



**ABBOTT**

Diagnostics Division

1730 TO MAY -2 12:28

Abbott Laboratories  
200 Abbott Park Road  
Abbott Park, Illinois 60064-3537

April 26, 2000

Dockets Management Branch (HFA-305)  
Food and Drug Administration  
Department of Health and Human Services  
Room 1-23  
12420 Parklawn Drive  
Rockville, MD 20857

## **Re: *Class II 510(k) Exemption Petition***

ABBOTT LABORATORIES submits this petition under Section 510(m)(2) of the Federal Food, Drug, and Cosmetic Act (the Act), as amended by Section 206 of the FDA Modernization Act of 1997, to request the Commissioner of the Food and Drugs to exempt devices classified as total triiodothyronine test system devices under CFR Section 862.1710, from the premarket notification requirement of Section 510(k) of the Act.

The information in this petition demonstrates that premarket notification is not necessary to provide assurance of the safety and effectiveness of devices classified as total triiodothyronine test systems.

For any written correspondence regarding this petition, please use the following address:

Denise Farmer  
Dept. 09V6, Bldg. AP31  
Abbott Laboratories  
200 Abbott Park Rd  
Abbott Park, IL 60064-6204

If there are any questions regarding this petition, please contact me at 847-938-5032 or by facsimile at 847-937-9616.

Sincerely,

Denise Farmer  
Regulatory Affairs Specialist  
ADD Regulatory Affairs  
ABBOTT LABORATORIES

cc: CDRH Document Mail Center (HFZ-401)  
9200 Corporate Blvd.  
Rockville, MD 20850

000-1280



## TABLE OF CONTENTS

- I. Statement of Grounds
  - A. Description of Device
  - B. Device History
  - C. Detection of Safety and Effectiveness Changes
  - D. Device Classification
  - E. Conclusion
- II. Environmental Impact
- III. References
- IV. Certification



## I. Statement of Grounds

The information in this petition demonstrates that premarket notification is not necessary to provide assurance of the safety and effectiveness of devices classified as total triiodothyronine test system devices. An analysis of the factors contained in Section III of FDA guidance documents, “Procedures for Class II Device Exemptions from Premarket Notification, Guidance for Industry and CDRH Staff” issued Feb. 19, 1998, is presented as part of this petition.

### A. Description of Device

A total triiodothyronine test system is a device intended to measure the hormone triiodothyronine in serum and plasma. Measurements obtained by this device are used in the diagnosis and treatment of thyroid disease such as hyperthyroidism.<sup>1</sup>

Relying on the definition of “generic type of device” found in the medical classification procedures a generic device means a grouping of devices that do not differ significantly in purpose, design, materials, energy source, function, or any other feature related to the safety and effectiveness, and for which similar regulatory controls are sufficient to provide reasonable assurance of safety and effectiveness.<sup>2</sup> In the case of total triiodothyronine devices, the generic type of devices include devices which measure both total triiodothyronine (TT3) and free triiodothyronine (FT3).

### B. Device History

There have been many different types of assays for measuring T3 over the years. The first were chemical methods that were often too insensitive or impractical for measuring the low T3 concentration present in serum. In the 1960’s competitive-binding assays were introduced which increased assay sensitivity and specificity. Following the competitive-binding assays, direct measurement assays were made available after the production of T3 antibodies. For many years, direct procedures for measuring free thyroid hormones were too cumbersome, time-consuming, and expensive for use in routine clinical laboratory. Today, the direct measurement of free thyroid hormones are common and many different assay techniques are employed.<sup>3</sup> In recent years, monoclonal T3 antibodies have been produced. Most current thyroid hormone assays employ radioactive iodine, an enzyme, or a fluorescent or chemiluminescent label attached to a hormone or antibody to that hormone. In either instance, the assay involves a high-affinity antibody specific for the hormone being measured.<sup>4</sup> As such, the use of TT3 and FT3 devices have been in existence for many years, and their use well-established.<sup>3,5,6,7</sup> Today, a “plethora of commercial kits are available and are routinely used in clinical practice.”<sup>8</sup>



A literature search revealed that triiodothyronine devices do not have a significant history of false or misleading claims associated with the inherent characteristics of the device. This search revealed articles comparing the performance of various triiodothyronine devices employing different assay technologies.<sup>9,10</sup> Characteristics of the device that are necessary for its safety and effectiveness are well established.<sup>11</sup> This literature search did not reveal a significant history of risks associated with triiodothyronine devices, however it did reveal that there are some substances which may cause slightly elevated results. T3 is usually a complementary assay to other thyroid function tests such as a thyroid stimulating hormone (TSH) test or a Free Thyroxine (FT4) test. A falsely elevated result would not result in injury and since it is usually a complementary test, the chance of a medical intervention would be low. However, if a medical intervention were to occur it would not cause an injury to the patient. These interferences and limitations are well documented in the literature.

The American Thyroid Association (ATA) issues guidelines for the use of laboratory tests in thyroid disorders. With the availability of highly sensitive TSH assays, the approach to thyroid function testing has changed from a FT4 Estimate and Total T4 to a TSH complemented by a Free Thyroxin. A sensitive TSH complemented by a FT4 represents the best and most efficient combination of blood tests for the diagnosis and follow up of most patients with thyroid disorders.<sup>12,13</sup> A T3 measurement alone is not a good measurement for thyroid function because T3 concentrations are affected by general health and even stress of individuals. T3 measurements are rarely needed, however they may be necessary for the diagnosis of hyperthyroidism or T3 toxicosis (a condition which is rarely seen in the United States). In addition, T3 measurements are not needed for the diagnosis or monitoring of hypothyroidism.<sup>14</sup>

A review of over 600,000 Medical Device Reports (MDR's) filed from 1977 to 2000 revealed only 40 Medical Device Reports (MDR's) filed under product code CDP (FDA product code for triiodothyronine devices). In none of these reports was there a report of patient injury. Of these 40, only 27 were directly related to the assay when the text was read. The remaining were caused by the instrument or the commodities used on the instrument although the product code identified was CDP. An additional 15 MDR's included "triiodothyronine" in the text, however the identified product was either an instrument or another thyroid device (such as triiodothyronine uptake, product code KHQ). These additional 15 did not refer to product code CDP. The low MDR rate and the lack of injury and significant risk support the safety and effectiveness of triiodothyronine devices.



### C. Detection of Safety and Effectiveness Changes

As *in vitro* diagnostic devices, triiodothyronine devices require routine testing of control material. Routine testing is an acceptable means for a user to readily detect changes in the device that could affect safety and effectiveness.<sup>15</sup> In accordance with *in vitro* diagnostic labeling requirements, “details of kinds of quality control procedures and materials required” will be included as part of the triiodothyronine device labeling.<sup>16</sup> In addition, state and Clinical Laboratory Improvement Amendments of 1988 requirements direct laboratories with specific instructions in regards to quality control procedures. In addition, T3 is usually a complementary test to other thyroid function tests such as a thyroid stimulating hormone (TSH) test or a Free Thyroxine (FT4) test.

### D. Device Classification

Triiodothyronine devices are classified as class II devices.<sup>1</sup> As described previously, these devices have been in use for many years and their use is well established. For these reasons, it is unlikely that changes to the device would result in a change in the device classification. Furthermore, a class II device that “has an intended use that is different from the intended use of a legally marketed device in that generic category...or...operates using a different fundamental scientific technology than that used by a legally marketed device in that generic category” would not be exempt from premarket notification.

### E. Conclusion

For the reasons cited within this petition triiodothyronine devices satisfy the requirements for exemption from the premarket notification requirement.

## II. Environmental Impact

Pursuant to 21 C.F.R. 25.24(a)(8) a petition for Class II exemption is subject to categorical exclusion of an environmental assessment.



### III. References

1. C.F.R. 862.1710
2. C.F.R 860.3(i)
3. Burtis, Carl A. and Ashwood, Edward R., eds., *Tietz Textbook of Clinical Chemistry*, 2nd Edition. (Philadelphia: W.B. Saunders Company, 1994), 1716, 1719,1727.
4. The National Academy of Clinical Biochemistry, *Standards of Laboratory Practice: Laboratory Support For the Diagnosis & Monitoring of Thyroid Disease*. (National Academy of Biochemistry, 1996), 27.
5. Sterling K, Tabachnick M: Resin uptake of I<sup>131</sup> triiodothyronine as a test of thyroid function. *J Clin, Endocrin Metab* 21:456, 1961.
6. Braverman LE, Foster AW, Mead LW: The charcoal T3 ratio. An in vitro test of thyroid function. *JAMA* 199:169, 1967.
7. Azukizawa M., Pekary AE, Hershman JM, Parker DC: Plasma thyrotropin, thyroxine, and triiodothyronine relationships in man. *J Clin Endocrin Metab* 51:135, 1976.
8. Browning Margaret C.K., Ford R.P, Callaghan S.J., Fraser, C.G.: Intra- and Interindividual Biological Variation of Five Analytes Used In Assessing Thyroid Function: Implications for Necessary Standards of Performance and the Interpretation of Results. *Clin Chem*, 32:962, 1986.
9. Zucchelli G.C., Giannesi, D., Clerico A., Mariani, G., Carpi, A, Galbati A., and Bianchi R.: Free Triiodothyronine (T3) Index Obtained from Measurements of T3 Resin Uptake and Total T3 Serum Concentration. *J Nucl Med and Allied Sciences*, 21:43, 1977.
10. Piketty Marie-Liesse, D'Herbomez M., Le Guillouzic D, Lebtahi R., Cosson E., Dumont A., Dilouya A., Helal B. : Clinical comparison of three labeled-antibody immunoassays of free triiodothyronine. *Clin Chem*, 42:933, 1966.
11. The National Academy of Clinical Biochemistry, *Standards of Laboratory Practice: Laboratory Support For the Diagnosis & Monitoring of Thyroid Disease*. (National Academy of Biochemistry, 1996), 28-33.
12. Surks I, Chopra IJ, Mariash CN, Nicoloff JT, Solomon DH. American Thyroid Association guidelines for use of laboratory tests in thyroid disorders. *JAMA*, 263: 1529, 1990.



## References (con't)

13. Hay ID, Bayer MF, Kaplan MM, Klee GG, Larsen PR, Spencer CA. American Thyroid Association assessment of current free thyroid hormone and thyrotropin measurements and guidelines for future clinical assays. *Clin Chem*, 37:2002, 1991.

14. The National Academy of Clinical Biochemistry, *Standards of Laboratory Practice: Laboratory Support For the Diagnosis & Monitoring of Thyroid Disease*. (National Academy of Biochemistry, 1996), 27, 29.



#### IV. Certification

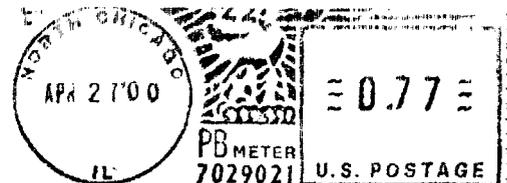
The undersigned certifies, that, to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioner which are unfavorable to the petition.

*Denise Farmer 4-26-00*  
Denise Farmer  
Dept. 09V6, Bldg. AP31  
Abbott Laboratories  
200 Abbott Park Road  
Abbott Park, IL 60064-6204  
(847)938-5032



Dept. 9V6 Bldg. AP31  
**ABBOTT LABORATORIES**  
200 Abbott Park Road  
Abbott Park, IL 60064-3537

**FIRST  
CLASS**



**FIRST CLASS MAIL**

**Dockets Management Branch (HFA-305)  
Food and Drug Administration  
Department of Health and Human Services  
Room 1-23  
12420 Parklawn Drive  
Rockville, MD 20857**