DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center- W066-G609
Silver Spring, MD 20993-0002

Abbott Molecular, Inc.
C/O Nancy Bengtson, Ph.D.
1300 E. Touhy Avenue
Des Plaines, IL 60018

July 29, 2013

Re: K123951- Order for Granting the Request for De Novo Classification
Vysis EGR1 FISH Probe Kit – SC (Specimen Characterization)
Evaluation of Automatic Class III Designation- *De Novo* Request
Regulation Number: 21 CFR 864.1870
Regulation Name: Early Growth Response 1 (EGR1) Gene Fluorescence In-Situ Hybridization (FISH) Test System For Specimen Characterization
Regulatory Classification: Class II
Product Code: PDO
Dated: April 1, 2013
Received: April 9, 2013

Dear Dr. Bengtson:

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 Vysis EGR1 FISH Probe Kit – SC (Specimen Characterization). The intended use of the Vysis EGR1 FISH Probe Kit – SC (Specimen Characterization) is it detects the LSI EGR1 probe target on chromosome 5q in bone marrow specimens. The Vysis EGR1 FISH Probe Kit – SC assay results characterize bone marrow specimens from patients with acute myeloid leukemia or myelodysplastic syndrome. The assay results are intended to be interpreted by a qualified pathologist or cytogeneticist. The device is not intended for high-risk uses such as selecting therapy, predicting therapeutic response or disease screening. The use of this product for diagnosis, monitoring or risk assessment has not been established. The Vysis EGR1 FISH Probe Kit – SC (Specimen Characterization) device is a prescription device under 21 CFR Part 801.109. FDA concludes that this device, and substantially equivalent devices of this generic type, should be classified into class II. This order, therefore, classifies the Vysis EGR1 FISH Probe Kit – SC (Specimen Characterization) into class II under the generic name, "Early Growth Response 1 (EGR1) Gene Fluorescence In-Situ Hybridization (FISH) Test System For Specimen Characterization."

FDA identifies this generic type of device as follows: Early Growth Response 1 (EGR1)

Gene Fluorescence In-Situ Hybridization (FISH) Test System For Specimen Characterization.

An early growth response 1 (EGR1) gene fluorescence in-situ hybridization (FISH) test system for specimen characterization is a device intended to detect the EGR1 probe target on chromosome 5q in bone marrow specimens from patients with acute myeloid leukemia (AML) or myelodysplastic syndrome (MDS). The assay results are intended to be interpreted only by a qualified pathologist or cytogeneticist. These devices do not include automated systems that directly report results without review and interpretation by a qualified pathologist or cytogeneticist. These devices also do not include any device intended for use to select patient therapy, predict patient response to therapy or to screen for disease as well as any device with a claim for a particular diagnosis, prognosis, monitoring or risk assessment.

Section 513(f)(2) of the FD&C Act provides that any person who submits a premarket notification under section 510(k) for a type of device that has not been previously classified may, within 30 days after receiving an order classifying the device in class III under section 513(f)(l), request FDA to classify the device under the criteria set forth in section 513(a)(1). FDA shall by order classify the device, which shall be the initial classification of the device type. Within 30 days after the issuance of an order classifying the device, FDA must publish a notice in the Federal Register announcing the classification.

In accordance with section 513(f)(1) and 513(i) of the FD&C Act, FDA issued an order on March 20, 2013, finding the Vysis EGR1 FISH Probe Kit – SC (Specimen Characterization) not substantially equivalent to any device within a type that was introduced or delivered for introduction into interstate commerce for commercial distribution before May 28, 1976, or that was subsequently reclassified into class I or class II, which means this device is automatically in class III under section 513(f)(1). On April 9, 2013, FDA filed your de novo request for classification of the Vysis EGR1 FISH Probe Kit – SC (Specimen Characterization) into class II. The petition was submitted under section 513(f)(2) of the FD&C Act. In order to classify the Vysis EGR1 FISH Probe Kit – SC (Specimen Characterization) 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 the Vysis EGR1 FISH Probe Kit – SC (Specimen Characterization) intended for use as follows:

> The Vysis EGR1 FISH Probe Kit – SC (Specimen Characterization) detects the LSI EGR1 probe target on chromosome 5q in bone marrow specimens. The Vysis EGR1 FISH Probe Kit – SC assay results characterize bone marrow specimens from patients with acute myeloid leukemia or myelodysplastic syndrome. The assay results are intended to be interpreted by a qualified pathologist or cytogeneticist. The device is not intended for high-risk uses such as selecting therapy, predicting therapeutic response or disease screening. The use of this product for

diagnosis, monitoring or risk assessment has not been established.

can be classified in class II with the establishment of special controls for this type of device. FDA believes that the class II special controls identified later in this order, along with the applicable general controls, provide reasonable assurance of the safety and effectiveness of the device type.

Table- Potentia1 Risks and Required Mitigations

Identified Potential Risk	**Required Mitigations**
False negative result	1) Premarket notification submissions must also include the following information: i) A detailed description of all probes included in the kit ii) Purpose of each probe iii) Probe molecular specificity iv) Probe specificity v) Probe limits vi) Probe sensitivity vii) Specification of required ancillary reagents, instrumentation and equipment viii) Specification of the specimen collection, processing, storage and slide preparation methods ix) Specification of the assay procedure x) Specification of control elements that are incorporated into the recommended testing procedures xi) Specification of risk mitigation elements: description of all additional procedures, methods, and practices incorporated into the directions for use that mitigate risks associated with testing xii) Specification of the criteria for test result interpretation and reporting xiii) Device analytical sensitivity data xiv) Device analytical specificity data xv) Device reference limit data xvi) Device precision/reproducibility data xvii) Device stability data to include *A)* Real-time Stability

	B) Freeze-Thaw Stability *C)* Transport and Temperature Stability *D)* Post-Hybridization Signal Stability *E)* Photostability of Probe xviii) Documentation that demonstrates the clinical validity of the device. The documentation must include data from clinical studies, a minimum of two peer-reviewed published literature references using the specific device seeking marketing clearance, or both. Documentation for the clinical studies and peer–reviewed published literature references cited must include the following elements: *A)* Documentation that the sponsor's probe was used in the literature reference *B)* Number & type of specimens *C)* Target population studied *D)* Upper reference limit *E)* Range of positive probe results 2) Your 21 CFR 809.10(b)(12) compliant labeling must include a statement summarizing the data identified in subparagraphs (1)(xiii)-(xviii) and a description of the studies supporting the information, including the pre-specified acceptance criteria for these performance studies, justification for the pre-specified acceptance criteria, and whether the pre-specified acceptance criteria were met. 3) Your 809.10 compliant labeling must include: i) A warning that reads "The assay results are intended to be interpreted only by a qualified pathologist or cytogeneticist." ii) A warning that reads "This device is not for high-risk uses such as selecting therapy, predicting therapeutic response or disease screening." iii) A warning that reads "The use of this device for diagnosis, monitoring or risk assessment has not been established."

False Positive Result	1) Premarket notification submissions must also include the following information: i) A detailed description of all probes included in the kit ii) Purpose of each probe iii) Probe molecular specificity iv) Probe specificity v) Probe limits vi) Probe sensitivity vii) Specification of required ancillary reagents, instrumentation and equipment viii) Specification of the specimen collection, processing, storage and slide preparation methods ix) Specification of the assay procedure x) Specification of control elements that are incorporated into the recommended testing procedures xi) Specification of risk mitigation elements: description of all additional procedures, methods, and practices incorporated into the directions for use that mitigate risks associated with testing xii) Specification of the criteria for test result interpretation and reporting xiii) Device analytical sensitivity data xiv) Device analytical specificity data xv) Device reference limit data xvi) Device precision/reproducibility data xvii) Device stability data to include: *A)* Real-time Stability *B)* Freeze-Thaw Stability *C)* Transport and Temperature Stability *D)* Post-Hybridization Signal Stability *E)* Photostability of Probe xviii) Documentation that demonstrates the clinical validity of the device. The documentation must include data from clinical studies, a minimum of two peer-reviewed published literature references using the specific device seeking marketing clearance, or both. Documentation for the clinical studies

	and peer–reviewed published literature references cited must include the following elements: *A)* Documentation that the sponsor's probe was used in the literature reference *B)* Number & type of specimens *C)* Target population studied *D)* Upper reference limit *E)* Range of positive probe results 2) Your 21 CFR 809.10(b)(12) compliant labeling must include a statement summarizing the data identified in subparagraphs (1)(xiii)-(xviii) and a description of the studies supporting the information, including the pre-specified acceptance criteria for these performance studies, justification for the pre-specified acceptance criteria, and whether the pre-specified acceptance criteria were met. 3) Your 809.10 compliant labeling must include: i) A warning that reads "The assay results are intended to be interpreted only by a qualified pathologist or cytogeneticist." ii) A warning that reads "This device is not for high-risk uses such as selecting therapy, predicting therapeutic response or disease screening." iii) A warning that reads "The use of this device for diagnosis, monitoring or risk assessment has not been established."

In addition to the general controls of the FD&C Act, an early growth response 1 (EGR1) gene fluorescence in-situ hybridization (FISH) test system for specimen characterization is subject to the following special controls:

1) Premarket notification submissions must also include the following information:
   i) A detailed description of all probes included in the kit
   ii) Purpose of each probe
   iii) Probe molecular specificity
   iv) Probe specificity
   v) Probe limits
   vi) Probe sensitivity

vii) Specification of required ancillary reagents, instrumentation and equipment
viii) Specification of the specimen collection, processing, storage and slide preparation methods
ix) Specification of the assay procedure
x) Specification of control elements that are incorporated into the recommended testing procedures
xi) Specification of risk mitigation elements: description of all additional procedures, methods, and practices incorporated into the directions for use that mitigate risks associated with testing
xii) Specification of the criteria for test result interpretation and reporting
xiii) Device analytical sensitivity data
xiv) Device analytical specificity data
xv) Device reference limit data
xvi) Device precision/reproducibility data
xvii) Device stability data to include:
A) Real-time Stability
B) Freeze-Thaw Stability
C) Transport and Temperature Stability
D) Post-Hybridization Signal Stability
E) Photostability of Probe
xviii) Documentation that demonstrates the clinical validity of the device. The documentation must include data from clinical studies, a minimum of two peer-reviewed published literature references using the specific device seeking marketing clearance, or both. Documentation for the clinical studies and peer–reviewed published literature references cited must include the following elements:
A) Documentation that the sponsor's probe was used in the literature reference
B) Number & type of specimens
C) Target population studied
D) Upper reference limit
E) Range of positive probe results

2) Your 21 CFR 809.10(b)(12) compliant labeling must include a statement summarizing the data identified in subparagraphs (1)(xiii)-(xviii) and a description of the studies supporting the information, including the pre-specified acceptance criteria for these performance studies, justification for the pre-specified acceptance criteria, and whether the pre-specified acceptance criteria were met.
3) Your 809.10 compliant labeling must include:
i) A warning that reads "The assay results are intended to be interpreted only by a qualified pathologist or cytogeneticist."
ii) A warning that reads "This device is not for high-risk uses such as selecting therapy, predicting therapeutic response or disease screening."
iii) A warning that reads "The use of this device for diagnosis, monitoring or risk assessment has not been established."

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 early growth response 1 (EGR1) gene fluorescence in-situ hybridization (FISH) test system for specimen characterization they intend to market and receive clearance to market from FDA prior to marketing the device.

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 market your device subject to the general control provisions of the FD&C Act and the special controls identified in this order.

If you have any questions concerning this classification order, please contact Shyam Kalavar at 301-796-6807.

Sincerely yours,

Reena Philip -S

for

Maria Chan, Ph.D.
Director
Division of Immunology and Hematology Devices
Office of *In Vitro* Diagnostics and
Radiological Health
Center for Devices and Radiological Health