SEP 22 1998

K981734

ATTACHMENT B

SUMMARY OF SAFETY AND EFFECTIVENESS

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VTEC-RPLA "SEIKEN"

Below summarizes and compares the performance of VTEC-RPLA "SEIKEN" and a similar device previously given FDA clearance for marketing in the US. The information contained in this summary was obtained from data prepared at and which is on file at Denka Seiken Co., Inc. This summary shows that the two reagent systems are substantially equivalent.

INTENDED USE

This *in vitro* diagnostic procedure is intended for the detection and identification of verotoxins or shiga-like toxins in culture isolates of *E. coli*. Such characterization is useful in the diagnosis of Enterohemorrhagic *E. coli* (EHEC) infections.

METHOD	**VTEC-RPLA "SEIKEN"**	**Premier EHEC**
Product code	230553	608096
Min. Detectable Conc.		
VT 1	25 pg/well	7 pg/well
VT2	25 pg/well	15 pg/well

Correlation

Specificity and sensitivity between the two tests were 100% and 100%, respectively.

VTEC-RPLA "SEIKEN" and Premier EHEC are similar in that both:

* Are reagent systems which can be used for the detection of verotoxins in culture isolates of *E. coli* to aid in the diagnosis of EHEC infections.
* Employ antibody-antigen reactions as part of the assay.

VTEC-RPLA "SEIKEN" and Premier EHEC are different in that:

* They use different culture conditions to prepare specimens
* VTEC-RPLA is based on reversed passive latex agglutination (RPLA) while the Premier EHEC is an enzyme immuno assay (EIA).
* The minimal detectable concentration for the VTEC-RPLA is approximately 25 pg/well ; that for the Premier EHEC is 7- 15 pg/well.
* VTEC-RPLA utilizes polyclonal antibodies specific for each verotoxin type, VT1 and VT2, and thus may be used to identify toxins; the Premier EHEC uses three types of antibody: an anti-VT monoclonal (EIA capture); anti-VT polyclonal (enzyme conjugate); and anti-rabbit IgG goat IgG conjugated with POD; the assay is specific for verotoxins but not type specific, ie cannot identify VT1 and VT2.
* Premier EHEC may be used to directly detect verotoxins in stools, in mixed cultures and in culture isolates while VTEC-RPLA is intended for use with culture isolates only.

PROTOCOL AND DATA SUMMARY

This section provides data generated by and for Denka Seiken Co., Ltd. characterizing the performance of VTEC-RPLA "SEIKEN". The protocols used for the data generation are given below, and the results are attached.

CORRELATION

Study 1 (in-house)

One hundred *Eschericia coli* strains (80 verotoxin-producing and 20 non-verotoxin producing) were obtained from the Japanese National Institute of Infectious Disease and tested in parallel using VTEC-RPLA "SEIKEN" and the Premier EHEC Reagent System. Specimens were prepared and tested according to the product inserts given in the kits. 100% sensitivity and 100% specificity were observed.

Study 2 (external)

One hundred and seventy eight *Eschericia coli* strains (147 verotoxin-producing and 31 non-verotoxin producing) isolated from humans were were tested by the Tokyo Metropolitan Research Laboratory of Public Health using VTEC-RPLA "SEIKEN", PCR and the vero cell assay. 100% sensitivity and 100% specificity were observed.

SENSITIVITY

Three reagent lots (Lot No. 3421, No. 3626 and No. 31222) and two verotoxin-producing strains, DK-EC-VT1 and DK-EC-VT2, obtained from Kyoto University Faculty of Medicine, were used in these studies. Verotoxin type 1 and verotoxin type 2 were purified from the respective strains above and preparations were adjusted to 100 ng/ml for testing. Each verotoxin preparation was tested with each reagent lot three times and all three lots showed titers of between 1:64 to 1:128 in all replicates.

SPECIFICITY

Three reagent lots (Lot No. 3421, No. 3626 and No. 31222) , eight verotoxin-producing and twelve non-producing strains of *E. coli* were used in these studies. Specimens were prepared using the CA-YE shaking broth recommended in the product insert and the resulting culture supernatants from each strain were lyophilized and subsequently tested in triplicate after reconstitution. Positive results were obtained from verotoxin-producing strains and, likewise, negative results only from non-producing strains.

REPRODUCIBILITY

Reagent lots and verotoxin specimens were the same as those described in SENSITIVITY above. Each verotoxin preparation was tested with each reagent lot five times and the resulting titers for all assays were between 1:64 to 1:128.
Also, performed were
Person--to--person: testing done by three operators
Day--to--day: testing done on five different days
Lot--to--lot: testing done with three different lots
All of the above studies showed agglutination titers of between 1:64 to 1:128.

DILUTION

Three verotoxin-producing strains, DK-EC-PS 1 (VT1), DK-EC- PS 4 (VT2) and DK-EC-PS 7 (VT1 and VT2), were cultured in CA-YE by the broth culture method and the supernatants obtained after cell-pelleting, in addition to ten-fold dilutions in saline, were each tested in a single examination. All ten-fold dilutions showed an agglutination titer at the expected range.

STABILITY

To establish storage conditions and the reagent shelf-life, the above three reagent lots were tested at 0, 3, 6, 9, 12 and 15 months with regards to sensitivity, specificity and reproducibility as described above. Reagents were store at 12 C. As there was no change in reagent performance throughout this time, the storage conditions and shelf-life were set at 2-10 C and one year after production, respectively.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

SEP 22 1998

Kevin Mangan
International Sales and Business Development
Denka Seiken Co., Ltd.
3-4-2, Nihonbashi-Kayabacho
Chuo-Ku
Tokyo, Japan 103-0025

Re: K981734
Trade Name: VTEC-RPLA "SEIKEN"
Regulatory Class: I
Product Code: GNA
Dated: August 14, 1998
Received: August 17, 1998

Dear Mr. Mangan:

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.

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 at (301) 443-6597 or at its internet address "http://www.fda.gov/cdrh/dsmamain.html"

Sincerely yours,

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

510(k) Number (if known) K981734

Device Name: VTEC-RPLA

Indications For Use:

VTEC-RPLA "SEIKEN" is an in vitro diagnostic device for the detection and identification of verotoxin 1 and 2 in culture isolates of E. coli and is intended as an aid in the diagnosis of Enterohemorrhagic E. coli (EHEC) infections.

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Woody Dubois

(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K981734

Prescription Use ____ OR Over-The-Counter Use ____
(Per 21 CFR 801.109)

(Optional Format 1-2-96)

8K-23