K971662
Nov 18, 1997

510(k) Summary

a.1. ***Submitter's Name:***

Diagnostic Hybrids, Inc.
1 President Street
Athens, OH 45701
614-593-1784
Attn.: J. L. Brown
Date of Preparation: April 23, 1997

a.2. ***Name of the device:***

Trade Name: ELVIS™ HSV ID/Typing Test System
Common Name: Enzyme Linked Virus Inducible System for Herpes Simplex Virus culture, identification and typing.
Classification Name: Not known.

a.3. ***Identification of the predicate device(s):***

The predicate device to which substantial equivalence is being claimed is:

HSV1/HSV2 Culture Identification/Typing Test
For pre-CPE and CPE applications.
Marketed and distributed by:

Syva Company
3401 Yerba Buena Road
P.O. Box 49013
San Jose, CA 95161

a.4. ***Description of the premarket notification device:***

The subject device provides Cells, Replacement Medium and Test Reagents for the culture, identification and typing of HSV isolated from patient specimens. It consists of ELVIS™ HSV Cells in a tube configuration [ELVIS™ HSV Gold Test, 510(k) No. K960578] and in shell vial and multiwell plate configurations [ELVIS™ HSV Test, 510(k) No. K941924],and reagents to which have been added HSV-typing monoclonal antibodies to permit the user to directly type the HSV-positive specimens.

ELVIS™ HSV Cells are genetically engineered Baby Hamster Kidney cells, which, when infected with either HSV-1 or HSV-2 are induced to generate and accumulate an endogenous, intracellular bacterial enzyme, β-galactosidase. Other related viruses are not capable of inducing this enzyme. In addition to the induction of this specific enzyme, HSV infection of cells results in the formation of HSV, type-specific proteins. The presence of these proteins can be detected microscopically by their fluorescence when HSV-type-specific, fluorescent labeled antibodies are used. Thus, when HSV-infected monolayers are fixed using Solution 1 and

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treated with Solution 2T, which contains the chromogenic substrate for the β-galactosidase enzyme, those cells infected with HSV are stained an indigo blue while uninfected cells remain colorless. Both type-2-specific, fluorescein labeled monoclonal antibodies and type-1-specific, non-labeled monoclonal antibodies are also incorporated in Solution 2T. This allows for the monoclonal antibodies to react with their specific antigens in the HSV-infected ELVIS™ Cells at the same time as the enzyme is causing the deposition of blue stain. After a 1 hour incubation period, which allows for these reactions to proceed in monolayers whose specimens contained viable HSV, the monolayers are examined for blue cells using standard light microscopy: those which do not contain blue cells are negative for HSV; those which contain blue cells are positive for HSV and can now be examined with a fluorescence microscope to determine the HSV type. If fluorescent cells are seen, the HSV in the specimen is type 2; if no fluorescent cells are seen, the HSV in the specimen is type 1. This can be confirmed by treating the monolayer with Solution 3 which contains fluorescein-labeled goat-antimouse antibodies which will react with the type 1-specific monoclonal antibodies in the HSV-1 infected cells.

Thus, the major change in the composition of the above legally marketed devices is the incorporation of the monoclonal antibodies into the Solution 2 which contains the chromogenic substrate for the β-galactosidase enzyme (which has been re-named Solution 2T. Additionally, two other reagents are included with the subject device, i.e., Solution 3, the fluorescein-labeled goat-antimouse antibody, and a Buffered Glycerol Mounting Medium used on the fixed and stained monolayers, to prevent them from drying before microscopic examination for fluorescence.

Because it is critical that the monoclonal antibodies be HSV-type specific, the laboratory and clinical development efforts were focused on demonstrating that the selected antibodies when present in Solution 2T yielded the same typing result as a predicate device, namely Syva's product. This product was selected as the one to show substantial equivalence to since it is estimated to account for about 75% of the total market for HSV typing antibodies. For the product to have such a major share of the market is indicative of its quality since its price has been maintained at a high level in the face of lower-priced competitive products.

a.5. ***Statement of the intended use.***

Herpes simplex virus (HSV) infections in humans can cause lesions at a variety of sites, e.g., oral-facial, genital,

visceral, eye, cutaneous and the central and peripheral nervous system. These lesions can be a result of the primary infection by the virus or they can result from a reactivation of the latent virus, causing recurrent episodes of the disease. There are two genetically- and antigenically-distinct forms of HSV, termed HSV type 1 (HSV-1) and HSV type 2 (HSV-2). HSV-2 is the most common cause of genital infections, due to venereal transmission; HSV-1 is commonly associated with the other disease locations although both serotypes have been shown to cause disease in all the locations of the body.

Studies have shown an increasing prevalence of genital HSV infections with a concomitant increase of the disease in neonates. The consequences of HSV infection can range from inconsequential (cold sores in otherwise healthy patients) to highly morbid and fatal (neonates). Since there is an effective antiviral chemotherapeutic agent (acyclovir) available to treat HSV infections, it becomes very important to have a rapid and accurate test for the detection and diagnosis of HSV.

Identification of the type of HSV infection is important in the management of the patient in that: (1) the prognosis and counseling of the patient depends on the HSV type since HSV-2 infections are often more painful, require a longer period of time to resolve and recur more frequently than HSV-1; (2) the most appropriate therapeutic agent can be selected by the physician since the effectiveness of an antiviral agent can differ for the two different types; and (3) the epidemiology of HSV infections can be tracked and studied for correlation to other diseases and populations.

a.6. ***Comparison of the technological characteristics.***

The following is a comparison of the technological characteristics of the predicate device to the subject device.

Item	***Predicate Device***	***Subject Device***
HSV-1 MAb		
Number:	1	2
Origin:	Mouse	Mouse
Antigen:	HSV-1 Glycoprotein C.	HSV-1 Glycoprotein C. HSV-1 induced nuclear antigen.
HSV-2		
Number:	2	2
Origin:	Mouse	Mouse
Antigen:	HSV-2 induced protein. HSV-2 Glycoprotein B.	HSV-2 Glycoprotein C. HSV-2 Glycoprotein G.

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Method:	Direct Fluorescent ImmunoAssay.	Direct Fluorescent ImmunoAssay for HSV-2. Indirect Fluorescent ImmunoAssay for HSV-1.
Fluorescent Label Site:	All 3 monoclonals.	HSV-2 monoclonals. Goat-antimouse antibodies

b.1. The non-clinical tests consist of those directed at defining the shelf life of the test kit components, the analytical sensitivity using Solution 2T and the specificity of the antibodies.

The tests for defining the shelf life of Solution 2T, Solution 3 and the Buffered Glycerol Mounting Medium are continuing at this time. Data on more than three lots stored at 2° to 8°C, ambient room temperature and 37°C are continuing to be generated. Currently, the real-time data support shelf lives in excess of 2 months for each reagent.

The test data demonstrating that the analytical sensitivity of the ELVIS™ Cells for detecting HSV using Solution 2T is not altered from that using Solution 2, i.e., without the antibody formulation are presented in the submission.

The test data demonstrating that the specificity of the antibodies used in the subject device yield results identical to those results using the predicate device are included in the submission. The data were obtained by testing the two devices concurrently using frozen positive clinical specimens and clinical isolates.

b.2. The clinical tests submitted consist of studies performed in 4 different laboratories on over 650 different clinical specimens. In the 218 HSV-positive specimens tested concurrently with the laboratory's standard test (using Syva's HSV1/HSV2 Culture Identification/Typing Test) and the **ELVIS™ HSV ID/Typing Test System**, there was complete agreement in the typing results between the two tests. In addition, the overall results show for the ELVIS™ HSV ID portion of the ID/Typing Test System a clinical sensitivity of 99.5% and a clinical specificity of 98.7% compared to the laboratory's standard test. The specimens tested were those normally submitted to the respective laboratories for HSV testing; **ELVIS™ HSV ID/Typing** tests were performed on those specimens for which there was sufficient residual sample. The above test results demonstrate that the **ELVIS™ HSV ID/Typing Test System** yields results substantially equivalent to the

predicate device.

b.3. The results from the clinical tests of the **ELVIS™ HSV ID/Typing Test System** as well as the users' experience with the System demonstrate that the subject device is safe and effective and performs at a level that is substantially equivalent to the predicate device and standard clinical test methods employed at each site.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

NOV 18 1997

Mr. James L. Brown
Vice President of
Product Development and
Regulatory Affairs
Diagnostic Hybrids Inc.
One President Street
Athens, Ohio 45701

Re: K971662
Trade Name: ELVIS HSV ID/Typing Test System
Regulatory Class: III Product Code: GQN
III GQL
Dated: August 26, 1997
Received: August 27, 1997

Dear Mr. Brown:

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 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 requirement, 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): K97-1662

Device Name: **ELVIS™ HSV ID/Typing Test System**

Indications for Use: **The ELVIS™ HSV ID/Typing Test System** is a qualitative test indicated for use in the isolation and identification of HSV from lesions and body fluids suspected of containing viable HSV-1 and/or HSV-2. Both serotypes have been isolated from various parts of the body, particularly when HSV-associated disease is indicated. Performance of this assay has not been established for use with antiviral therapy or prenatal monitoring.

(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K971662

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

Concurrence of CDRH, Office of Device Evaluation (ODE)

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