EVALUATION OF AUTOMATIC CLASS III DESIGNATION FOR VYSIS EGR1 FISH PROBE KIT – SC (SPECIMEN CHARACTERIZATION)

Decision Summary

A. 510(k) Number K123951

B. Purpose of the Submission: Clearance of new assay

C. Measurand: LSI EGR1 probe target on chromosome 5q in bone marrow specimens

D. Type of Test: Flourescence in-situ hybridization (FISH)

E. Applicant: Abbott Molecular Inc.

F. Device Name: Vysis EGR1 FISH Probe Kit - SC (Specimen Characterization)

G. Regulatory Information:

FDA identifies this type of device as:
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.

1. New Regulation Number: 21 CFR 864.1870
2. Classification: Class II (special controls)
3. Product code: PDO
4. Panel: Hematology and Pathology Devices Panel

H. Intended Use:

1. Intended use(s):

   The Vysis EGR1 FISH Probe Kit – SC 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. This 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.

2. Indication(s) for use:

   Same as intended use

3. Special conditions for use statement(s):

   Warnings included in the labeling are as follows:
   - The assay results are intended to be interpreted only by a qualified pathologist or cytogeneticist.
   - The Vysis EGR1 FISH Probe Kit – SC is not 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.
   - Caution: Federal law restricts this device to sale by or on the order of a physician or other practitioner licensed by the law of the State in which he practices, to use or order the use of the device.

4. Special instrument requirements:

   Fluorescence microscope equipped with appropriate excitation and emission filters

I. Device Description:

The Vysis EGR1 FISH Probe Kit – Specimen Characterization uses fluorescence in situ hybridization (FISH) DNA probe technology to detect probe target LSI EGR1 (containing early growth response 1 gene; location chromosome 5q31). The LSI D5S23, D5S721 probe (location chromosome 5p15.2) serves as a control.

The Vysis EGR1 FISH Probe Kit – SC (List No. 04N37-001) consists of the following components which are sufficient to process 20 assays:
1. Vysis LSI EGR1 SpectrumOrange/D5S23, D5S721 Spectrum Green Probes
2. Vysis LSI/WCP Hybridization Buffer
3. DAPI II Counterstain
4. NP-40

5. 20X SSC Salt

Items 2 through 5 above are general purposes reagents.

DNA Probes: Vysis LSI EGR1 SpectrumOrange/ D5S23, D5S721 SpectrumGreen.

a. The SpectrumOrange-labeled LSI EGR1 probe, approximately 209 kb in length (chr5:137654208-137862738; February 2009 Assembly; UCSC Human Genome Browser) is located at 5q31 and contains the complete EGR1 gene.
b. The SpectrumGreen-labeled LSI D5S23, D5S721 probe, approximately 561 kb in length (chr5:9397109-9958407; February 2009 Assembly; UCSC Human Genome Browser) is located at 5p15.2.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   No predicate device exists for this intended use

2. Predicate 510(k) number(s):

   Not applicable

3. Comparison with predicate:

   Not Applicable

K. Standard/Guidance Document Referenced (if applicable):

Not Applicable

L. Test Principle:

Alterations in chromosome 5 are common aberrations in myelodysplastic syndromes (MDS) and acute myeloid leukemia (AML). Chromosome band 5q31 contains the early growth response 1 gene (EGR1). The Vysis locus specific identifier (LSI) EGR1 SpectrumOrange Probe and D5S23, D5S721 SpectrumGreen Probe are components of the Vysis EGR1 FISH Probe Kit, and are used to detect the target EGR1 using FISH DNA probe technology. The results of this assay are used to characterize bone marrow specimens.

Bone marrow cells from AML patients attached to microscope slides using standard cytogenetic procedures are used for this assay. The resulting cellular DNA is denatured to single-stranded form and subsequently allowed to hybridize with the LSI EGR1 and LSI D5S23, D5S721 probes. Following hybridization, the unbound probe is removed by a series of washes, and the nuclei are counterstained with DAPI, a DNA-specific stain that fluoresces blue. Hybridization of the LSI EGR1 and LSI D5S23, D5S721 probes is viewed using a fluorescence microscope equipped with

appropriate excitation and emission filters, allowing visualization of the orange and green fluorescent signals.

The expected signal pattern in a cell with two copies of the EGR1 gene covered by the probes using the Vysis EGR1 FISH Probe Kit is 2 orange and 2 green signals (2R2G). In a cell with the 5q alteration, one orange signal (LSI EGR1) and two green signals (LSI D5S23, D5S721) will be expected. Enumeration of the orange LSI EGR1 and green LSI D5S23, D5S721 signals provide a mechanism for determining absolute copy number of the probe targets and the presence of chromosomal alterations of interest.

M. Performance Characteristics (if/when applicable):

The sponsor provided the following information to support the analytical performance of the device:

1. Analytical performance:

   a. *Precision/Reproducibility:*
   Repeatability and reproducibility of the Vysis EGR1 FISH Probe Kit were tested as shown in the table below:

Study	Study Protocol	Conclusion
Precision: Intra-Day and Inter-Day	• 6 Bone marrow specimens - 2 high positive (HP1 & 2) (69.3%, 49.9% positivity) - 2 low positive (LP1 & 2) (12% positivity) - 2 negative (Neg1 & 2) • 3 test sites • 5 different testing days • 1 lot of probe • Red and green signal patterns of 200 nuclei evaluated by 2 technologists (each technologist evaluated 100 nuclei per panel member) • Pre-specified acceptance criteria: Agreement with the expected result of greater than or equal to 90% for the high positive specimen category for each site and 90% for the negative specimen category across all sites with no more than 3 discordant results occurring at one site.	Acceptance criteria met

Study	Study Protocol	Conclusion
Reproducibility: Inter-Site	• Testing configuration same as above • In addition, 2 replicates of each panel member were tested • Pre-specified acceptance criteria: Same as above	Acceptance criteria met
Lot to Lot Reproducibility	• 6 Bone marrow specimens - 2 high positive (HP1 & 2) (69.3%, 49.9% positivity) - 2 low positive (LP1 & 2) (12% positivity) - 2 negative (Neg1 & 2) • 3 lots of probe • 4 replicates • 1 site • 2 operators per site • Pre-specified acceptance criteria: Same as above	Acceptance criteria met

Between Site Analysis of Variance

Sample Type	N	Mean %[a]	SD[b]
High Positive 1	30	70.0	5.44
High Positive 2	30	47.6	0.74
Low Positive 1	30	18.1	1.03
Low Positive 2	30	14.9	0.00
Negative 1	30	0.7	0.99
Negative 2	30	0.9	1.5

[a] Percentage of cells with 1R2G signal pattern

[b] SD = standard deviation

Within-day/Between-day Analysis of Variance

Sample Type	N	Mean %[a]	Within-Day Component SD[b]	Between-Day Component SD
High Positive 1	30	70.0	3.28	4.01
High Positive 2	30	47.6	5.56	0.00
Low Positive 1	30	18.1	3.00	3.82
Low Positive 2	30	14.9	3.25	1.54
Negative 1	30	0.7	0.71	0.00
Negative 2	30	0.9	0.66	1.42

[a] Percentage of cells with 1R2G signal pattern

[b] SD = standard deviation

Lot-to-Lot Analysis of Variance

Sample Type	N	Mean %[a]	SD[b]
High Positive 1	12	66.2	0.00
High Positive 2	12	47.4	3.04
Low Positive 1	12	12.7	0.00
Low Positive 2	12	12.3	1.12
Negative 1	12	0.0	0.00
Negative 2	12	0.1	0.20

[a] Percentage of cells with 1R2G signal pattern
[b]SD = standard deviation

b. Linearity/assay reportable range:

Not applicable

c. Traceability, Stability, Expected values (controls, calibrators, or methods):

Kit stability
The kit stability was assessed as detailed in the table below:

Study	StudyProtocol	Conclusion
Real-Time Stability	• Attributes evaluated: signal intensity, target background, cross-hybridization, specificity, overall readability • 3 lots of the device • 3 specimens • The Vysis EGRI FISH Probe Kit dating is determined by the component with the shortest expiration dating. • Pre-specified acceptance criteria: Acceptable quality of all attributes for all samples tested	Acceptance criteria met for 12 month stability
In-Use Freeze-Thaw Stability	• A series of 20 freeze-thaw cycles was performed on the probes, hybridization buffer and DAPI II counterstain. • 1 lot of the device • 3 specimens • Attributes evaluated: Same as above • Pre-specified acceptance criteria: Same as above	Acceptance criteria met throughout and at the end of 20 freeze-thaw cycles
Transport and Temperature Extreme	• Device components were removed from -20ºC and cycled for 48 hours on dry ice, 72 hours at 25ºC, 72	Acceptance criteria met

Stability	hours at 40ºC, and -20ºC for 24 hours prior to testing • 1 lot of the device • 3 specimens • Attributes evaluated: Same as above • Pre-specified acceptance criteria: Same as above	
Post-hybridization Signal Stability	• A single slide from each of 3 bone marrow specimens was tested at baseline and then stored at -20ºC ± 10ºC protected from light • The samples were tested at three time points -Day **7,** Day 14, and Day 25 • 1 lot of the device • Attributes evaluated: Same as above • Pre-specified acceptance criteria: Same as above	Acceptance criteria met for Post-hybridization stability of 3 weeks
Probe Photostability	• The device was exposed continuously under white fluorescent light (to mimic standard laboratory conditions) at 15-30ºC for different time lengths (0 hours, 3 hours, 8 hours, 24 hours and 48 hours) • 1 lot of the device • Attributes evaluated: Same as above • Pre-specified acceptance criteria: Same as above	Acceptance criteria met for Photo-stability of 48 hours

Controls:
The Vysis EGR1 FISH Probe Kit also contains the LSI D5S23, D5S721 probe (location chromosome 5p15.2) which serves as a control. Observation of at least 1R signal and 1G signal, assures that the assay conditions are adequate to allow both the orange and green labeled probes to bind properly to their respective targets.

d. Detection limit:

The analytical sensitivity of the Vysis LSI EGRI SpectrumOrange/D5S23, D5S721SpectrumGreen probes was established using interphase nuclei prepared from 25 bone marrow specimens that were either karyotypically normal or 5pl5 and 5q31 deletion-free. The orange and green signal patterns of nuclei for these 25 specimens were evaluated by two technologists. Each

technologist evaluated 100 nuclei per specimen for a total of 200 nuclei per specimen and 5000 scoreable nuclei from normal specimens. The analytical sensitivity was calculated as the percentage of scoreable interphase nuclei with the expected 2 red/2 green signal pattern.

Probe	Total Number of Nuclei Scored	Number of Nuclei With Expected Signal Pattern	Analytical Sensitivity (95% Confidence Interval)
Vysis EGR1/D5S23, D5S721	5000	4979	99.6% (99.4, 99.7)

e. Analytical specificity:

Analytical specificity is defined as the percentage of signals that hybridize to the correct locus and no other location. The analytical specificity of the Vysis LSI EGR1 SpectrumOrange/D5S23, D5S721 SpectrumGreen probes for their respective chromosome target loci was established using metaphase chromosomes prepared from peripheral blood cultures of five karyotypically normal males that were pooled prior to dropping on microscope slides. The hybridization location of each FISH signal on chromosomes of 100 consecutive metaphase nuclei was evaluated by one technologist for a total of 200 target loci.

For each probe and sample, the number of metaphase chromosome FISH signals hybridized to the correct locus and the number of metaphase chromosome FISH signals hybridized to the incorrect locus were enumerated.

The analytical specificity of each probe was calculated as the number of metaphase chromosome FISH signals hybridized to the correct locus divided by the total number of metaphase chromosome FISH signals hybridized and multiplied by 100 to give a percentage. The analytical specificity of the Vysis LSI EGR1 SpectrumOrange/D5S23, D5S721 SpectrumGreen Probes was 100%.

Probe	Target	Total No. of Metaphase Chromosome Hybridized	No. of Metaphase Chromosome Hybridized to Correct Locus	Analytical Specificity (95% Confidence Intervals)
D5S23, D5S721	5p15.2	200	200	100% (98, 100)
EGR1	5q31	200	200	100% (98, 100)

f. Assay cut-off:

Same as reference range (see #5 below)

2. Comparison studies:

   a. Method comparison with predicate device:

   Not applicable

   b. Matrix comparison:

   Not applicable

3. Clinical studies:

   a. Clinical Sensitivity:

   Not applicable

   b. Clinical specificity:

   Not applicable

   c. Other clinical supportive data (when a. and b. are not applicable):

   The sponsor provided three peer-reviewed published papers to support the clinical validity of the device in characterizing bone marrow specimens from patients with AML. All three papers used the Abbott Vysis EGR1 FISH Probe Kit. The information is listed in the table below:

Conditions	Data Source 1 Sun et. al	Data Source 2 Galvan et. al	Data Source 3 Vance et. al
Was the specific device under review in the submission used in the study?	Yes	Yes	Yes
Was the specimen type in the study representative of the claimed specimen type(s)	Yes	Yes	Yes
Target population (disease status)	Known or suspected del(5q) having MDS or AML	MDS, therapy-related MDS (t-MDS) and AML patients	AML
Upper reference limit (percentage and per 200 nuclei)	6% or 12 1R2G patterns per 200 scoreable interphase nuclei	6% or 12 1R2G patterns per 200 scoreable interphase nuclei	6% or 12 1R2G patterns per 200 scoreable interphase nuclei
Total Number of specimens tested for each claimed type	320 bone marrow specimens	28 bone marrow specimens	181 bone marrow specimens*
Number of specimens with a positive probe result [5q- (1R2G)]	66	23 MDS – 6 t-MDS – 3 t-MDS&MM – 1 AML – 13	8 AML – 8
Range of positive probe results	Not available	MDS: 35 – 81.5% t-MDS: 25 – 75% t-MDS&MM: 76% AML: 20 – 99%	45 - 91 %

MDS – Myelodysplastic syndrome
AML – Acute myeloid leukemia
t-MDS – Therapy related MDS
MM – Multiple Myeloma
* Line data unpublished, but this data was provided in the 510(k) submission

Sun Y, Cook JR. *Fluorescence in situ hybridization for del(5q) in myelodysplasia/acute myeloid lukemia: Comparison of EGR1 vs. CSF1R probes and diagnostic yield over metaphase cytogenetics alone. Leuk Res* 2010; 34: 340–343.

Galvan AB, Mallo M, Arenillas L, et al. *Does monosomy 5 really exist in myelodysplastic syndromes and acute myeloid leukemia? Leuk Res* 2010; 34: 1242– 1245.

Vance GH, Haesook K, Hicks GA, et al. *Utility of interphase FISH to stratify patients into cytogenetic*

risk categories at diagnosis of AML in an Eastern Cooperative Oncology Group (ECOG) clinical trial (E1900). Leuk Res 2007; 31:605-609.

4. Clinical cut-off**:**

   Not applicable

5. Expected values/Reference range:

   The upper reference limit is defined as the maximum quantity of scoreable interphase nuclei with an altered signal pattern from either karyotypically normal specimens or 5p15.2 and 5q31 deletion-free specimens. The upper reference limit is expressed in terms of a percentage or the actual number of atypical nuclear FISH signal pattern per the standard number of nuclei tested.

   The upper reference limit for this assay is 6% or 12 1R2G patterns per 200 scoreable interphase nuclei. Published literature was used to establish the reference range for this assay.

   In order to validate the 6% upper reference limit of the Vysis EGR1 FISH Probe Kit, the assay was performed on interphase nuclei from 25 bone marrow specimens from either karyotypically normal specimens or 5p15.2 and 5q31 deletion-free specimens. The signal patterns of 200 nuclei were evaluated by counting the number of orange and green signals. Each of two technologists evaluated 100 nuclei per specimen. Among the 25 normal specimens, none produced 1R2G signals at or above the 6% upper reference limit.

N. Other Supportive Instrument Characteristics Data Not Covered In The "Performance Characteristics" Section above:

None

O. Proposed Labeling:

Labeling satisfies the requirements of 21 CFR 809.10, 21 CFR 801.109, including an appropriate prescription statement as required by 21 CFR 801.109(b), and the special controls for this type of device.

P. Risks to Health and Mitigation Measures:

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."

Q. Benefit/Risk Analysis:

Summary of the Benefits	**Summary of the Risks**	**Summary of Other Factors**	**Conclusions**
AML and MDS patients may potentially benefit in the intended use population by use of the device to characterize bone marrow specimens with assay results interpreted by a qualified pathologist or cytogeneticist.	Erroneous device results could adversely influence expectation of more or less favorable clinical course of AML or MDS patients due to false negative or false positive results.	In addition to cited clinical studies using the device probes, analytical evaluation and labeling supports the intended use. De novo regulatory approach leverages device use by a qualified pathologist or cytogeneticist in the context of histopathological evaluation (e.g., immunohistochemistry).	Yes. Based on the supporting clinical studies for the diagnostic device along with review of the analytical performance and labeling, the probable benefits outweigh the probable risks.

R. Conclusion:

The request for Evaluation of Automatic Class III Designation for this device is granted. The device is classified as Class II under regulation 21 CFR 864.1870 with special controls. The device is classified under the following:

Product Code:	PDO
Device Type:	Early growth response 1 (EGR1) gene fluorescence in-situ hybridization (FISH) test system for specimen characterization
Class:	II (special controls)
Regulation:	21 CFR 864.1870

(a) *IDENTIFICATION*: 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.

(b) *CLASSIFICATION*: Class II (special controls). EGR1 Gene FISH test system for specimen characterization must comply with the following special controls:

1) Premarket notification submissions must 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 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. Target population must include the intended use population

D) Upper reference limit

F) Range of positive probe results

2) 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) 21 CFR 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.”