



May 4, 2022

Fujirebio Diagnostics, Inc.
Stacey Dolan
Senior Manager Regulatory Affairs
201 Great Valley Parkway
Malvern, Pennsylvania 19355

Re: DEN200072

Trade/Device Name: Lumipulse **G** β -Amyloid Ratio (1-42/1-40)
Regulation Number: 21 CFR 866.5840
Regulation Name: Alzheimer's disease pathology assessment test
Regulatory Class: Class II
Product Code: QSE
Dated: November 19, 2020
Received: November 20, 2020

Dear Stacey Dolan:

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 Lumipulse **G** β -Amyloid Ratio (1-42/1-40), a prescription device with the following indications for use:

The Lumipulse **G** β -Amyloid Ratio (1-42/1-40) is an *in vitro* cerebral spinal fluid (CSF) test that combines the results of Lumipulse **G** β -Amyloid 1-42 and Lumipulse **G** β -Amyloid 1-40 assays into a ratio of β -amyloid₁₋₄₂ to β -amyloid₁₋₄₀ concentrations using the LUMIPULSE **G**1200 System.

The Lumipulse **G** β -Amyloid Ratio (1-42/1-40) is intended to be used in adult patients, aged 55 years and older, presenting with cognitive impairment who are being evaluated for Alzheimer's disease (AD) and other causes of cognitive decline.

A test result ≥ 0.073 is a negative result which is consistent with a negative amyloid positron emission tomography (PET) scan result. A negative result reduces the likelihood that a patient's cognitive impairment is due to AD.

A test result ≤ 0.058 is a positive result which is consistent with a positive amyloid PET scan result. A positive result does not establish a diagnosis of AD or other cognitive disorder.

A test result between 0.059 and 0.072 is considered as a likely positive result as it is more likely consistent with a positive amyloid PET scan result. A likely positive result does not establish a

diagnosis of AD or other cognitive disorders and has increased uncertainty in regard to amyloid PET positivity.

The Lumipulse $G\beta$ -Amyloid Ratio (1-42/1-40) results must be interpreted in conjunction with other patient clinical information.

This test is not intended as a screening or stand-alone diagnostic test.

FDA concludes that this device should be classified into Class II. This order, therefore, classifies the Lumipulse $G\beta$ -Amyloid Ratio (1-42/1-40), and substantially equivalent devices of this generic type, into Class II under the generic name Alzheimer's disease pathology assessment test.

FDA identifies this generic type of device as:

Alzheimer's disease pathology assessment test. An Alzheimer's disease (AD) pathology assessment test is an *in vitro* diagnostic device intended to measure one or more analytes in human specimens to assess whether a patient presenting with cognitive impairment and being evaluated for AD and other causes of cognitive decline would test positive or negative for amyloid plaques or neurofibrillary tangles at the time of testing, as measured by FDA-approved positron emission tomography (PET) imaging agents. The device is intended to assess the underlying AD-associated pathology in conjunction with clinical assessment to increase diagnostic certainty.

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 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 request FDA to make a risk-based classification of the device under section 513(a)(1) of the Act. On December 13, 2016, the 21st Century Cures Act removed a requirement that a De Novo request be submitted within 30 days of receiving an NSE determination. 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 announcing the classification.

On November 20, 2020, FDA received your De Novo requesting classification of the Lumipulse $G\beta$ -Amyloid Ratio (1-42/1-40). The request was submitted under section 513(f)(2) of the FD&C Act. In order to classify the Lumipulse $G\beta$ -Amyloid Ratio (1-42/1-40) 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 Lumipulse $G\beta$ -Amyloid Ratio (1-42/1-40) 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	Mitigation Measures
Failure to correctly interpret test results can lead to false positive results (leading to workup and anxiety regarding a serious diagnosis that is incorrect) or false negative results (leading to delays in getting treatment and delays planning early in the course of this progressive disease)	Special controls (1) and (2)
Incorrect test results that provide false positive results (leading to workup and anxiety regarding a serious diagnosis that is incorrect) or false negative results (leading to delays in getting treatment and delays planning early in the course of this progressive disease)	Special controls (1) and (2)

In combination with the general controls of the FD&C Act, the Alzheimer's disease pathology assessment test is subject to the following special controls:

- (1) Design verification and validation must include:
 - (i) Detailed documentation of studies demonstrating analytical performance, including precision, linearity, assay interference, cross-reactivity, detection capability, specimen and reagent stability, and hook effect, as applicable. For devices measuring multiple analytes, the detailed documentation must include studies demonstrating the analytical performance of the device in regard to each individual analyte, including precision, linearity, assay interference, cross-reactivity, detection capability, specimen and reagent stability, and hook effect, as applicable.
 - (ii) Detailed documentation of studies demonstrating clinical performance in the intended use patient population. All eligible subjects must meet the appropriate study inclusion and exclusion criteria that define the intended use population. Relevant demographic and patient characteristics must be documented, including the time from specimen collection for testing with the subject device to PET imaging acquisition; patient cognitive, neurological, and psychiatric assessments; Apolipoprotein E (APOE) carrier status; and patient education level. All specimens must be tested with the users of the subject device blinded to the disease status and PET scan results of the subject from whom the specimen was obtained. Each PET scan must use an FDA-approved PET tracer and must be independently evaluated in a blinded manner and interpreted according to the FDA-required labeling for the PET tracer. For banked specimens, details on storage conditions and storage period must be documented. In addition, documentation must include evidence to support the stability of the archived specimens for the duration of storage.
 - (iii) Detailed documentation of studies, which are performed using specimens from persons established to be cognitively normal, that establish the upper and lower limits of reference intervals for the output provided by the device. For banked specimens, the detailed documentation must include details on storage conditions and storage period. In addition, the detailed documentation must include evidence to support the stability of the archived specimens for the duration of storage.
- (2) The labeling required under 21 CFR 809.10(b) must include:

- (i) An intended use that provides a description of the measurand(s) (i.e., AD pathology biomarker(s)) the device measures in the specified human specimens, the results provided to the user (including information to facilitate clinical interpretation of all device outputs), the clinical indications appropriate for test use, and the specific population(s) for which the device is intended.
- (ii) Limiting statements indicating that:
 - (A) This device is not intended to be used as a stand-alone test and the test results must be interpreted in conjunction with other diagnostic tools and clinical information.
 - (B) The safety and effectiveness of the device have not been established for predicting development of dementia or other neurologic conditions or for monitoring the effect of any therapeutic product.
 - (C) A positive result is associated with the presence of amyloid plaques or neurofibrillary tangles in the brain but does not establish a diagnosis of AD as would be established by neuropathological examination.
- (iii) A detailed summary of the performance testing, including results, required under paragraph (1).

Although this letter refers to your product as a device, please be aware that some granted products may instead be combination products. If you have questions on whether your product is a combination product, contact CDRHProductJurisdiction@fda.hhs.gov.

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 Alzheimer's disease pathology 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) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see <https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products>); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; 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/medical-devices/device-advice-comprehensive-regulatory-assistance>) and CDRH Learn (<https://www.fda.gov/training-and-continuing-education/cdrh-learn>). 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 (<https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice>) for more information or contact DICE by email (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 Woosung (David) Cho at 301-796-5998.

Sincerely,

Lea Carrington
Director
Division of Immunology and Hematology Devices
OHT7: Office of In Vitro Diagnostics
and Radiological Health
Office of Product Evaluation and Quality
Center for Devices and Radiological Health