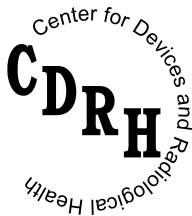


# **Class II Special Control Guidance Document for B-Type Natriuretic Peptide Premarket Notifications; Final Guidance for Industry and FDA Reviewers**

**Document issued on: November 30, 2000**



**U.S. Department of Health and Human Services  
Food and Drug Administration  
Center for Devices and Radiological Health**

**Clinical Chemistry and Toxicology Branch  
Division of Clinical Laboratory Devices  
Office of Device Evaluation**

## **Preface**

### **Public Comment**

Comments and suggestions may be submitted at any time for Agency consideration to Dockets Management Branch, Division of Management Systems and Policy, Office of Human Resources and Management Services, Food and Drug Administration, 5630 Fishers Lane, Room 1061, (HFA-305), Rockville, MD, 20852. When submitting comments, please refer to the exact title of this guidance document. Comments may not be acted upon by the Agency until the document is next revised or updated.

For questions regarding the use or interpretation of this guidance contact Dr. Jean Cooper, (301) 594-1243.

### **Additional Copies**

Additional copies are available from the Internet on the CDRH home page: <http://www.fda.gov/cdrh> or CDRH Facts on Demand at 1-800-899-0381 or 301-827-0111 from a touch-tone telephone. Press 1 to enter the system and enter the document number 1072 followed by the pound sign (#). Follow the remaining voice prompts to complete your request.

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*This document is intended to provide guidance. It represents the Agency's current thinking on this topic. It does not create nor confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statute, regulations, or both.*

## **Background**

On November 20, 2000, FDA classified B-Type Natriuretic Peptide *in vitro* diagnostic devices from Class III designation to Class II.

This guidance document describes a means by which B-Type Natriuretic Peptide (BNP) devices may comply with the requirements of class II special controls. Designation of this guidance document as a special control means that manufacturers of B-Type Natriuretic Peptide devices, who follow the recommendations listed in this document before introducing their device into commercial distribution in the United States, will be able to market their device after they have submitted a premarket notification submission, referred to as a 510(k), and received a finding of “substantial equivalence” for their device. Manufacturers should comply with either the recommendations of this guidance or some alternate means that provide equivalent assurance of safety and effectiveness.

## **The Least Burdensome Approach**

The issues identified in this guidance document represent those that we believe need to be addressed before your device can be approved/cleared for marketing. In developing the guidance, we carefully considered the relevant statutory criteria for Agency decision-making. We also considered the burden that may be incurred in your attempt to comply with the guidance and address the issues we have identified. We believe that we have considered the least burdensome

approach to resolving the issues presented in the guidance document. If, however, you believe that information is being requested that is not relevant to the regulatory decision for your pending application or that there is a less burdensome way to address the issues, you should follow the procedures outlined in the “A Suggested Approach to Resolving Least Burdensome Issues” document. It is available on our Center web page at:  
<http://www.fda.gov/cdrh/modact/leastburdensome.html>

## **Scope**

FDA identifies this generic type of device as a clinical chemistry device under 21 CFR §862.1117, product code NBC. This generic type of device, a B-Type Natriuretic Peptide device is used as an aid in the diagnosis of patients with congestive heart failure.

## **Risks to Health**

FDA has identified two risks to health associated with this type of device, a falsely low BNP and a falsely elevated BNP. A falsely low BNP could potentially delay diagnosis and treatment of congestive heart failure (CHF), but this risk is generally most applicable to asymptomatic patients. These patients would eventually become symptomatic due to progression of their disease, at which point further testing and treatment would be initiated. A falsely elevated BNP could result in unnecessary additional testing, e.g. a non-invasive echocardiogram, in a patient without CHF. This possibility can be decreased by ruling out conditions known to be associated with an increased BNP level. The risks to health are minimized by premarket evaluation of a statistically valid, age-matched control clinical study of the population targeted in the intended use and by labeling describing the sensitivity, specificity, the area under the receiver operator characteristics (ROC) curve, and confidence intervals obtained when data from these studies are analyzed.

## **Special Controls Guidance**

FDA believes the following controls, when combined with the general controls of the Food Drug and Cosmetic Act, will provide reasonable assurance of the safety and effectiveness of this type of device: labeling, design controls, and clinical information.

1. The sale, distribution, and use of this device are restricted to prescription use in accordance with 21 CFR §801.109.
2. Labeling in accordance with 21 CFR §809.10 (b). In addition, labeling should include:

- appropriate literature citations
  - an intended use statement with test methodology and specimen type
  - an adequate description of the New York Heart Association (NYHA) classification in the interpretation of results and reference intervals
  - a summary of results from the clinical studies
  - the descriptive statistics: sensitivity, specificity, the area under the ROC curve, and confidence intervals
  - descriptive statistics for different subgroups including healthy, non-CHF with other diseases, and CHF population
3. Clinical study information in the submission should include:
- statistically valid age matched controls
  - NYHA classification
  - statistically valid sample size for every subgroup by race and gender
4. Analytical/Laboratory performance studies should include:
- expected values
  - estimates of precision
  - assay specificity, cross reactivity, interfering substances
  - linearity/ recovery
  - method and reagent description
  - description of the standardization method of the calibrators
  - kit stability information

## **Premarket Notification**

FDA has determined that premarket notification is necessary to provide reasonable assurance of the safety and effectiveness of this generic type of device, and therefore, the device type is not exempt from the premarket notification requirements. Thus, persons who intend to market a device of this type need to submit a premarket notification to FDA and receive agency clearance prior to marketing the device.