

10/21/98

# Ramco Laboratories Inc.

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Fax No.: 713-526-1528

## 510(k) SUMMARY

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92

The assigned 510(k) number is: K981208

<b>Submitter:</b>	Ramco Laboratories, Inc. 4507 Mt. Vernon Houston, TX 77006
Phone #:	(713) 526-9677
Fax #:	(713) 526-1528
Contact Person:	Jeffrey B. Grubb, President
Date Prepared:	March 27, 1998
Device Name:	Transferrin Receptor Assay
Trade Name:	<b><i>TfR</i></b>
Common Name:	TfR Assay
Classification Name:	sTfR Immunological Test System
Predicate Device Name:	Quantikine IVD sTfR Immunoassay R&D Systems, Inc. 614 McKinley Place N.E. Minneapolis, MN 55413 510(k) #K970718

The ***TfR*** assay is an *in vitro* enzyme immunoassay based upon the double antibody sandwich method. Plasma or serum samples are diluted in buffer and pipetted into microwells pre-coated with polyclonal antibody to transferrin receptor. Horseradish peroxidase conjugated antibody specific for serum transferrin receptor (STR) is added to the wells and incubated. During this incubation, the STR binds to the polyclonal antibodies adsorbed to the wells and the HRP-conjugated second antibodies bind to the captured STR.

Any unbound STR and excess HRP-conjugate are washed from the wells. Enzyme substrate is added to the wells and allowed to incubate, a stop solution is then added to stop the reaction and the intensity of the yellow product is measured in a microplate reader. The optical density of the resulting solution is directly proportional to the concentration of the STR in the standard samples. A standard curve is generated from the STR standards provided in the assay and the concentration of STR in the unknown sample is determined by comparing the unknown's optical density reading with the standard curve graph.

The *TfR* assay is an *in vitro* enzyme immunoassay for quantifying the concentration of transferrin receptor in human serum or plasma to aid in the diagnosis of iron deficiency anemia, particularly in the presence of other disease states.

Ramco Laboratories, Inc. is claiming substantial equivalence of its *TfR* assay the R&D Systems (Minneapolis, Minnesota) Quantikine IVD sTfR Immunoassay ("QSI") which obtained 510(k) clearance on May 27, 1997 (K970718, Class II).

Both *TfR* and QSI's intended use is to quantitatively determine the level of transferrin receptor in human serum or plasma to aid in the diagnosis of iron deficiency anemia. Both are based on the microplate sandwich enzyme immunoassay technique, use calibrators to generate a log-log curve from which the quantity of an unknown sample is read, use a monoclonal transferrin antibody conjugated to horseradish peroxidase, use a microplate reader with a 450nm filter to read the results, and supply controls which, like the unknown samples, must be diluted prior to use. Finally, both assays offer a prescribed normal range, the upper limit of which is the indicator for the presence or absence of iron deficiency anemia.

Both *TfR* and QSI use a monoclonal antibody in its conjugate. However, *TfR* uses a polyclonal transferrin receptor antibody to coat the microplate, making it a polyclonal-monoclonal assay, while QSI uses a monoclonal antibody to coat the plate making it a double monoclonal. *TfR* provides 7 standards consisting of TfR, isolated from human placenta, contained in a phosphate buffer with BSA and normal rabbit serum and calibrated in ng/ml while QSI provides 6 standards, consisting of human serum transferrin receptor, contained in buffered animal serum and calibrated in nmol/L. The assay results are reported in  $\mu\text{g/ml}$  in the *TfR* assay compared to nmol/L for QSI. Samples and controls are diluted 100:1 prior to use in the *TfR* assay compared to 50:1 for QSI. Finally, *TfR* is a single-stage compared to QSI which is a two-stage assay.

Over an 18 month period of time, patient samples were collected. These samples were segregated into one of three categories: 1) Anemia of Chronic Disease ("ACD"), clinically defined as Serum Iron < 60, Iron Binding Capacity < 350 and Hemoglobin < 12; 2) Iron Deficiency Anemia ("IDA"), clinically defined as Serum Iron < 60, Iron Binding Capacity > 350 and Hemoglobin < 12; and 3) neither IDA nor ACD, samples that had either Serum Iron > 60 or Hemoglobin > 12.

Of the above samples, *TfR* results were obtained for 38 of the IDA, 175 of the ACD, and 70 of the "Neither IDA nor ACD" samples (283 total), while QSI results were obtained for 23 of the IDA, 119 of the IDA and 13 of the "Neither IDA nor ACD" samples (155 total).

Performing a linear regression of all values for the 155 samples for which a *TfR* and QSI value has been obtained yields an  $R^2$  of 88.2% (See Table 17).

Of the 38 IDA samples, QSI results were obtained for 23. *TfR* is in agreement ( $> 8.3\mu\text{g/ml}$ ) with the clinical definition of IDA 30 out of 38 times or 78.9% while QSI is in agreement with the clinical definition 18 out of 23 times or 78.3%. Of these 23 samples, *TfR* delivered the same individual result as QSI for 22 out of 23 samples.

The IDA population was further refined to those samples where QSI and ferritin results concurred ( $\text{STR} > 28.1$  and ferritin  $< 30$ ). This reduced the population to 17 samples. Of these 17 samples, *TfR* concurred with the individual QSI results 17 out of 17 times or 100.0%.

Of the 175 ACD samples, QSI results were obtained for 119. *TfR* is in agreement ( $< 8.3\mu\text{g/ml}$ ) with the clinical definition of ACD 145 out of 175 times or 82.9% while QSI is in agreement with the clinical definition 81 out of 119 times or 68.1%. Of these 119 samples, *TfR* delivered the same individual result as QSI.

The ACD population was further refined to those samples where QSI and ferritin results concurred ( $\text{STR} < 28.1$  and ferritin  $> 30$ ). This reduced the population to 80 samples. Of these 80 samples, *TfR* concurred with the individual QSI results 79 out of 80 times or 98.8%.

Of the 70 "Neither IDA nor ACD" samples, QSI results were obtained for 13. Of these 13 samples, *TfR* delivered the same individual result as QSI 12 out of 13 times or 92.3%

When all samples results are taken as a whole, *TfR* delivered the same individual result as QSI 140 out of 155 times or 90.3%. When only those cases are used where QSI and ferritin are in agreement, *TfR* and QSI give the same result 96 out of 97 times or 98.97%.



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

OCT 21 1998

Food and Drug Administration  
2098 Gaither Road  
Rockville MD 20850

Mr. Jeffrey B. Grubb  
President  
Ramco Laboratories, Inc.  
4507 Mt. Vernon  
Houston, Texas 77006

Re: K981208/S1  
Trade Name: TfR  
Regulatory Class: II  
Product Code: JNM  
Dated: July 29, 1998  
Received: July 31, 1998

Dear Mr. Grubb:

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.

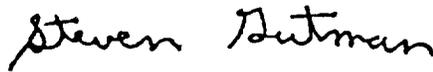
If your device is classified (see above) into either class II (Special Controls) or class III (Premarket Approval), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 895. A substantially 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.

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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,

A handwritten signature in cursive script that reads "Steven Gutman".

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

INDICATIONS FOR USE STATEMENT

510(k) Number: K 981208

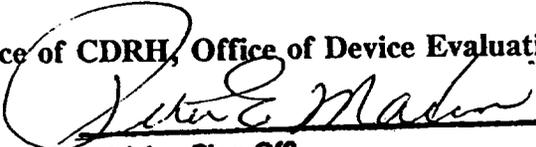
Device Name: TfR

Indications for Use: The *TfR* assay is an *in vitro* enzyme immunoassay for quantifying the concentration of transferrin receptor in human serum or plasma to aid in the diagnosis of iron deficiency anemia, particularly in the presence of other disease states.

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Concurrence of CDRH, Office of Device Evaluation (ODE)

  
\_\_\_\_\_  
(Division Sign-Off)

Division of Clinical Laboratory Devices

510(k) Number

K 981208

Prescription Use

OR

Over-The-Counter Use