

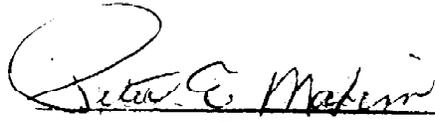
**Varelisa® TPO Antibodies - Device Modification  
510(k) Submission  
Section 1. Indications For Use Statement**

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510(k) Number:                     K993585                    

Device Name: **Varelisa® TPO Antibodies**

The Varelisa TPO Antibodies EIA kit is designed for the quantitative and qualitative determination of TPO (thyroid peroxidase) antibodies in serum or plasma to aid in the diagnosis of thyroid diseases such as Autoimmune Thyroiditis and Graves' Disease.



(Division Sign-Off)

Director of Clinical Laboratory Devices                     K993585                      
510(k) Number

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Concurrence of CDRH, Office of Device Evaluation (ODE)

Prescription Use  OR Over-The-Counter Use

(Per 21 CFR 801.109)

Varelisa® TPO Antibodies - Device Modification  
 510(k) Submission  
 Section 9. Summary of Safety and Effectiveness

JAN - 5 2000

9. 510(K) SUMMARY OF SAFETY AND EFFECTIVENESS

This summary of safety and effectiveness information is being submitted in accordance with the requirements of The Safety Medical Devices Act of 1990 (SMDA 1990) and 21 CFR Part 807.92.

Assigned 510(k) Number: 15993585

**Date of Summary Preparation:** October 11, 1999

**Distributor:** Pharmacia & Upjohn  
 Diagnostics Division, US Operation  
 7425-248-1  
 7000 Portage Road  
 Kalamazoo, MI 49001

**Manufacturer:** Pharmacia & Upjohn Diagnostics GmbH Co. KG  
 Munzingerstrasse 7  
 D-79111 Freiburg, Germany

**Company Contact Person:** Karen E. Matis  
 Manager, Regulatory Affairs and Quality  
 Management  
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 7000 Portage Road  
 7425-248-01  
 Kalamazoo, MI 49001  
 (614) 794-3324 (Phone)  
 (614) 794-0266 (Fax)

**Device Name:** Varelisa® TPO Antibodies

**Common Name:** Thyroid autoantibody immunological test system.

**Classification:**

<u>Product Name</u>	<u>Product Code</u>	<u>Class</u>	<u>CFR</u>
Varelisa® TPO Antibodies	82JZO	II	866.5870

**Varelisa® TPO Antibodies - Device Modification  
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**Substantial Equivalence to:**

elias™ TM Antibodies

**Indications For Use Statement:**

The Varelisa TPO Antibodies EIA kit is designed for the quantitative and qualitative determination of TPO (thyroid peroxidase) antibodies in serum or plasma to aid in the diagnosis of thyroid diseases such as Autoimmune Thyroiditis and Graves' Disease.

**General Description of the Device**

The Varelisa TPO Antibodies assay is an indirect noncompetitive enzyme immunoassay for the quantitative and qualitative determination of TPO (thyroid peroxidase) antibodies in serum or plasma.

The determination of TPO antibodies is of central importance for the clinical diagnosis of thyroid diseases. The presence of TPO antibodies suggests the possibility of autoimmune diseases such as Autoimmune Thyroiditis and Graves' Disease.

**Varelisa® TPO Antibodies Test Principle**

Varelisa TPO Antibodies is an indirect noncompetitive enzyme immunoassay. The wells of a microplate are coated with human recombinant TPO antigen. Antibodies specific for TPO present in a patient sample bind to this antigen.

In a second step an enzyme labeled second antibody (Conjugate) binds to the antigen-antibody complex which leads to the formation of an enzyme labeled antigen-antibody sandwich complex.

The enzyme labeled antigen-antibody complex converts the added substrate to form a colored solution. The rate of color formation from the chromogen is a function of the amount of Conjugate complexed with the bound antibody and thus is proportional to the initial concentration of the respective antibodies in the patient sample.

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**Device Comparison:**

elias TMAb Assay (the predicate/ original device) and Varelisa® TPO Antibodies Assay (the new/ modified device) are both indirect noncompetitive enzyme immunoassays for the determination of anti-thyroid antibodies in serum or plasma to aid in the diagnosis of thyroid diseases such as autoimmune thyroiditis and Grave's Disease.

The essential difference between both assays is the use of human recombinant TPO (new device) instead of the purified thyroid microsomal antigen (predicate device). This modification was initiated due to the fact that Thyroid Peroxidase is the accepted target of the "thyroid microsomal" antibodies<sup>1</sup>. In addition, the recombinant protein technology assures an antigen preparation free from contamination with Thyroglobulin.

An important common feature between the predicate and modified assays is the standardization against the Anti-Thyroid Microsome Serum, NIBSC Research Standard 66/387, assuring comparability of the assay results.

In a correlation study, a high degree of similarity was demonstrated: comparing 183 positive and negative samples, an  $R^2$ -value of 0.90 (Pearson's coefficient of correlation: 0.95) was obtained. Slight differences in the values are due to the different antigen sources (recombinant TPO antigen and microsome preparation, respectively). Omitting 7 samples (out of 183 samples) which were found equivocal in Varelisa TPO Antibodies (for elias TM Abs no equivocal range is defined), the overall agreement was 98.9%.

All defined negative samples were found negative in both assays and the evaluation of the results obtained for 39 blood donor samples gave mean values of 0.4 IU/ml for both assays.

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<sup>1</sup> Czamocka, B., Ruf, J., Ferrand, M., et al. (1985) Purification of the human thyroid peroxidase and its identification as the microsomal antigen involved in autoimmune thyroid diseases. FEBS Lett. 190, 147-152



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

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Diagnostics Division, US Operations  
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7425-248-01  
Kalamazoo, Michigan 49001-0199

JAN - 5 2000

Food and Drug Administration  
2098 Gaither Road  
Rockville MD 20850

Re: K993585  
Trade Name: Varelisa® TPO Antibodies  
Regulatory Class: II  
Product Code: JZO  
Dated: October 20, 1999  
Received: October 22, 1999

Dear Ms. Matis:

We have reviewed your Section 510(k) notification of intent to market the device referenced above and we 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). You may, therefore, market the device, subject to the general controls provisions of the Act. 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.

If your device is classified (see above) into either class II (Special Controls) or class III (Premarket Approval), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 895. A substantially equivalent determination assumes compliance with the Current Good Manufacturing Practice requirements, as set forth in the Quality System Regulation (QS) for Medical Devices: General regulation (21 CFR Part 820) and that, through periodic QS inspections, the Food and Drug Administration (FDA) will verify such assumptions. Failure to comply with the GMP regulation may result in regulatory action. In addition, FDA may publish further announcements concerning your device in the Federal Register. Please note: this response to your premarket notification submission does not affect any obligation you might have under sections 531 through 542 of the Act for devices under the Electronic Product Radiation Control provisions, or other Federal laws or regulations.

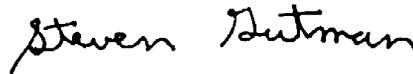
Page 2

Under the Clinical Laboratory Improvement Amendments of 1988 (CLIA-88), this device may require a CLIA complexity categorization. To determine if it does, you should contact the Centers for Disease Control and Prevention (CDC) at (770) 488-7655.

This letter will allow you to begin marketing your device as described in your 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4588. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification"(21 CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers Assistance at its toll-free number (800) 638-2041 or (301) 443-6597, or at its internet address "<http://www.fda.gov/cdrh/dsma/dsmamain.html>".

Sincerely yours,



Steven I. Gutman, M.D, M.B.A.  
Director  
Division of Clinical  
Laboratory Devices  
Office of Device Evaluation  
Center for Devices and  
Radiological Health

Enclosure