K970877

SEP 22 1997

# 510 (k) Summary
# Safety and Effectiveness

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

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|---|---|
| **Name:**<br>**Address:** | Diagnostic Products Corporation<br>5700 West 96th Street<br>Los Angeles, California 90045 |
| **Telephone Number:** | (213) 776-0180 |
| **Contact Person:** | Edward M. Levine, Ph.D. |
| **Date of Preparation:** | March 7, 1997 |
| **Device Name:**<br>**Trade:**<br>**Catalog Number:**<br>**Common:** | <br>IMMULITE® CEA<br>LKCE1 (100 tests); LKCE5 (500 tests)<br>Reagent system for the determination of carcinoembryonic antigen in human serum. |
| **Classification:** | Class II device (866.3780) |
| **Manufacturer:** | Diagnostic Products Corporation<br>5700 West 96th Street<br>Los Angeles, California 90045 |
| **Establishment Registration #:** | DPC's Registration # is 2017183 |
| **Substantially Equivalent Predicate Device:** | Abbott Laboratories' IMx® CEA |
| **Description of Device:** | IMMULITE CEA is a clinical device for use with the IMMULITE Automated Immunoassay Analyzer. |
| **Intended Use of the Device:** | IMMULITE CEA is designed for the quantitative detection of carcinoembryonic antigen in human serum. It is intended strictly for *in vitro* diagnostic use as an aid in the management of cancer patients and in the assessment of prognosis. |

## Summary and Explanation of the Test:

Carcinoembryonic antigen (CEA) comprises a heterogeneous family of glycoproteins ranging in weight from 175,000 to 200,000 daltons due to varying carbohydrate and amino acid content. Its biological function is not well defined, but it may play a role in intercellular recognition, regulation of the immune response, and metastasis of colorectal cancer. The name derives from the previous belief that CEA occurred only in gastrointestinal carcinomas and the fetal digestive tract. Elevated levels have since been detected in a number of malignant and nonmalignant conditions of the gastrointestinal tract and other sites. These conditions include various hepatic diseases; inflammatory lesions, particularly of the gastrointestinal tract; infections; trauma; infarction; collagen vascular disease; renal impairment; and smoking (current and past). CEA also occurs at low levels in normal colon and other tissues. Serum values in healthy adults are generally less than 5 ng/mL.[1] Though serum values exceeding five times the normal range usually indicate malignancy, values seen in malignant and nonmalignant conditions can overlap considerably, ruling out the use of CEA as a screen for malignancy. The value of CEA measurement lies, instead, in patient prognosis, status assessment, and monitoring.

Until 1980, the only assay method for CEA used in the United States was a radioimmunoassay requiring extraction. Since then, several other nonextraction RIAs and sandwich-type EIAs have been developed for use on serum and plasma samples.

CEA levels at diagnosis of colorectal carcinoma (CRC) correlate with prognosis. Elevated preoperative serum CEA predicts increased risk of recurrence or hepatic metastases. The site of the primary cancer may influence interpretation of elevated CEA: in colon carcinomas, high CEA levels indicate a poor prognosis, but not necessarily so in rectal carcinomas. In addition, monitoring levels during chemotherapy before surgery can be informative, and failure of CEA to fall during preoperative radiotherapy usually indicates the presence of a tumor outside the field of radiation and a poorer prognosis. Preoperative elevated CEA has also been observed to correlate inversely with estimated mean time to recurrence, and to correlate directly with degree of tumor stage, thickness, and differentiation in CRC patients at diagnosis. CEA is not always elevated, however, in sera of those with poorly differentiated CRCs, which produce less CEA but which are more aggressive than moderately or well-differentiated carcinomas. Rising CEA is deemed the most accurate indicator of recurrence in CRC. Levels decrease to normal in nearly all patients after complete resection of CRCs, usually within 4 to 6 weeks after surgery. Failure to decline after surgery may suggest incomplete resection, and increasing levels can precede recurrent CRCs an average of 4 to 6 months before they are clinically evident in about two-thirds of cases. Rising CEA levels have also been used to assist in selecting candidates for second-look surgery, in conjunction with antibody imaging using radiolabeled antibodies against CEA to provide information on tumor location. Several studies have suggested a correlation between the rate of rise in CEA and the presence or probability of hepatic metastases; more rapid rises are seen with hepatic metastases than with localized recurrences and resectable localized tumors. In some cases, it has been CEA that signaled the asymptomatic recurrences.

**Summary and Explanation of the Device:**

DPC's IMMULITE CEA is an in vitro diagnostic medical device for use with DPC's IMMULITE Automated Immunoassay Analyzer, a random access instrument which performs chemiluminescent immunoassays. The assay is designed for the quantitative measurement of carcinoembryonic antigen (CEA) in serum and is intended as an aid in the management of patients with cancer and in the assessment of prognosis. The IMMULITE CEA assay is a solid-phase, two-site sequential chemiluminescent immunometric assay. The solid phase consists of a polystyrene bead (coated with a monoclonal antibody specific for CEA) which is enclosed within an IMMULITE Test Unit (LCE1) which acts as a reaction vessel. The patient serum sample (or CEA Adjustors, LCEL and LCEH) and reagent (LCEA, buffer/serum matrix, with preservative) are incubated for approximately 30 minutes at 37°C in the Test Unit. With intermittent agitation, CEA in the sample becomes bound to the surface of the bead. Unbound serum is then removed by a centrifugal wash. A second reagent (LCEB, an alkaline phosphatase-labeled anti-ligand) is introduced and the Test Unit is incubated for an additional 30 minutes. Unbound conjugate is removed by a centrifugal wash, after which a chemiluminescent substrate (LSUB, a phosphate ester of adamantyl dioxetane) is added and the Test Unit is incubated for a further 10 minutes. The substrate undergoes hydrolysis in the presence of alkaline phosphatase to yield an unstable intermediate. The continuous production of this intermediate results in the sustained emission of light. The bound complex (and thus also the photon output as measured by the luminometer) is proportional to the concentration of CEA in the sample. The concentration of CEA in the patient sample is obtained using a stored master calibration curve within the IMMULITE analyzer. The IMMULITE CEA assay has a calibration range up to 550 nanograms of CEA per milliliter.

**Performance Equivalence - Technology Comparison:**

Diagnostic Products Corporation (DPC) asserts that **IMMULITE® CEA** is substantially equivalent to the **IMx®** CEA kit marketed by Abbott Laboratories *(Abbott Park, IL)*.

Each product is designed for the quantitative measurement of carcinoembryonic antigen (CEA) in serum and is intended as an aid in the management of patients with cancer and in the assessment of prognosis.

**IMMULITE® CEA** is a chemiluminescent enzyme immunoassay and **IMx® CEA** is a microparticle enzyme immunoassay (MEIA). The technology in DPC's IMMULITE CEA is identical to technology used in previously cleared and commercially marketed IMMULITE® products.

In the IMx CEA assay, the patient sample and Anti-CEA coated microparticles are added to the incubation well of a reaction cell. CEA in the specimen binds to the anti-CEA coated microparticles forming an antibody-antigen complex. An aliquot of the antigen-antibody complex is transferred to the glass fiber matrix. The microparticles bind irreversibly to the glass fiber matrix. The matrix is washed to remove unbound materials. The anti-CEA/alkaline phosphatase conjugate is dispensed onto the matrix and binds to the antigen-antibody complex. Finally, the matrix is washed to remove unbound materials, and the substrate, 4-Methylumbelliferyl Phosphate, is added to the matrix, and the fluorescent product is measured by the optical assembly.

**Performance Equivalence - Method Comparison:**

The clinical performance of the IMMULITE CEA procedure was compared to the Abbott IMx® CEA. Linear regression analysis of the 374 specimens that were within the calibration range of both the IMMULITE and IMx® assays yielded:

$$\text{IMMULITE}^{®} = 1.19 * \text{IMx}^{®} - 0.67 \text{ ng/mL}$$

with a correlation coefficient (r) of 0.987.

**Conclusion:**

The conclusions drawn from the clinical and nonclinical studies demonstrate that the device is safe, effective, and performs as well as, or better, than the current legally marketed device.

Edward M. Levine 3/7/97

*Edward M. Levine, Ph.D.* *Date*
*Director of Clinical Affairs*

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

SEP 22 1997

Edward M. Levine, Ph.D.
Director of Clinical Affairs
Diagnostic Products Corporation
5700 West 96th Street
Los Angeles, California 90045

Re: K970877
Trade Name: IMMULITE® CEA
Regulatory Class: II
Product Code: DHX
Dated: July 2, 1997
Received: July 3, 1997

Dear Dr. Levine:

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): K970877

Device Name: **IMMULITE CEA**

Indications For Use:

**DPC's IMMULITE CEA is intended for use with the IMMULITE Automated Immunoassay Analyzer. The IMMULITE CEA is a solid-phase, chemiluminescent enzyme immunoassay designed for the quantitative detection of carcinoembryonic antigen in human serum. It is intended strictly for *in vitro* diagnostic use as an aid in the management of cancer patients and in the assessment of prognosis.**

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

Concurrence of CDRH, Office of Device Evaluation (ODE)

(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K970877

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