Summary of Safety and Effectiveness

As required by 21 CFR 807.92, the following 510(k) Summary is provided:

1. Submitters Information

Contact person:	William J. Pignato Director of Regulatory Affairs
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Date Summary Prepared: April 30, 1999

2. Device Information

Proprietary Name:	Chiron Diagnostics ACS: 180 Folate
Common Name:	Folate Immunological test system
Device Classification:	Class II

3. Predicate Device Information

Name:	Chiron Diagnostics ACS: 180 Folate Immunoassay
Manufacturer:	Chiron Diagnostics Corporation

4. Device Description

Folate, with vitamin B12, is essential for DNA synthesis, which is required for normal red blood cell maturation. Humans obtain folate from dietary sources including fruits, green and leafy vegetables, yeast, and organ meats. Folate is absorbed through the small intestine and stored in the liver.

Low folate intake, malabsorption as a result of gastrointestinal diseases, pregnancy, and drugs such as phenytoin are causes of folate deficiency. Folate deficiency is also associated with chronic alcoholism. Folate and vitamin B12 deficiency impair DNA synthesis, causing macrocytic anemias. These anemias are characterized by abnormal maturation of red blood cell precursors in the bone marrow, the presence of megaloblasts, and decreased red blood cell survival.

Since both folate and vitamin B12 deficiency can cause macrocytic anemia, appropriate treatment depends on the differential diagnosis of the deficiency. Serum folate measurement provides an early index of folate status. However, folate is much more concentrated in red blood cells than in serum so the red blood cell folate measurement

more closely reflects tissue stores. Red blood cell folate concentration is considered the most reliable indicator of folate status.

5. **Statement of Intended Use**

For the quantitative determination of folate in serum or EDTA plasma and red blood cells using the Folate BA (Biotin Avidin) assay on the Chiron Diagnostics ACS:180® Automated Chemiluminescence Systems.

6. **Summary of Technological Characteristics**

The Chiron Diagnostics ACS:180 Folate assay is a competitive immunoassay using direct chemiluminescent technology. Folate in the patient sample competes with acridinium ester-labeled folate in the Lite Reagent for a limited amount of biotin-labeled folate binding protein. Biotin-labeled folate binding protein binds to avidin which is covalently coupled to paramagnetic particles in the Solid Phase. In the ACS:180 Folate assay the sample is pretreated to release the folate from endogenous binding proteins in the sample.

The system performs the following steps for calibrators, quality control samples, and patient samples:

dispenses 150 µL of sample into a cuvette
dispenses 50 µL of DTT
dispenses 100 µL of folate binding protein and 200 µL of Solid Phase and incubates for 5.0 minutes at 37°C
dispenses 100 µL of Lite Reagent and incubates for 2.5 minutes at 37°C
separates, aspirates, and washes the cuvettes with reagent water[6]
dispenses 300 µL each of Reagent 1 and Reagent 2 to initiate the chemiluminescent reaction
reports results according to the selected option, as described in the system operating instructions or in the online help system

An inverse relationship exists between the amount of folate present in the patient sample and the amount of relative light units (RLUs) detected by the system.

6. **Performance Characteristics**

Expected Results

To determine the reference range for the ACS:180 Folate assay for serum and RBC folate, data was obtained on 263 serum and 109 red blood cell folate samples, respectively. The normal ranges are based on 95% confidence intervals and the deficient ranges represent the observed ranges.

Category	N	Mean (ng/mL)	Range (ng/mL)	Mean (nmol/L)	Range (nmol/L)
Serum folate					
deficient*	32	1.08	0.0–2.31	2.45	0.0–5.24
normal	231	9.89	4.25–23.8	22.4	9.65–54.0
RBC folate					
deficient*	10	64.4	9–157	146	20.4–356
normal	99	545	322–886	1237	731–2011

* Diagnosed by bone and/or peripheral blood smear pathology and other criteria including:

- megaloblastic anemia
- folate deficient diet
- malabsorption
- alcoholism
- Tropical Sprue
- abnormal blood parameters including mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and hematocrit (HCT).

Laboratories should consider these reference ranges as guidelines only. The data was obtained on apparently healthy males and females from the United States. Due to population demographic factors, assay methods, calibration, and reagent specificity, each laboratory should establish its own reference ranges for the diagnostic evaluation of patient results.

Sensitivity and Assay Reportable Range

The ACS:180 Folate assay measures folate concentrations up to 20 ng/mL (45.4 nmol/L) with a minimum detectable concentration of 0.25 ng/mL (0.6 nmol/L). Analytical sensitivity is defined as the concentration of folate that corresponds to the RLUs that are two standard deviations less than the mean RLUs of 20 replicate determinations of the folate zero standard in 7 assays with 3 lots of reagents.

Method Comparison

For 258 serum samples in the range of 0 to 20 ng/mL (0 to 45.4 nmol/L), the relationship between the ACS:180 Folate assay and an alternate folate assay is described by the equation:

ACS:180 Folate = 0.92 (alternate chemiluminescent method) + 0.21 ng/mL
Correlation coefficient (r) = 0.95

For 189 red blood cell samples in the range of 9.0 to 882 ng/mL (20.4 to 2002 nmol/L), the relationship between the ACS:180 Folate assay and an alternate folate assay is described by the equation:

ACS:180 RBC Folate = 0.93 (alternate chemiluminescent method) + 52.8 ng/mL
Correlation coefficient (r) = 0.96

Precision

Four samples were assayed six times with three lots of reagents in 23 runs on four systems (n = 138 for each sample), over a period of three days. The following results were obtained:

Mean Folate (ng/mL)	Mean Folate (nmol/L)	Within-run % CV	Total % CV
1.91	4.34	7.95	9.24
5.94	13.5	5.36	8.79
10.6	24.1	5.61	6.60
15.4	35.0	4.88	5.36

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

JUN 30 1999

Mr. William J. Pignato
Director of Regulatory Affairs
Chiron Diagnostics Corporation
63 North Street
Medfield, Massachusettes 02052-1688

Re: K991582
Trade Name: Chiron Diagnostics ACS: 180® Folate Assay
Regulatory Class: II
Product Code: CGN, JIS
Dated: April 30, 1999
Received: May 7, 1999

Dear Mr. Pignato:

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 (301) 443-6597, or at its internet address "http://www.fda.gov/cdrh/dsma/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): K991582

Device Name: Chiron Diagnostics ACS:180 Folate Assay

Indications for Use:

For the quantitative determination of folate in serum or EDTA plasma and red blood cells using the Folate BA (Biotin Avidin) assay on the Chiron Diagnostics ACS:180® Automated Chemiluminescence Systems.

Jean Cooper

(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K991582

(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) (Optional Format 1-2-96)