

K970883  
MAY 21, 1997

### 510(k) Summary

**BOEHRINGER  
MANNHEIM  
CORPORATION**



**Introduction**

According to the requirements of 21 CFR 807.92, the following information provides sufficient detail to understand the basis for a determination of substantial equivalence.

**1.  
Submitter  
name,  
address,  
contact**

Boehringer Mannheim Corporation  
2400 Bisso Lane  
P.O. Box 4117  
Concord, CA 94524-4117  
(510) 674 - 0690, extension 8240  
Fax: (510) 687-1850  
Contact Person: Yvette Lloyd

Date Prepared: March 6, 1997

**2.  
Device name**

Proprietary name: CEDIA® Digoxin II Assay

Common name: Homogeneous enzyme immunoassay for the determination of Digoxin.

Classification name: Enzyme immunoassay, Digoxin

**3.  
Predicate  
device**

The Boehringer Mannheim CEDIA® Digoxin II is substantially equivalent to other products in commercial distribution intended for similar use. Most notably it is substantially equivalent to the currently marketed Abbott TDx® Digoxin II Assay (K882233).

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510(k) Summary, Continued

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**4.  
Device  
Description**

The CEDIA<sup>®</sup> Digoxin II Assay is based on the bacterial enzyme  $\beta$ -galactosidase, which has been genetically engineered into two inactive fragments. These fragments spontaneously reassociate to form fully active enzyme that, in the assay format, cleaves a substrate, generating a color change that can be measured spectrophotometrically. In the assay, digoxin in the sample competes with analyte conjugated to one inactive fragment of  $\beta$ -galactosidase for antibody binding site. If analyte is present in the sample, it binds to antibody, leaving the inactive enzyme fragments free to form active enzyme. If analyte is not present in the sample, antibody binds to analyte conjugated on the inactive fragment, inhibiting the reassociation of inactive  $\beta$ -galactosidase fragments, and no active enzyme is formed.

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**510(k) Summary, Continued**

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**5.  
Intended use**

Immunoassay for the in vitro quantitative determination of Digoxin in human serum and plasma.

**6.  
Comparison  
to predicate  
device**

The Boehringer Mannheim CEDIA® Digoxin II Assay is substantially equivalent to other products in commercial distribution intended for similar use. Most notably it is substantially equivalent to the currently marketed Abbott TDx® Digoxin II Assay (K882233).

The following table compares the CEDIA® Digoxin II Assay with the predicate device, Abbott TDx® Digoxin II Assay. Specific data on the performance of the test have been incorporated into the draft labeling in attachment 5. Labeling for the predicate device is provided in attachment 6.

**Similarities:**

- Intended Use: Immunoassay for the in vitro quantitative determination of Digoxin
- Sample type: Serum and plasma
- Assay range: 0.15 - 4 ng/mL

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510(k) Summary, Continued

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6. Comparison to predicate device cont.

**Differences:**

Feature	CEDIA® Digoxin II	TDx Digoxin II
Reaction test principle	Spectrophotometric 570 nm	Fluorescence Polarization
Instrument required	Hitachi 911	Abbott TDx

**Performance Characteristics:**

Feature	CEDIA® Digoxin II			TDx Digoxin II		
Precision	Modified NCCLS (ng/mL):			NCCLS (ng/mL):		
Level	<u>Level 1</u>	<u>Level 2</u>	<u>Level 3</u>	<u>Low</u>	<u>Mid</u>	<u>High</u>
N	120	120	120	50	50	50
Within run	1.1	1.8	3.8	0.70	1.44	3.66
%CV	4.25	2.22	1.56	5.75	3.15	1.87
Total	1.1	1.8	3.8	0.70	1.44	3.66
%CV	5.44	3.58	2.34	7.67	3.98	1.91

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510(k) Summary, Continued

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6.  
Comparison  
to predicate  
device, (cont.)

**Performance Characteristics:**

Feature	CEDIA® Digoxin II	TDx Digoxin II
Lower Detection Limit	0.15 ng/mL	0.2 ng/mL
Linearity	0.15 - 4 ng/mL	0.0 - 4.0 ng/mL
Method Comparison	Vs Abbott TDx Digoxin  <u>Least Squares</u> $y = 0.98x - 0.12$ $r = 0.955$ $N = 99$  <u>Deming's:</u> $y = 1.02x - 0.17$ $r = 0.955$ $N = 99$	Vs Baxter Dade Stratus  $y = 0.94x + 0.08$ $r = 0.962$ $N = 200$

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510(k) Summary, Continued

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CORPORATION**



6.  
Comparison  
to predicate  
device, (cont.)

Performance Characteristics:

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Feature	CEDIA® Digoxin II	TDx Digoxin II
Interfering substances	No interference at: (within $\pm 10\%$ of baseline) <i>15</i>	No interference at:
Bilirubin	66 mg/dL	20 mg/dL
Hemoglobin	1000 mg/dL	1000 mg/dL
<i>Triglyceride</i> Lipemia	100 mg/dL	2500 mg/dL
Total Protein	10 g/dL	N/A
Rheumatoid Factor	100 IU/mL	N/A
Specificity	% Cross-reactivity	% Cross-reactivity
Digoxigenin	60.5	up to 200
$\beta$ -Acetyldigoxin	77.0	not tested
$\alpha$ -Acetyldigoxin	75.3	not tested
Gitalin	2.1	not tested
Digoxigenin- Mono-Digitoxiside	102.5	
Digitoxin-Bis- Digitoxiside	86.3	up to 200
Digitoxin	1.5	up to 200
$\beta$ -Methyldigoxin	76.3	4.8
3-Epe-Digoxigenin	37.6	not tested
3- Dehydrodigoxigenin	82.6	not tested
Epi-Digoxigenin- Glucuronide	42.9	not tested

*Handwritten initials*



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration  
2098 Gaither Road  
Rockville MD 20850

MAY 21 1997

Yvette R. Lloyd  
Regulatory Affairs Specialist  
Boehringer Mannheim Corporation  
2400 Bisso Lane  
P.O. Box 4117  
Concord, California 94524-4117

Re: K970883  
CEDIA® Digoxin II Assay  
Regulatory Class: II  
Product Code: KXT  
Dated: April 18, 1997  
Received: April 24, 1997

Dear Ms. Lloyd:

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 (Pre-market 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 Good Manufacturing Practice for Medical Devices: General (GMP) regulation (21 CFR Part 820) and that, through periodic GMP 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 pre-market 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 (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

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510(k) Number (if known): N/A

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Device Name: CEDIA® Digoxin II Assay

**Indications For Use:**

The CEDIA Digoxin II homogeneous enzyme immunoassay is for the quantitation of digoxin in human serum or plasma using automated clinical chemistry analyzers. Measurements are used in the diagnosis and treatment of digoxin overdose and in monitoring levels of digoxin to ensure proper therapy.

Digoxin is widely prescribed for the treatment of congestive heart failure and various disturbances of cardiac rhythm. Therapeutic use of digoxin improves the strength of myocardial contraction and results in the beneficial effects of increased cardiac output, decreased heart size, decreased venous pressure and decreased blood volume. Digoxin therapy also results in stabilized and slowed ventricular pulse rate.

Although the availability of crystalline digoxin has permitted the standardization of drug dosage, therapeutic administration inadvertently, yet frequently, results in toxicity. Importantly, symptoms of digoxin toxicity often mimic the cardiac arrhythmias for which the drug was originally prescribed. Studies suggest that up to 25% of all hospitalized patients treated with digoxin experienced some degree of toxicity, and that the mortality rate among toxic patients was more than twice that of nontoxic patients. Digoxin concentrations of 0.9 to 2.0 ng/mL in serum or plasma are normally considered to be therapeutic. Symptoms of human toxicity generally only appear at concentrations above 2.0 ng/mL; however, concentrations as low as 1.4 ng/mL may be toxic for others.

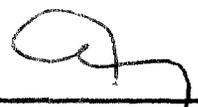
Concurrence of CDRH, Office of Device Evaluation (ODE)

Prescription Use    
 (Per 21 CFR 801.109)

OR

Over-The-Counter Use

(Optional Format 1-2-96)

  
\_\_\_\_\_  
(Division Sign-Off)  
Division of Clinical Laboratory Devices

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INDICATIONS FOR USE, Continued:

Toxicity of digoxin may reflect several factors: a) The drug has a low therapeutic ratio (i.e., a very small difference exists between therapeutic and toxic tissue levels). b) Individuals vary in their response to digoxin. c) Absorption of various tablet forms of digoxin may vary over a two-fold range. d) Susceptibility to digitalis toxicity apparently increases with age.

In combination with other clinical data, monitoring serum or plasma levels may provide the physician with useful information to aid in adjusting patient dosage, and achieving optimal therapeutic effect, while avoiding both subtherapeutic and harmful toxic drug levels.

The CEDIA Digoxin II Assay performance has not been established with body fluids other than human serum and plasma (Na or Li heparin; Na EDTA). Digoxin-like immunoreactive substances (DLIS) have been identified in blood from patients in renal failure, liver failure, and pregnant women in the third trimester. Studies have established that the presence of DLIS in a sample can result in a false elevation of digoxin when assayed by commercially available immunoassay.

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Concurrence of CDRH, Office of Device Evaluation (ODE)

Prescription Use \_\_\_\_\_  
(Per 21 CFR 801.109)

OR

Over-The-Counter Use \_\_\_\_\_

(Optional Format 1-2-96)