-T3 | 50000 | 0.002 | rT3 | 190000 | 0.007 | 3-iodo-L-tyrosine | 10000000 | 0.000 | 3,5-diiodo-L-tyrosine | 10000000 | 0.000 | 3,3',5-triiodothyroacetic acid | 100000 | 0.000 | 3,3',5,5'-tetraiodothyroacetic acid | 100000 | 0.001 | <table><tr><td>Cross-reactant</td><td>Concentration tested ng/dL</td><td>Cross-reactivity %</td></tr><tr><td>L-T3</td><td>50000</td><td>0.005</td></tr><tr><td>D-T3</td><td>50000</td><td>0.002</td></tr><tr><td>rT3</td><td>190000</td><td>0.007</td></tr><tr><td>3-iodo-L-tyrosine</td><td>10000000</td><td>0.000</td></tr><tr><td>3,5-diiodo-L-tyrosine</td><td>10000000</td><td>0.000</td></tr><tr><td>3,3',5-triiodothyroacetic acid</td><td>100000</td><td>0.000</td></tr><tr><td>3,3',5,5'-tetraiodothyroacetic acid</td><td>100000</td><td>0.001</td></tr></table> | Cross-reactant | Concentration tested ng/dL | Cross-reactivity % | L-T3 | 50000 | 0.005 | D-T3 | 50000 | 0.002 | rT3 | 190000 | 0.007 | 3-iodo-L-tyrosine | 10000000 | 0.000 | 3,5-diiodo-L-tyrosine | 10000000 | 0.000 | 3,3',5-triiodothyroacetic acid | 100000 | 0.000 | 3,3',5,5'-tetraiodothyroacetic acid | 100000 | 0.001 |
|                                     | Cross-reactant                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | Concentration tested ng/dL                                                                                                                      | Cross-reactivity %         |                    |      |       |       |      |       |       |     |        |       |                   |          |       |                       |          |       |                                |        |       |                                     |        |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                |                            |                    |      |       |       |      |       |       |     |        |       |                   |          |       |                       |          |       |                                |        |       |                                     |        |       |
|                                     | L-T3                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 50000                                                                                                                                           | 0.005                      |                    |      |       |       |      |       |       |     |        |       |                   |          |       |                       |          |       |                                |        |       |                                     |        |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                |                            |                    |      |       |       |      |       |       |     |        |       |                   |          |       |                       |          |       |                                |        |       |                                     |        |       |
|                                     | D-T3                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 50000                                                                                                                                           | 0.002                      |                    |      |       |       |      |       |       |     |        |       |                   |          |       |                       |          |       |                                |        |       |                                     |        |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                |                            |                    |      |       |       |      |       |       |     |        |       |                   |          |       |                       |          |       |                                |        |       |                                     |        |       |
|                                     | rT3                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 190000                                                                                                                                          | 0.007                      |                    |      |       |       |      |       |       |     |        |       |                   |          |       |                       |          |       |                                |        |       |                                     |        |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                |                            |                    |      |       |       |      |       |       |     |        |       |                   |          |       |                       |          |       |                                |        |       |                                     |        |       |
|                                     | 3-iodo-L-tyrosine                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 10000000                                                                                                                                        | 0.000                      |                    |      |       |       |      |       |       |     |        |       |                   |          |       |                       |          |       |                                |        |       |                                     |        |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                |                            |                    |      |       |       |      |       |       |     |        |       |                   |          |       |                       |          |       |                                |        |       |                                     |        |       |
|                                     | 3,5-diiodo-L-tyrosine                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 10000000                                                                                                                                        | 0.000                      |                    |      |       |       |      |       |       |     |        |       |                   |          |       |                       |          |       |                                |        |       |                                     |        |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                |                            |                    |      |       |       |      |       |       |     |        |       |                   |          |       |                       |          |       |                                |        |       |                                     |        |       |
|                                     | 3,3',5-triiodothyroacetic acid                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | 100000                                                                                                                                          | 0.000                      |                    |      |       |       |      |       |       |     |        |       |                   |          |       |                       |          |       |                                |        |       |                                     |        |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                |                            |                    |      |       |       |      |       |       |     |        |       |                   |          |       |                       |          |       |                                |        |       |                                     |        |       |
|                                     | 3,3',5,5'-tetraiodothyroacetic acid                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 100000                                                                                                                                          | 0.001                      |                    |      |       |       |      |       |       |     |        |       |                   |          |       |                       |          |       |                                |        |       |                                     |        |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                |                            |                    |      |       |       |      |       |       |     |        |       |                   |          |       |                       |          |       |                                |        |       |                                     |        |       |
|                                     | Cross-reactant                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | Concentration tested ng/dL                                                                                                                      | Cross-reactivity %         |                    |      |       |       |      |       |       |     |        |       |                   |          |       |                       |          |       |                                |        |       |                                     |        |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                |                            |                    |      |       |       |      |       |       |     |        |       |                   |          |       |                       |          |       |                                |        |       |                                     |        |       |
|                                     | L-T3                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 50000                                                                                                                                           | 0.005                      |                    |      |       |       |      |       |       |     |        |       |                   |          |       |                       |          |       |                                |        |       |                                     |        |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                |                            |                    |      |       |       |      |       |       |     |        |       |                   |          |       |                       |          |       |                                |        |       |                                     |        |       |
|                                     | D-T3                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 50000                                                                                                                                           | 0.002                      |                    |      |       |       |      |       |       |     |        |       |                   |          |       |                       |          |       |                                |        |       |                                     |        |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                |                            |                    |      |       |       |      |       |       |     |        |       |                   |          |       |                       |          |       |                                |        |       |                                     |        |       |
| rT3                                 | 190000                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 0.007                                                                                                                                           |                            |                    |      |       |       |      |       |       |     |        |       |                   |          |       |                       |          |       |                                |        |       |                                     |        |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                |                            |                    |      |       |       |      |       |       |     |        |       |                   |          |       |                       |          |       |                                |        |       |                                     |        |       |
| 3-iodo-L-tyrosine                   | 10000000                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 0.000                                                                                                                                           |                            |                    |      |       |       |      |       |       |     |        |       |                   |          |       |                       |          |       |                                |        |       |                                     |        |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                |                            |                    |      |       |       |      |       |       |     |        |       |                   |          |       |                       |          |       |                                |        |       |                                     |        |       |
| 3,5-diiodo-L-tyrosine               | 10000000                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 0.000                                                                                                                                           |                            |                    |      |       |       |      |       |       |     |        |       |                   |          |       |                       |          |       |                                |        |       |                                     |        |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                |                            |                    |      |       |       |      |       |       |     |        |       |                   |          |       |                       |          |       |                                |        |       |                                     |        |       |
| 3,3',5-triiodothyroacetic acid      | 100000                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 0.000                                                                                                                                           |                            |                    |      |       |       |      |       |       |     |        |       |                   |          |       |                       |          |       |                                |        |       |                                     |        |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                |                            |                    |      |       |       |      |       |       |     |        |       |                   |          |       |                       |          |       |                                |        |       |                                     |        |       |
| 3,3',5,5'-tetraiodothyroacetic acid | 100000                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 0.001                                                                                                                                           |                            |                    |      |       |       |      |       |       |     |        |       |                   |          |       |                       |          |       |                                |        |       |                                     |        |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                |                            |                    |      |       |       |      |       |       |     |        |       |                   |          |       |                       |          |       |                                |        |       |                                     |        |       |
|                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                 |                            |                    |      |       |       |      |       |       |     |        |       |                   |          |       |                       |          |       |                                |        |       |                                     |        |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                |                            |                    |      |       |       |      |       |       |     |        |       |                   |          |       |                       |          |       |                                |        |       |                                     |        |       |
|                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                 |                            |                    |      |       |       |      |       |       |     |        |       |                   |          |       |                       |          |       |                                |        |       |                                     |        |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                |                            |                    |      |       |       |      |       |       |     |        |       |                   |          |       |                       |          |       |                                |        |       |                                     |        |       |
|                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                 |                            |                    |      |       |       |      |       |       |     |        |       |                   |          |       |                       |          |       |                                |        |       |                                     |        |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                |                            |                    |      |       |       |      |       |       |     |        |       |                   |          |       |                       |          |       |                                |        |       |                                     |        |       |
|                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                 |                            |                    |      |       |       |      |       |       |     |        |       |                   |          |       |                       |          |       |                                |        |       |                                     |        |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                |                            |                    |      |       |       |      |       |       |     |        |       |                   |          |       |                       |          |       |                                |        |       |                                     |        |       |
|                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                 |                            |                    |      |       |       |      |       |       |     |        |       |                   |          |       |                       |          |       |                                |        |       |                                     |        |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                |                            |                    |      |       |       |      |       |       |     |        |       |                   |          |       |                       |          |       |                                |        |       |                                     |        |       |
|                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                 |                            |                    |      |       |       |      |       |       |     |        |       |                   |          |       |                       |          |       |                                |        |       |                                     |        |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                |                            |                    |      |       |       |      |       |       |     |        |       |                   |          |       |                       |          |       |                                |        |       |                                     |        |       |
|                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                 |                            |                    |      |       |       |      |       |       |     |        |       |                   |          |       |                       |          |       |                                |        |       |                                     |        |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                |                            |                    |      |       |       |      |       |       |     |        |       |                   |          |       |                       |          |       |                                |        |       |                                     |        |       |
|                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                 |                            |                    |      |       |       |      |       |       |     |        |       |                   |          |       |                       |          |       |                                |        |       |                                     |        |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                |                            |                    |      |       |       |      |       |       |     |        |       |                   |          |       |                       |          |       |                                |        |       |                                     |        |       |
|                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                 |                            |                    |      |       |       |      |       |       |     |        |       |                   |          |       |                       |          |       |                                |        |       |                                     |        |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                |                            |                    |      |       |       |      |       |       |     |        |       |                   |          |       |                       |          |       |                                |        |       |                                     |        |       |
|                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                 |                            |                    |      |       |       |      |       |       |     |        |       |                   |          |       |                       |          |       |                                |        |       |                                     |        |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                |                            |                    |      |       |       |      |       |       |     |        |       |                   |          |       |                       |          |       |                                |        |       |                                     |        |       |

| Feature     | Predicate Device:<br>Elecsys FT4 II (k131244)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | Candidate Device:<br>Elecsys FT4 III                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
|-------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Limitations | <p>The assay is unaffected by icterus (bilirubin &lt; 701 µmol/L or &lt; 41 mg/dL), hemolysis (Hb &lt; 0.621 mmol/L or &lt; 1.0 g/dL), lipemia (Intralipid &lt; 2000 mg/dL), biotin (&lt; 81.8 nmol/L or &lt; 20 ng/mL), albumin &lt; 6.3 g/dL, IgG &lt; 7 g/dL, IgA &lt; 1.6 g/dL and IgM &lt; 1 g/dL.</p> <p>Criterion: Recovery within ± 10 % of initial value.</p> <p>Samples should not be taken from patients receiving therapy with high biotin doses (i.e. &gt; 5 mg/day) until at least 8 hours following the last biotin administration.</p> <p>No interference was observed from rheumatoid factors up to a concentration of 1200 IU/mL and samples from dialysis patients.</p> <p>Any influence that might affect the binding behavior of the binding proteins can alter the result of the fT4 tests (e.g. drugs, NTIs (Non Thyroid Illness) or patients suffering from FDH (Familial Dysalbuminemic Hyperthyroxinemia) or increased TBG in pregnancy).</p> <p>The test cannot be used in patients receiving treatment with lipid-lowering agents containing D T4. If the thyroid function is to be checked in such patients, the therapy should first be discontinued for 4-6 weeks to allow the physiological state to become re-established.</p> <p>Autoantibodies to thyroid hormones can interfere with the assay.</p> <p>In vitro tests were performed on 17 commonly used pharmaceuticals. No interference with the assay was found.</p> | <p>Bilirubin ≤ 701 µmol/L or ≤ 41 mg/dL</p> <p>Hemoglobin ≤ 0.621 mmol/L or ≤ 1000 mg/dL</p> <p>Intralipid ≤ 2000 mg/dL</p> <p>Rheumatoid factors ≤ 1200 IU/mL</p> <p>IgG ≤ 7 g/dL</p> <p>IgA ≤ 1.6 g/dL</p> <p>IgM ≤ 1 g/dL</p> <p>Criterion: Recovery of ≤ ± 0.6 pmol/L of initial value ≤ 6 pmol/L and ± 10 % of initial value &gt; 6 pmol/L.</p> <p>Any influence that might affect the binding behavior of the binding proteins can alter the result of the fT4 tests (e.g. drugs, NTIs (Non Thyroid Illness) or patients suffering from FDH (Familial Dysalbuminemic Hyperthyroxinemia)).</p> <p>The test cannot be used in patients receiving treatment with lipid-lowering agents containing D T4. If the thyroid function is to be checked in such patients, the therapy should first be discontinued for 4-6 weeks to allow the physiological state to become re-established</p> <p>Autoantibodies to thyroid hormones can interfere with the assay.</p> <p>Pharmaceutical substances In vitro tests were performed on 16 commonly used pharmaceuticals. No interference with the assay was found.</p> |

| Feature               | Predicate Device:<br>Elecsys FT4 II (k131244)                                                                                                                                                  | Candidate Device:<br>Elecsys FT4 III                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                       |                       |        |       |             |   |            |    |                  |     |             |      |             |     |            |     |              |     |                |     |                |     |            |       |
|-----------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|-----------------------|--------|-------|-------------|---|------------|----|------------------|-----|-------------|------|-------------|-----|------------|-----|--------------|-----|----------------|-----|----------------|-----|------------|-------|
| Special thyroid drugs | The following special thyroid drugs were tested with concentrations shown in the table below. No interference with the assay was found.<br>Criterion: Recovery within ± 10 % of initial value. | In addition, the following special thyroid drugs were tested. No interference with the assay was found. <table><tr><th>Drug</th><th>Concentration (µg/mL)</th></tr><tr><td>Iodide</td><td>0.200</td></tr><tr><td>Carbimazole</td><td>6</td></tr><tr><td>Thiamazole</td><td>80</td></tr><tr><td>Propylthiouracil</td><td>300</td></tr><tr><td>Perchlorate</td><td>2000</td></tr><tr><td>Propranolol</td><td>240</td></tr><tr><td>Amiodarone</td><td>200</td></tr><tr><td>Prednisolone</td><td>100</td></tr><tr><td>Hydrocortisone</td><td>200</td></tr><tr><td>Flurocortolone</td><td>100</td></tr><tr><td>Octreotide</td><td>0.300</td></tr></table> | Drug                  | Concentration (µg/mL) | Iodide | 0.200 | Carbimazole | 6 | Thiamazole | 80 | Propylthiouracil | 300 | Perchlorate | 2000 | Propranolol | 240 | Amiodarone | 200 | Prednisolone | 100 | Hydrocortisone | 200 | Flurocortolone | 100 | Octreotide | 0.300 |
|                       | Drug                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | Concentration (µg/mL) |                       |        |       |             |   |            |    |                  |     |             |      |             |     |            |     |              |     |                |     |                |     |            |       |
|                       | Iodide                                                                                                                                                                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 0.200                 |                       |        |       |             |   |            |    |                  |     |             |      |             |     |            |     |              |     |                |     |                |     |            |       |
|                       | Carbimazole                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 6                     |                       |        |       |             |   |            |    |                  |     |             |      |             |     |            |     |              |     |                |     |                |     |            |       |
|                       | Thiamazole                                                                                                                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 80                    |                       |        |       |             |   |            |    |                  |     |             |      |             |     |            |     |              |     |                |     |                |     |            |       |
|                       | Propylthiouracil                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 300                   |                       |        |       |             |   |            |    |                  |     |             |      |             |     |            |     |              |     |                |     |                |     |            |       |
|                       | Perchlorate                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 2000                  |                       |        |       |             |   |            |    |                  |     |             |      |             |     |            |     |              |     |                |     |                |     |            |       |
|                       | Propranolol                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 240                   |                       |        |       |             |   |            |    |                  |     |             |      |             |     |            |     |              |     |                |     |                |     |            |       |
|                       | Amiodarone                                                                                                                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 200                   |                       |        |       |             |   |            |    |                  |     |             |      |             |     |            |     |              |     |                |     |                |     |            |       |
|                       | Prednisolone                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 100                   |                       |        |       |             |   |            |    |                  |     |             |      |             |     |            |     |              |     |                |     |                |     |            |       |
|                       | Hydrocortisone                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 200                   |                       |        |       |             |   |            |    |                  |     |             |      |             |     |            |     |              |     |                |     |                |     |            |       |
|                       | Flurocortolone                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 100                   |                       |        |       |             |   |            |    |                  |     |             |      |             |     |            |     |              |     |                |     |                |     |            |       |
|                       | Octreotide                                                                                                                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 0.300                 |                       |        |       |             |   |            |    |                  |     |             |      |             |     |            |     |              |     |                |     |                |     |            |       |
|                       |                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                       |                       |        |       |             |   |            |    |                  |     |             |      |             |     |            |     |              |     |                |     |                |     |            |       |
|                       |                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                       |                       |        |       |             |   |            |    |                  |     |             |      |             |     |            |     |              |     |                |     |                |     |            |       |
|                       |                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                       |                       |        |       |             |   |            |    |                  |     |             |      |             |     |            |     |              |     |                |     |                |     |            |       |
|                       |                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                       |                       |        |       |             |   |            |    |                  |     |             |      |             |     |            |     |              |     |                |     |                |     |            |       |
|                       |                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                       |                       |        |       |             |   |            |    |                  |     |             |      |             |     |            |     |              |     |                |     |                |     |            |       |
|                       |                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                       |                       |        |       |             |   |            |    |                  |     |             |      |             |     |            |     |              |     |                |     |                |     |            |       |
|                       |                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                       |                       |        |       |             |   |            |    |                  |     |             |      |             |     |            |     |              |     |                |     |                |     |            |       |
|                       |                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                       |                       |        |       |             |   |            |    |                  |     |             |      |             |     |            |     |              |     |                |     |                |     |            |       |
|                       |                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                       |                       |        |       |             |   |            |    |                  |     |             |      |             |     |            |     |              |     |                |     |                |     |            |       |
|                       |                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                       |                       |        |       |             |   |            |    |                  |     |             |      |             |     |            |     |              |     |                |     |                |     |            |       |
|                       |                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                       |                       |        |       |             |   |            |    |                  |     |             |      |             |     |            |     |              |     |                |     |                |     |            |       |
|                       |                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                       |                       |        |       |             |   |            |    |                  |     |             |      |             |     |            |     |              |     |                |     |                |     |            |       |

| Feature                                                                                                                                                                                                                                                         | Predicate Device:<br>Elecsys FT4 II (k131244)                                                                                                                         | Candidate Device:<br>Elecsys FT4 III                                                                                                                                                                                                                                                                                                                                                                                                                                         |                             |                               |      |     |     |  |     |     |     |     |      |             |      |      |      |     |     |             |      |      |      |     |     |             |      |      |      |     |     |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------|-------------------------------|------|-----|-----|--|-----|-----|-----|-----|------|-------------|------|------|------|-----|-----|-------------|------|------|------|-----|-----|-------------|------|------|------|-----|-----|
| Biotin                                                                                                                                                                                                                                                          | Samples should not be taken from patients receiving therapy with high biotin doses (i.e. > 5 mg/day) until at least 8 hours following the last biotin administration. | <i>Biotin interference</i>                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                             |                               |      |     |     |  |     |     |     |     |      |             |      |      |      |     |     |             |      |      |      |     |     |             |      |      |      |     |     |
|                                                                                                                                                                                                                                                                 |                                                                                                                                                                       | % Bias for samples containing various concentrations of Biotin                                                                                                                                                                                                                                                                                                                                                                                                               |                             |                               |      |     |     |  |     |     |     |     |      |             |      |      |      |     |     |             |      |      |      |     |     |             |      |      |      |     |     |
|                                                                                                                                                                                                                                                                 |                                                                                                                                                                       | <table><tr><th rowspan="2">Sample<br/>ng/dL<br/>(pmol/L)</th><th colspan="5">Biotin concentrations (ng/mL)</th></tr><tr><th>52</th><th>65</th><th>78</th><th>91</th><th>104</th></tr><tr><td>0.96 (12.4)</td><td>1.2</td><td>2.1</td><td>3.6</td><td>5.7</td><td>8.5</td></tr><tr><td>1.66 (21.4)</td><td>-1.8</td><td>-1.4</td><td>1.3</td><td>3.0</td><td>7.3</td></tr><tr><td>2.61 (33.6)</td><td>-0.5</td><td>0.6</td><td>2.3</td><td>4.7</td><td>7.5</td></tr></table>  | Sample<br>ng/dL<br>(pmol/L) | Biotin concentrations (ng/mL) |      |     |     |  | 52  | 65  | 78  | 91  | 104  | 0.96 (12.4) | 1.2  | 2.1  | 3.6  | 5.7 | 8.5 | 1.66 (21.4) | -1.8 | -1.4 | 1.3  | 3.0 | 7.3 | 2.61 (33.6) | -0.5 | 0.6  | 2.3  | 4.7 | 7.5 |
|                                                                                                                                                                                                                                                                 |                                                                                                                                                                       | Sample<br>ng/dL<br>(pmol/L)                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                             | Biotin concentrations (ng/mL) |      |     |     |  |     |     |     |     |      |             |      |      |      |     |     |             |      |      |      |     |     |             |      |      |      |     |     |
|                                                                                                                                                                                                                                                                 |                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | 52                          | 65                            | 78   | 91  | 104 |  |     |     |     |     |      |             |      |      |      |     |     |             |      |      |      |     |     |             |      |      |      |     |     |
|                                                                                                                                                                                                                                                                 |                                                                                                                                                                       | 0.96 (12.4)                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | 1.2                         | 2.1                           | 3.6  | 5.7 | 8.5 |  |     |     |     |     |      |             |      |      |      |     |     |             |      |      |      |     |     |             |      |      |      |     |     |
|                                                                                                                                                                                                                                                                 |                                                                                                                                                                       | 1.66 (21.4)                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | -1.8                        | -1.4                          | 1.3  | 3.0 | 7.3 |  |     |     |     |     |      |             |      |      |      |     |     |             |      |      |      |     |     |             |      |      |      |     |     |
|                                                                                                                                                                                                                                                                 |                                                                                                                                                                       | 2.61 (33.6)                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | -0.5                        | 0.6                           | 2.3  | 4.7 | 7.5 |  |     |     |     |     |      |             |      |      |      |     |     |             |      |      |      |     |     |             |      |      |      |     |     |
|                                                                                                                                                                                                                                                                 |                                                                                                                                                                       | % Bias for samples containing various concentrations of Biotin                                                                                                                                                                                                                                                                                                                                                                                                               |                             |                               |      |     |     |  |     |     |     |     |      |             |      |      |      |     |     |             |      |      |      |     |     |             |      |      |      |     |     |
|                                                                                                                                                                                                                                                                 |                                                                                                                                                                       | <table><tr><th rowspan="2">Sample<br/>ng/dL<br/>(pmol/L)</th><th colspan="5">Biotin concentrations (ng/mL)</th></tr><tr><th>117</th><th>150</th><th>300</th><th>600</th><th>1200</th></tr><tr><td>0.96 (12.4)</td><td>10.9</td><td>17.6</td><td>57.1</td><td>256</td><td>*</td></tr><tr><td>1.66 (21.4)</td><td>7.6</td><td>16.1</td><td>53.7</td><td>291</td><td>*</td></tr><tr><td>2.61 (33.6)</td><td>9.7</td><td>15.9</td><td>56.5</td><td>*</td><td>*</td></tr></table> | Sample<br>ng/dL<br>(pmol/L) | Biotin concentrations (ng/mL) |      |     |     |  | 117 | 150 | 300 | 600 | 1200 | 0.96 (12.4) | 10.9 | 17.6 | 57.1 | 256 | *   | 1.66 (21.4) | 7.6  | 16.1 | 53.7 | 291 | *   | 2.61 (33.6) | 9.7  | 15.9 | 56.5 | *   | *   |
| Sample<br>ng/dL<br>(pmol/L)                                                                                                                                                                                                                                     | Biotin concentrations (ng/mL)                                                                                                                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                             |                               |      |     |     |  |     |     |     |     |      |             |      |      |      |     |     |             |      |      |      |     |     |             |      |      |      |     |     |
|                                                                                                                                                                                                                                                                 | 117                                                                                                                                                                   | 150                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 300                         | 600                           | 1200 |     |     |  |     |     |     |     |      |             |      |      |      |     |     |             |      |      |      |     |     |             |      |      |      |     |     |
| 0.96 (12.4)                                                                                                                                                                                                                                                     | 10.9                                                                                                                                                                  | 17.6                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 57.1                        | 256                           | *    |     |     |  |     |     |     |     |      |             |      |      |      |     |     |             |      |      |      |     |     |             |      |      |      |     |     |
| 1.66 (21.4)                                                                                                                                                                                                                                                     | 7.6                                                                                                                                                                   | 16.1                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 53.7                        | 291                           | *    |     |     |  |     |     |     |     |      |             |      |      |      |     |     |             |      |      |      |     |     |             |      |      |      |     |     |
| 2.61 (33.6)                                                                                                                                                                                                                                                     | 9.7                                                                                                                                                                   | 15.9                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 56.5                        | *                             | *    |     |     |  |     |     |     |     |      |             |      |      |      |     |     |             |      |      |      |     |     |             |      |      |      |     |     |
| * = Values above the measuring range. % Bias can not be calculated.                                                                                                                                                                                             |                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                             |                               |      |     |     |  |     |     |     |     |      |             |      |      |      |     |     |             |      |      |      |     |     |             |      |      |      |     |     |
| ** Specimens with biotin concentrations up to 104 ng/mL demonstrated ≤ 10% bias in results. Biotin concentrations greater than 104 ng/mL can lead to higher positive bias for fT4 results.                                                                      |                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                             |                               |      |     |     |  |     |     |     |     |      |             |      |      |      |     |     |             |      |      |      |     |     |             |      |      |      |     |     |
| Some studies have shown that serum concentrations of biotin can reach 355 ng/mL within the first hour after biotin ingestion for subjects consuming supplements of 20 mg biotin per day and up to 1160 ng/mL for subjects after a single dose of 300 mg biotin. |                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                             |                               |      |     |     |  |     |     |     |     |      |             |      |      |      |     |     |             |      |      |      |     |     |             |      |      |      |     |     |
| Do not test samples from patients who take biotin.                                                                                                                                                                                                              |                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                             |                               |      |     |     |  |     |     |     |     |      |             |      |      |      |     |     |             |      |      |      |     |     |             |      |      |      |     |     |

## **4. NON-CLINICAL PERFORMANCE EVALUATION**

Non-clinical performance evaluation for Elecsys FT4 III executed with the study briefly summarized.

### **4.1. Precision**

#### **4.1.1. Repeatability and Intermediate Precision**

Precision was evaluated on a single **cobas e 411** analyzer according to CLSI guideline EP05-A3 using one reagent lot for evaluation. The protocol consisted of testing 2 replicates of each of two levels of control, PreciControl Universal and five human sera per run, 2 runs per day for 21 days. The samples were run in randomized order on the **cobas e 411** analyzer. Serum samples used were native single donors, native serum pools, and spiked serum pools.

### **4.2. Human Anti-Mouse Antibodies (HAMA)**

Not Applicable (no mouse antibodies used)

### **4.3. Endogenous Interferences**

#### **4.3.1. Biotin**

The purpose of this study was to evaluate endogenous substances for potential interference with the parameters measured with the Elecsys FT4 III on the **cobas e 411** immunoassay analyzer using human serum samples (single donors, native as well as spiked).

For each interfering substance three human serum samples containing low, mid and high concentrations of fT4 were tested in accordance with CLSI EP07-A2.

### **4.4. Sample Matrix Comparison**

The effect on quantitation of analyte in the presence of anticoagulants with the Elecsys FT4 III immunoassay was determined by comparing values obtained from samples (native single donors and pools as well as spiked samples) drawn into Serum, Li-Heparin, K2-and K3-EDTA plasma primary tubes. 53 serum/plasma pairs per sample material were tested in singleton with one reagent lot on one **cobas e 411** immunoassay analyzer.

#### 4.5. Method Comparison to Predicate

A method comparison was performed using the Elecsys FT4 III assay (candidate device, Y) and the Elecsys FT4 II assay (predicate device, X) to assess the bias between the two assays.

A total of 141 serum samples (138 native human serum samples and 3 spiked sample pools) were measured in singleton on the **cobas e 411** analyzer in one run covering the entire measuring range. FT4 values ranged between 2.31 and 91.9 pmol/L for the Reference Method (X).

#### 4.6. Reagent Stability

To test reagent stability, four studies were executed with two studies completed including:

- Study 1: Reagent stability after first opening at 2-8°C (84 days)
- Study 2: On board reagent stability (28 days)
- Study 3: Alternate storage in the refrigerator / on the analyzer (56 days, not exceeding 120 hours onboard)
- Study 4: A real-time stability study is ongoing to support shelf-life stability claim.

##### 4.6.1. Reagent Stability After First Opening

Elecsys FT4 III reagent kits can be used after first opening for up to 84 days when stored at 2-8°C. Reagent stability after first opening for the Elecsys FT4 III assay was tested on one **cobas e 411** immunoassay analyzer.

A fresh reagent rackpack was placed on the analyzer and calibrated. Reference values for the samples tested were determined. After initial measurement the kit was removed from the analyzer and kept at 2-8 °C for 36, 63 and 85 days. After 36, 63 and 85 days the kit was placed on the analyzer again, calibrated and the test samples were determined.

Samples tested in duplicate include six human serum (HS) samples and two controls (PreciControl Universal) for run qualification. The human samples used were native single donor serum, native serum pools, and spiked serum pools.

#### 4.6.2. Reagent On-board stability (28 days)

Elecsys FT4 III reagent kits can be stored on board of the analyzers for up to 28 days. A new calibration of the kit kept on-board is recommended every 7 days.

Reagent On-board Stability for the Elecsys FT4 III assay was tested on one **cobas e 411** immunoassay analyzer.

A fresh reagent rackpack was placed on the analyzer and calibrated. All samples were measured on day 0. On day 8, 15, 22 and 29, the same samples were measured with the same reagent kit kept at  $20^{\circ}\text{C} \pm 3^{\circ}\text{C}$  (on-board condition) using the calibration curves established on day 0, 8, 15, 22 and 29, respectively.

Samples tested include five human serum (HS) samples and two controls (PreciControl Universal) for run qualification. Each sample was tested in two-fold determination. Human serum samples used were native single donor serum, native serum pools, and spiked serum pools.

#### 4.6.3. Alternate storage in the refrigerator / on the analyzer (56 days, not exceeding 120 hours onboard)

Elecsys FT4 III reagent kits can be stored in total for 56 days when stored alternatively in the refrigerator and on the analyzer, with a total time onboard the analyzer not exceeding 120 hours.

Reagent refrigerator / on-board Stability for the Elecsys FT4 III assay was tested on one **cobas e 411** immunoassay analyzer.

A fresh reagent rackpack was placed on the analyzer and calibrated. All samples were measured on day 0. On day 24, 29, 36, 43, 50 and 57, the same samples were measured with the same reagent kit kept in the refrigerator at  $2-8^{\circ}\text{C}$  and at  $20^{\circ}\text{C} \pm 3^{\circ}\text{C}$  (on-board condition) for 57 days not exceeding 120 hours under on-board condition using the calibration curves established on day 24, 29, 36, 43, 50 and 57, respectively.

Samples tested include five human serum (HS) samples and two controls (PreciControl Universal) for run qualification. Each sample was tested in two-fold determination. Human

serum samples used were native single donor serum, native serum pools, and spiked serum pools.

#### 4.6.4. Reagent Real-time Stability

In the ongoing real-time stability study, the Elecsys FT4 III reagent is stored at 2-8°C. The stored assay reagents are tested at time point T=0 (after manufacturing) and at specified intervals over the shelf life of the device up to the planned shelf life plus one month. Testing will be performed using three human serum samples (stored at -20°C).

Data for the time-points at 0, 7, 10 and 13 months tested in duplicate are available. The average on-test recovery value will be calculated as absolute deviation / percent recovery compared to the reference value measured at T=0 for the human serum samples.

#### 4.7. Calibration Stability

To test calibration stability, two studies were completed, including:

- Study 1. Lot calibration stability
- Study 2. On-board calibration stability

##### 4.7.1. Lot calibration study

Calibration of an Elecsys FT4 III reagent lot is recommended every 28 days (4 weeks). During that time period fresh reagent kits of the same lot can be used without calibration using the calibration curve of the day 0 reagent kit.

Elecsys FT4 III was calibrated with a fresh reagent kit on day 0 using a **cobas e 411** immunoassay analyzer. After 36 days (5 weeks) a new reagent kit of the same lot was used and recovery of samples was determined using the calibration curve of day 0.

Five human serum (HS) samples and two controls (PreciControl Universal) for run qualification were tested; each sample was tested with two-fold determination. Human serum samples used were single donor serum, native serum pools, and spiked serum pools.

#### 4.7.2. On-board Calibration Stability

Elecsys FT4 III reagent kits can be stored on board of the analyzers for up to 7 days without a new calibration.

Reagent On-board Calibration stability for the Elecsys FT4 III assay was tested on one **cobas e 411** immunoassay analyzer.

A fresh reagent rackpack was placed on the analyzer and calibrated. All samples were measured on day 0. On day 8 the same samples were measured with the same reagent kit kept at  $20^{\circ}\text{C} \pm 3^{\circ}\text{C}$  (on-board condition) using the calibration curve established on day 0.

Samples tested include five human serum (HS) samples and two controls (PreciControl Universal) for run qualification. Each sample was tested in two-fold determination. Human serum samples used were single donor serum, native serum pools, and spiked serum pools.

#### 4.8. Biotin

The Elecsys FT4 II was cleared under k131244; Elecsys FT4 III is a modification of this assay with only minor changes in the assay buffer composition to increase the Biotin resistance. For this purpose the D-Biotin concentration in the R2 reagent buffer was reduced.

### 5. EXTERNAL (CLINICAL) TESTING

Not Applicable

### 6. CLINICAL PERFORMANCE EVALUATION

Not Applicable

### 7. ADDITIONAL INFORMATION

The Elecsys FT4 III is intended to be used with the following calibrators and controls:

- FT4 III CalSet
- Elecsys FT4 CalCheck
- PreciControl Universal

FT4 III CalSet, product code JIS, is a Class II 510(k) Exempt device and therefore, is not included with this submission.

The Elecsys FT4 CalCheck, product code JJX, is a Class I 510(k) Exempt device and therefore, is not included with this submission.

PreciControl Universal, product code JJY, is a Class I 510(k) Exempt device and therefore, is not included with this submission.

## **8. CONCLUSIONS**

The information provided in this 510(k) Premarket Notification will support a determination of substantial equivalence for the Elecsys FT4 III. The data supports a safe, effective device which performs as well as or better than the predicate device.