

IMMEDIATE RESPONSE DIAGNOSTICS

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Food and Drug Administration
Center for Devices and Radiological Health
Document Mail Center, ODE (HFZ-401)
9200 Corporate Boulevard
Rockville, MD 20850

Subject: Request for Evaluation of Automatic Class III Designation for the Triage® B-Type Natriuretic Peptide (BNP) Test (K003475)

To Whom it May Concern,

In response to the Not Substantially Equivalent letter dated November 13, 2000, Biosite Diagnostics, Incorporated would like to request that FDA make a risk-based classification of the Triage® B-Type Natriuretic Peptide (BNP) Test (K003475), in accordance with Section 207 of the Food and Drug Administration Modernization Act of 1997. We suggest that the Triage® BNP Test be re-classified as a Class II device.

The Triage® B-Type Natriuretic Peptide (BNP) Test is intended for use as an aid in the diagnosis of congestive heart failure (CHF). The BNP test is a non-invasive, low-risk test that measures circulating levels of BNP, which are elevated in individuals with both symptomatic and asymptomatic CHF. According to statistics published by the American Heart Association, in the United States, approximately 4.6 million people suffer from CHF, with 550,000 new cases diagnosed annually. There is a significant mortality rate associated with the disease, as it accounts for 260,000 deaths each year. CHF also ranks among the costliest of all the cardiovascular diseases. In 1996, \$3.6 billion was paid to Medicare beneficiaries for the disease, according to the Health Care Financing Administration.

Currently, physicians most frequently diagnose CHF by interpreting clinical signs and symptoms and echocardiography data to identify heart dysfunction. Clinical signs and symptoms of CHF, including dyspnea and pedal edema, are not specific for CHF, making the differential diagnosis of CHF from non-cardiac disorders such as chronic obstructive pulmonary disease (COPD) difficult. Echocardiography is an expensive non-invasive procedure that allows physicians to identify individuals with systolic heart dysfunction, but it is not sensitive to diastolic dysfunction, which accounts for approximately 1/3 of CHF cases. Data from clinical studies, as presented in K003475 have demonstrated that the Triage® BNP Test has excellent discriminatory ability for individuals with or without CHF. A receiver operating characteristic (ROC) curve for the BNP test that included individuals with and without CHF yielded an area under the curve of 0.944±0.007, indicating that the test has an excellent ability to distinguish individuals with CHF from those without CHF. The Triage® BNP Test demonstrated an overall sensitivity of 82.4% and a specificity of 95.6% when using a cutoff of 100 pg/ml to distinguish these groups. Furthermore, the data indicate that elevations in BNP concentration are not associated with non-specific and potentially co-morbid diseases including COPD, renal insufficiency, hypertension,

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and diabetes, and there were no indications of changes in the BNP concentration associated with racial differences in individuals without CHF. Finally, BNP concentrations were found to be significantly elevated in individuals with CHF that had no evidence of systolic dysfunction by echocardiography, indicating that the Triage[®] BNP Test has the ability to aid physicians in the identification of patients whose cause of CHF is diastolic heart dysfunction. The ROC curve for distinguishing individuals with diastolic heart failure from individuals without CHF yielded an area under the curve of 0.894 ± 0.018 , indicating that the BNP test has excellent discriminatory ability in these two groups.

The Triage[®] BNP Test itself is a low-risk *in vitro* diagnostic product that measures the BNP concentration in a patient blood sample in approximately 15 minutes. Because BNP is a sensitive and specific marker of CHF and the Triage[®] BNP Test has a rapid turn-around time, the test will greatly benefit patients by allowing physicians to make a diagnostic decision for CHF earlier. This will result in earlier treatment for individuals with CHF and lower health care costs for individuals without CHF because these individuals may not be candidates for expensive diagnostic procedures. Furthermore, the Triage[®] BNP Test will not be used as a stand-alone test for the diagnosis of CHF, but rather as an aid in the diagnosis of CHF used in conjunction with other methods that are currently available to physicians, including the evaluation of clinical signs and symptoms and echocardiography.

Based on the data presented in K003475 and the rationale described herein, Biosite Diagnostics, Incorporated suggests that the Triage[®] BNP Test be re-classified as a Class II device and be subject to 510(k) requirements.

Sincerely,



Jeffrey R. Dahlen, Ph.D.
Principal Scientist, Clinical & Regulatory Affairs
Biosite Diagnostics, Incorporated