



Banyan Biomarkers, Inc.  
Steven Richieri  
President  
16470 West Bernardo Drive  
Suite 100  
San Diego, California 92127

February 14, 2018

Re: DEN170045  
Trade/Device Name: Banyan BTI  
Regulation Number: 21 CFR 866.5830  
Regulation Name: Brain trauma assessment test  
Regulatory Class: Class II  
Product Code: QAT  
Dated: August 24, 2017  
Received: August 28, 2017

Dear Steven Richieri:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your De Novo request for classification of the Banyan BTI, a prescription device with the following indications for use:

The Banyan BTI is an *in vitro* diagnostic chemiluminescent enzyme-linked immunosorbent assay (ELISA). The assay provides a semi-quantitative measurement of the concentrations of ubiquitin C-terminal hydrolase-L1 (UCH-L1) and glial fibrillary acidic protein (GFAP) in human serum, and is used with the Synergy 2 Multi-mode Reader.

The assay results obtained from serum collected within 12 hours of suspected head injury are used, along with other available clinical information, to aid in the evaluation of patients 18 years of age and older with suspected traumatic brain injury (Glasgow Coma Scale score 13-15). A negative assay result is associated with the absence of acute intracranial lesions visualized on a head CT (computed tomography) scan.

The Banyan BTI is for prescription use only.

FDA concludes that this device should be classified into Class II. This order, therefore, classifies the Banyan BTI, and substantially equivalent devices of this generic type, into Class II under the generic name “Brain trauma assessment test.”

FDA identifies this generic type of device as: **Brain trauma assessment test.**

A brain trauma assessment test is a device that consists of reagents used to detect and measure brain injury biomarkers in human specimens. The measurements aid in the evaluation of patients with suspected mild traumatic brain injury in conjunction with other clinical information to assist in determining the need for head imaging per current standard of care.

Section 513(f)(2) of the Food, Drug and Cosmetic Act (the FD&C Act) was amended by section 607 of the Food and Drug Administration Safety and Innovation Act (FDASIA) on July 9, 2012. This new law provides two options for De Novo classification. First, any person who receives a "not substantially equivalent" (NSE) determination in response to a 510(k) for a device that has not been previously classified under the Act may, within 30 days of receiving notice of the NSE determination, request FDA to make a risk-based classification of the device under section 513(a)(1) of the Act. Alternatively, any person who determines that there is no legally marketed device upon which to base a determination of substantial equivalence may request FDA to make a risk-based classification of the device under section 513(a)(1) of the Act without first submitting a 510(k). FDA shall, within 120 days of receiving such a request, classify the device. This classification shall be the initial classification of the device. Within 30 days after the issuance of an order classifying the device, FDA must publish a notice in the Federal Register classifying the device type.

On August 28, 2017, FDA received your De Novo requesting classification of the Banyan BTI. The request was submitted under section 513(f)(2) of the FD&C Act. In order to classify the Banyan BTI into class I or II, it is necessary that the proposed class have sufficient regulatory controls to provide reasonable assurance of the safety and effectiveness of the device for its intended use. After review of the information submitted in the De Novo request, FDA has determined that, for the previously stated indications for use, the Banyan BTI can be classified in class II with the establishment of special controls for class II. FDA believes that class II (special) controls provide reasonable assurance of the safety and effectiveness of the device type. The identified risks and mitigation measures associated with the device type are summarized in the following table:

Identified Risks to Health	Identified Mitigations
Inaccurate test results that provide false positive or false negative results	General controls and special control (1)
Failure to correctly interpret test results can lead to false positive or false negative results	General controls and special control (2)

In combination with the general controls of the FD&C Act, a Brain trauma assessment test is subject to the following special controls:

- (1) The 21 CFR 809.10(b) compliant labeling must include detailed descriptions of and results from performance testing conducted to evaluate precision, accuracy, linearity, analytical sensitivity, interference, and cross-reactivity. This information must include the following:
  - (i) Performance testing of device precision must, at minimum, use one unmodified clinical specimen from the intended use population with concentration of the brain injury biomarker(s) near the medical decision point. Contrived specimens that have been generated from pooling of multiple samples or spiking of purified analyte to cover the measuring range may be used, but the contrived samples must be prepared to mimic clinical specimens as closely as possible. This testing must evaluate repeatability and reproducibility using a protocol from an FDA-recognized standard.
  - (ii) Device performance data must be demonstrated through a clinical study and must include the following:
    - (a) Data demonstrating clinical validity including the clinical sensitivity and specificity, and positive and negative predictive value of the test in the intended use population of patients with suspected mild traumatic brain injury (i.e., Glasgow Coma Score (GCS) of 13–15), or equivalent standard of care for determination of severity of Traumatic Brain Injury (TBI).
    - (b) Study must be performed using the operators and in settings that are representative of the types of operators and settings for which the device is intended to be used.
    - (c) All eligible subjects must meet the well-defined study inclusion and exclusion criteria that define the intended use population. The prevalence of diseased or injured subjects in the study population must reflect the prevalence of the device's intended use population, or alternatively, statistical measures must be used to account for any bias due to enrichment of subpopulations of the intended use population.
    - (d) All eligible subjects must have undergone a head CT scan or other appropriate clinical diagnostic standard used to determine the presence of an intracranial lesion as part of standard of care and must also be evaluated by the subject device. All clinical diagnostic standards used in the clinical study must follow standard clinical practice in the U.S.
    - (e) Relevant demographic variables and baseline characteristics including medical history and neurological history. In addition, head injury characteristics, neurological assessments, and physical evidence of trauma must be provided for each subject. This information includes but is not limited to the following: time since head injury, time from head injury to CT scan, time from head injury to blood draw, GCS score or equivalent, experience of loss of consciousness, presence of confusion, episodes of vomiting, post-traumatic amnesia characteristics, presence of post traumatic seizures, drug or alcohol intoxication, mechanism of injury, acute intracranial lesion type, neurosurgical lesion, and cranial fracture.
    - (f) Each CT scan or other imaging result must be independently evaluated in a blinded manner by at least two board-certified radiologists to determine whether it is positive or negative as defined by the presence or absence of acute intracranial lesions. This independent review

must be conducted without access to test results of the device. Prior to conducting the review, the criteria and procedures to be followed for scoring the images must be established, including the mechanism for determining consensus.

- (g) All the clinical samples must be tested with the subject device blinded to the TBI-status and the neurological-lesion-status of the subject.
  - (h) Details on how missing values in data are handled must be provided.
  - (i) For banked clinical samples, details on storage conditions and storage period must be provided. In addition, a specimen stability study must be conducted for the duration of storage to demonstrate integrity of archived clinical samples. The samples evaluated in the assay test development must not be used to establish the clinical validity of the assays.
- (iii) Performance testing of device analytical specificity must include the most commonly reported concomitant medications present in specimens from the intended use population. Additionally, potential cross-reacting endogenous analytes must be evaluated at the highest concentration reported in specimens from the intended use population.
- (iv) Expected/reference values generated by testing a statistically appropriate number of samples from apparently healthy normal individuals.
- (2) The 21 CFR 809.10(a) and 809.10(b) compliant labeling must include the following limitations:
- (i) A limiting statement that this device is not intended to be used a stand-alone device but as an adjunct to other clinical information to aid in the evaluation of patients who are being considered for standard of care neuroimaging.
  - (ii) A limiting statement that reads “A negative result is generally associated with the absence of acute intracranial lesions. An appropriate neuroimaging method is required for diagnosis of acute intracranial lesions.”
  - (iii) As applicable, a limiting statement that reads “This device is for use by laboratory professionals in a clinical laboratory setting.”

Section 510(m) of the FD&C Act provides that FDA may exempt a class II device from the premarket notification requirements under section 510(k) of the FD&C Act, if FDA determines that premarket notification is not necessary to provide reasonable assurance of the safety and effectiveness of the device type. FDA has determined premarket notification is necessary to provide reasonable assurance of the safety and effectiveness of the device type and, therefore, the device is not exempt from the premarket notification requirements of the FD&C Act. Thus, persons who intend to market this device type must submit a premarket notification containing information on the Brain trauma assessment test they intend to market prior to marketing the device.

Please be advised that FDA's decision to grant this De Novo request does not mean that FDA has made a determination that your device complies with other requirements of the FD&C Act or any Federal statutes

and regulations administered by other Federal agencies. You must comply with all the FD & C Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the FD&C Act); 21 CFR 1000-1050.

A notice announcing this classification order will be published in the Federal Register. A copy of this order and supporting documentation are on file in the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Room 1061, Rockville, MD 20852 and are available for inspection between 9 a.m. and 4 p.m., Monday through Friday.

As a result of this order, you may immediately market your device as described in the De Novo request, subject to the general control provisions of the FD&C Act and the special controls identified in this order.

For comprehensive regulatory information about medical devices and radiation-emitting products, please see Device Advice (<https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/>) and CDRH Learn (<http://www.fda.gov/Training/CDRHLearn>). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (<http://www.fda.gov/DICE>) for more information or contact DICE by email ([DICE@fda.hhs.gov](mailto:DICE@fda.hhs.gov)) or phone (1-800-638-2041 or 301-796-7100).

If you have any questions concerning the contents of the letter, please contact Sic Chan at 301-796-7015.

Sincerely,

For,  
Lea Carrington  
Director  
Division of Immunology and Hematology Devices  
Office of In Vitro Diagnostics and Radiological Health  
Center for Devices and Radiological Health