

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION  
DECISION SUMMARY  
ASSAY ONLY TEMPLATE**

**A. 510(k) Number:**

k063224

**B. Purpose for Submission:**

New device

**C. Measurand:**

Controls for assays detecting cytochrome P450 2D6 gene mutations and variants

**D. Type of Test:**

Quality control material for genetic testing

**E. Applicant:**

Gentris Corporation

**F. Proprietary and Established Names:**

GentriSure CYP2D6 \*4A/\*2AxN Human Genomic DNA Reference Control

GentriSure CYP2D6 \*29/\*2AxN Human Genomic DNA Reference Control

GentriSure CYP2D6 \*2M/\*17 Human Genomic DNA Reference Control

GentriSure CYP2D6 \*3A/\*4A Human Genomic DNA Reference Control

GentriSure CYP2D6 \*6B/\*41 Human Genomic DNA Reference Control

GentriSure CYP2D6 \*1/\*5 Human Genomic DNA Reference Control

**G. Regulatory Information:**

1. Regulation section:

21 CFR § 866.5910; Quality control material, genetics, DNA

2. Classification:

Class II

3. Product code:

NZB, Quality control material, genetics, DNA

4. Panel:

Immunology (82)

**H. Intended Use:**

1. Intended use(s):

See indication(s) for use below.

2. Indication(s) for use:

The GentiSure™ Human Genomic DNA Reference Control (HGDRC) is an independent, external run control that is intended for use in assessing the performance diagnostic assays that detect cytochrome p450 2D6 (CYP2D6) genetic polymorphisms. This control is not intended to be used as a substitute for controls provided with licensed test kits. *GentiSure* HGDRC can be used for assay validation, staff training and proficiency testing, and as a quality control in routine *in vitro* diagnostic testing.

3. Special conditions for use statement(s):

Not applicable.

4. Special instrument requirements:

Not applicable.

**I. Device Description:**

*GentiSure* CYP2D6 Human Genomic DNA Reference Controls are isolated from B-lymphoblastoids derived from properly consented individual donors. Ten different CYP2D6 alleles are represented in these controls: \*4A/\*2AxN, \*29/\*2AxN, \*2M/\*17, \*3A/\*4A, \*6B/\*41 and \*1/\*5.

The *GentiSure* CYP2D6 Human Genomic DNA Reference Control is suspended in a 10mM Tris-EDTA (pH 8.0) buffered solution containing 0.05% sodium azide. The DNA is aliquoted into 0.5mL, RNAase-, DNAase-, and endotoxin-free conical tubes with screw caps containing silicone O-rings. The minimum fill volume for each tube is 10 mL at a concentration of 50 ng/mL, which is sufficient to perform up to 10 reactions containing 50 ng each.

**J. Substantial Equivalence Information:**

1. Predicate device name(s):

Maine Molecular Quality Controls, Inc. INTROL CF Panel I Control

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

k060070

3. Comparison with predicate:

Differences	Predicate device	Proposed device
Physical composition	Synthetic (recombinant) DNA with carrier DNA, preservatives, dye and stabilizers	Purified DNA in buffer with sodium azide
Gene encoded; number of variations tested	<i>CFTR</i> ; 38 mutations, 4 variants	CYP450 2D6; 11 alleles
Assay steps controlled	Extraction, DNA analysis	DNA analysis

Similarities	Predicate device	Proposed device
Recommended storage	2-8°C	same
Method to validate presence mutations	Bi-directional sequencing	same

**K. Standard/Guidance Documents Referenced (if applicable):**

None referenced.

**L. Test Principle:**

Not applicable.

**M. Performance Characteristics (if/when applicable):**

1. Analytical performance:

a. *Precision/Reproducibility:*

The performance of the Human Genomic DNA Reference Controls (HGDRCs) was tested using three different methods, including FDA cleared AmpliChip® CYP450 Test. The HGDRCs performed in the expected manner across all the platforms, taking into consideration the limitations for each of the assays. Furthermore, the correct genotype results were reproducible from lab-to-lab, lot-to-lot and from run-to-run. Overall a total of 682 data points were obtained in this study, including data points that yielded a “no call” and data from repeat testing. By comparing the observed genotypes to the known genotypes based on bi-directional sequencing data, an overall concordance of 97.1% was determined. In all instances, miscalled genotype results could be explained based on limitations inherent to the assays being used.

AmpliChip

Reference Control	Expected Call	Total No. of Test Points	No. of "No Calls"	Total Genotype Calls	No. of Correct Calls	No. of Miscalls	% Concordance <sup>1</sup>
*4A/*2AxN	*4/*2xN	11	0	11	10	1	90.9
*29/*2AxN	*29/*2xN	9	0	9	9	0	100.0
*2M/*17	*17/*41 <sup>2</sup>	9	0	9	9	0	100.0
*3A/*4A	*3/*4	9	0	9	9	0	100.0
*6B/*41	*6/*41	11	1	10	10	0	100.0
*1/*5	*1/*5	9	0	9	9	0	100.0
<b>TOTAL</b>		58	1	57	56	1	98.2

<sup>1</sup> % Concordance = (No. of Correct Calls)/(total genotype calls) x 100

<sup>2</sup> AmpliChip is not able to distinguish CYP2D6 \*2M from \*41, therefore \*2M is called \*41.

b. *Linearity/assay reportable range:*

Not applicable.

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

Bidirectional sequencing of the Human Genomic DNA Reference Control (HGDR) materials was used to validate the presence of mutant or wild type sequence.

The Human Genomic DNA Reference Controls include the following 2D6 mutations and polymorphisms:

<b>Allele Nucleotide changes, Gene M33388</b>	<b>Nucleotide changes, Gene M33388</b>	<b>Allele Nucleotide changes, Gene M33388</b>	<b>Nucleotide changes, Gene M33388</b>
<i>CYP2D6*2A</i>	-1584C>G; -1235A>G; -740C>T; -678G>A; <i>CYP2D7</i> gene conversion in intron 1; 1661G>C; 2850C>T; 4180G>C	<i>CYP2D3A</i>	<b>2549delA</b>
<i>CYP2D6*2M</i>	-1584C; -1237_-1236insAA; -1235A>G; -750_-749delGA; -740C>T; -678G>A; <i>CYP2D7</i> gene conversion in intron 1; 310G>T; 746C>G; 843T>G; 1661G>C; 2850C>T; 2988G; 3384A>C; 3584G>A; 3790C>T; 4180G>C; 4481G>A	<i>CYP2D6*4A</i>	100C>T; 974C>A; 984A>G; 997C>G; 1661G>C; <b>1846G&gt;A</b> ; 4180G>C
<i>CYP2D6*2XN</i> (N=2, 3, 4, 5 or 13)	1661G>C; 2850C>T; 4180G>C	<i>CYP2D6*17</i>	<b>1023C&gt;T</b> ; 1661G>C; <b>2850C&gt;T</b> ; 4180G>C
<i>CYP2D6*5</i>	<b>CYP2D6 deleted</b>	<i>CYP2D6*29</i>	1659G>A; 1661G>C; 2850C>T; 3183G>A; 4180G>C
<i>CYP2D6*6B</i>	<b>1707delT</b> ; 1976G>A	<i>CYP2D6*41</i>	-1584C; -1235A>G; -740C>T; -678G>A; <i>CYP2D7</i> gene conversion in intron 1; 1661G>C; 2850C>T; <b>2988G&gt;A</b> ; 4180G>C
<i>CYP2D6*10A</i>	<b>100C&gt;T</b> ; 1661G>C; 4180G>C		

Prior to product release, each HGDR is tested for concentration, purity, and DNA integrity. In addition, a functional quality control test is performed in order to demonstrate that a 6.7kb CYP2D6-specific PCR product can be amplified from the HGDR.

**Stability:** Stability of three different lots of the control material were evaluated and confirmed by four methods: evaluation of DNA integrity or degradation by observation on agarose gel, generation of appropriate PCR

amplicon, bi-directional sequencing and additional methodologies to evaluate specific alleles.

**Real time stability study:** The shelf life of the control material is 2 months at 2-8°C. Real time stability testing is on-going.

Stability testing protocols include the following:

*Undiluted Bulk Stability:* During routine manufacturing, undiluted bulk DNA product will be stored at -30°C. A portion of the undiluted bulk will be removed to generate the diluted bulk DNA. The remaining undiluted concentrate DNA is tested for stability.

*Filled Product (2-8°C):* The normal storage conditions for product in the stability study will be 2-8°C/ambient humidity as this is the storage condition recommended to the end user in the package insert.

*Filled Product (-30°C):* In order to mimic in-house inventory storage conditions, product stored at -30°C will be tested.

*Open vial stability:* To ensure open vial stability in end-user handling and laboratory conditions, a portion of each lot was opened and closed a minimum of 10 times.

*Heat-stress testing:* The effect of potential temperature extremes (45°C for five days) representing what the product may be subjected to during shipment is under testing.

*Freeze-thaw testing:* A portion of each lot was frozen (-30°C) overnight and then thawed by placing at room temperature for 2 hours. This was repeated two additional times for a total of three freeze/thaw cycles.

- d. *Detection limit:*  
Not applicable.
  - e. *Analytical specificity:*  
Not applicable.
  - f. *Assay cut-off:*  
Not applicable.
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):

4. Clinical cut-off:

Not applicable.

5. Expected values/Reference range:

Not applicable.

**N. Proposed Labeling:**

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

**O. Conclusion:**

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.