

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

A. 510(k) Number:

K061686

B. Purpose for Submission:

To detect *vanA* and *vanB* genes in rectal swabs

C. Measurand:

vanA and *vanB* genes

D. Type of Test:

Qualitative Nucleic Acid Amplification Test of the *vanA* and *vanB* genes directly from rectal swabs.

E. Applicant:

GeneOhm Sciences Canada Inc.

F. Proprietary and Established Names:

IDI-VanR™ Assay

G. Regulatory Information:

1. Regulation section:

866.1640

2. Classification:

II

3. Product code:

NIJ – System, test, genotypic detection, resistant markers

4. Panel:

H. Intended Use:

1. Intended use(s):

The IDI-VanR® Assay is a qualitative in vitro test for the rapid detection of vancomycin-resistance (*vanA* and *vanB*) genes directly from rectal swabs. The IDI-vanR® Assay detects the presence of the *vanA* and *vanB* genes that can be associated with vancomycin-resistant enterococci (VRE). The assay is performed on an automated real-time PCR instrument with rectal swabs from patients at risk for VRE colonization. The IDI-VanR® Assay can be used as an aid to identify, prevent and control vancomycin-resistant colonization in healthcare settings. Concomitant cultures are necessary to recover organisms for epidemiological typing, susceptibility testing and for further confirmatory identification. The IDI-VanR® Assay is not intended to diagnose VRE infections nor to guide or monitor treatment for VRE infections.

2. Indication(s) for use:

The IDI-VanR® Assay is a qualitative in vitro test for the rapid detection of vancomycin-resistance (*vanA* and *vanB*) genes directly from rectal swabs. The IDI-vanR® Assay detects the presence of the *vanA* and *vanB* genes that can be associated with vancomycin-resistant enterococci (VRE). The assay is performed on an automated real-time PCR instrument with rectal swabs from patients at risk for VRE colonization. The IDI-VanR® Assay can be used as an aid to identify, prevent and control vancomycin-resistant colonization in healthcare settings. Concomitant cultures are necessary to recover organisms for epidemiological typing, susceptibility testing and for further confirmatory identification. The IDI-VanR® Assay is not intended to diagnose VRE infections nor to guide or monitor treatment for VRE infections.

3. Special conditions for use statement(s):

Samples must be collected using the Copan Transystem™ swabs. (Liquid Stuart, Liquid Amies, Amies Agar Gel without Charcoal, or Amies Agar Gel with Charcoal).

Prescription Use Only

4. Special instrument requirements:

Assay is performed with the SmartCycler® instrument

I. Device Description:

The IDI-VanR™ Assay is performed on rectal swabs with a procedure that includes

specimen lysis, amplification of the *vanA* and *vanB* targets, and detection of fluorogenic target-specific hybridization probes. The amplification, detection and interpretation of the signals are done automatically by the Cepheid SmartCycler® instrument software. A positive and negative control is included in each IDI-*vanR*™ Assay run. An Internal Control is also included in each assay tube. The inclusion of these three controls will monitor every step of the PCR procedure and the functionality of every reagent. External controls are recommended to monitor the cell lysis and DNA extraction steps. The procedure takes about 60 to 75 minutes.

J. Substantial Equivalence Information:

1. Predicate device name(s):

Bile Esculin Azide agar with 6 µg/mL vancomycin

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

K972359

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended Use	Screening for vancomycin resistance	Same
Type of test	Qualitative	Same

Differences		
Item	Device	Predicate
Technology	PCR amplification with detection of fluorogenic target-specific hybridization	Growth based phenotypic detection
Controls	Positive, negative and internal controls are part of the assay. Specimen processing controls are recommended which include positive and negative <i>Enterococci spp.</i> isolates	<i>E. faecalis</i> ATCC 51299 – positive; <i>E. faecalis</i> ATCC 29212 – negative
Mode of detection	Presence of <i>vanA</i> and or <i>vanB</i> genes	Growth or no growth in the presence of 6 µg/mL vancomycin
Specimen Type	Rectal swab	Rectal swab or stool

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

Not Applicable

L. Test Principle:

Following specimen lysis and *vanA* and *vanB* amplification, the DNA targets are detected with molecular beacons, a hairpin-forming single-stranded oligonucleotides labeled as one end with a quencher and at the other end with a fluorescent reporter dye (fluorophore). In the absence of target, the fluorescence is quenched. In the presence of target, the hairpin structure opens upon beacon/target hybridization, resulting in emission of fluorescence. For the detection of *vanA* amplicons, the molecular beacon contains the fluorophore FAM at the 5' end and the non-fluorescent quencher moiety DABCYL at the opposite end of the oligonucleotide. For the detection of the *vanB* amplicons, the molecular beacon contains the fluorophore Texas Red at the 5' end and the quencher DABCYL at the 3' end. Each beacon-target hybrid fluoresces at a wavelength characteristic of the fluorophore used in the particular molecular beacon. The amount of fluorescence depends on the amount of specific amplicons present at that time. The SmartCycler® software simultaneously monitors the fluorescence emitted by each beacon, interprets all data, and provides a final result at the end of the cycling program.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Ten samples containing negative matrix consisting of 3 low positive specimens and 5 high positive specimens and a negative and positive control were frozen and sent to three sites. Testing was performed in triplicate on three separate days at each site with three lots. Both *vanA* and *vanB* genes were included to ensure that all primers and probes of the IDI-*vanR*™ Assay were assessed. The overall reproducibility was > 95% with 3 invalid positive control results.

b. *Linearity/assay reportable range:*

Not Applicable

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

The table below describes internal controls that are part of the assay with the various parts controlled.

Step controlled		Positive Control	Negative Control	Internal Control
Specimen Preparation	Cell lysis			
	DNA extraction			
	Inactivation of heat labile inhibitors		X	X
PCR	Denaturation step	X		X
	Primer/target annealing	X		X
	Elongation Step	X		X
	Probe/amplicon annealing	X		X
Presence of non heat labile PCR inhibitors				X
Reagent contamination			X	
Environmental contamination with GBS amplicon			X	

Since Cell lysis and DNA extraction are not controlled, the Package Insert will carry a statement that the user may test a positive and negative strain as recommended or required by other regulations. The recommendations include the testing of ATCC 51299 *E. faecalis* as a positive specimen processing control and for *E. gallinarum* ATCC 700425 as an external negative control.

d. Detection limit:

Internal studies determined that the genomic limits of detection (LOD) for specific *vanA* and *vanB* are 5 and 10 DNA copies per reaction, respectively. The bacterial LOD for *vanA* and *vanB* are 1.6 and 1.4 CFU/reaction.

e. Analytical specificity:

Analytical specificity of the IDI-*vanR*™ Assay was determined with well-characterized isolates of vancomycin-sensitive closely related genera, and other pathogenic and commensal flora found in the rectum and stools. These included *Enterococcus spp.* with the presence of other *van* genes (*vanC*, *vanD*, *vanE*, *vanG*). All provided a negative test result.

Potentially interfering substances were tested using materials that may be found in the rectum (petroleum jellies, creams, blood, suppositories). Blood showed a reduction in the IC% Endpoint and hydrocortisone provided unresolved results when the swab was heavily covered in it.

f. Assay cut-off:

Acceptance Criteria for the IDI-*VanR*™ were established during assay development and pre-validated at one external site with 216 specimens prior to the clinical trial. The acceptance criteria includes; Endpoint threshold, 2nd derivative threshold, minimum cycle threshold, maximum cycle threshold, and % IC NC endpoint.

2. Comparison studies:

a. *Method comparison with predicate device:*

A clinical study was conducted at 4 diverse sites from units with high VRE prevalence such as intensive care units. Each site performed routine VRE screening (culture on selective media [Bile Esculin azide agar with 6 µg/mL vancomycin (BEAV) plate) followed by phenotypic identification and detection of vancomycin and teicoplanin resistance]. An enriched culture method was also inoculated (Bile Esculin Azide broth with vancomycin 8 µg/mL) and further cultured if the original culture was negative. A total of 968 rectal swab specimens were collected with one of the recommended swabs (refer to “Materials required but not provided”), screened for vancomycin-resistance with the reference culture method described above and with the IDI-VanR™ assay. Compared to the culture method, the IDI-VanR™ assay identified 97.3% of the positive specimens (by either culture technique), and 91.4% of the specimens negative (by both culture techniques). For the population tested, these results produced a negative predictive value of 99.6% and positive predictive value of 59.1%.

		IDI-VanR™					TOTAL
		VAN A	VAN B	VAN A+B	NEGATIVE	UNRESOLVED	
Reference Method	VanA	80	0	18	3	0	101
	VanB	0	4	3	0	0	7
	VanA + B	0	0	2	0	0	2
	Negative	14	58	2	783	1	858
	Total :	94	62	25	786	1	968

The IDI-vanR™ “vanB “only column in the table above would be recommended for further confirmation according to the interpretation of this result. Of the 62 vanB only positives, 4 were culture vanB positive with the rest not positive fro VRE by culture.

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):*

Not Applicable

4. Clinical cut-off:

Not Applicable

5. Expected values/Reference range:

The prevalence of VRE in the study population was 11.1%. The overall *vanA* prevalence was 10.6% and *vanB* was 0.9%.

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.

