Quidel Corporation
% Selena Liu
Senior Regulatory Affairs Specialist
QuidelOrtho Corporation
9975 Summers Ridge Road
San Diego, California 92121

Re: K232286
Trade/Device Name: Savanna HSV 1+2/VZV Assay, Savanna HSV 1+2/VZV Control Set, Savanna Instrument
Regulation Number: 21 CFR 866.3309
Regulation Name: Herpes Virus Nucleic Acid-Based Cutaneous And Mucocutaneous Lesion Panel
Regulatory Class: Class II
Product Code: PGI
Dated: November 21, 2023
Received: November 21, 2023

Dear Selena Liu:

We have reviewed your section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (the Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database available at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Additional information about changes that may require a new premarket notification are provided in the FDA guidance documents entitled "Deciding When to Submit a 510(k) for a Change to an Existing Device"

(https://www.fda.gov/media/99812/download) and "Deciding When to Submit a 510(k) for a Software Change to an Existing Device" (https://www.fda.gov/media/99785/download).

Your device is also subject to, among other requirements, the Quality System (QS) regulation (21 CFR Part 820), which includes, but is not limited to, 21 CFR 820.30, Design controls; 21 CFR 820.90, Nonconforming product; and 21 CFR 820.100, Corrective and preventive action. Please note that regardless of whether a change requires premarket review, the QS regulation requires device manufacturers to review and approve changes to device design and production (21 CFR 820.30 and 21 CFR 820.70) and document changes and approvals in the device master record (21 CFR 820.181).

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR Part 803) for devices or postmarketing safety reporting (21 CFR Part 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 Part 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR Parts 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, 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).

Sincerely,

Ryan C. Karsner -S

Digitally signed by Ryan C. Karsner -S
Date: 2023.12.20 11:54:38 -05'00'

Ryan Karsner, MD
Deputy Assistant Director
Division of Microbiology Devices
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Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 07/31/2026
See PRA Statement below.

510(k) Number *(if known)*
K232286

Device Name
Savanna HSV 1+2/VZV Assay
Savanna HSV 1+2/VZV Assay Control Set, Savanna Instrument

Indications for Use *(Describe)*
The Savanna HSV 1+2/VZV Assay is an automated, rapid multianalyte real-time PCR test for the simultaneous qualitative detection and differentiation of herpes simplex virus type 1, herpes simplex virus type 2, and varicella-zoster virus DNA isolated from human cutaneous or mucocutaneous lesion samples obtained from symptomatic patients suspected of active herpes simplex virus 1, herpes simplex virus 2 and/or varicella-zoster infection. This in vitro diagnostic test is intended to aid in the diagnosis of patients with signs or symptoms of herpes simplex virus type 1, herpes simplex virus type 2, and varicella-zoster virus infection.
The Savanna HSV 1+2/VZV Assay is intended to aid in the diagnosis of herpes simplex virus 1, herpes simplex virus 2 and varicella-zoster virus active infections. The results of this test should not be used as the sole basis for diagnosis, treatment or other management decisions and must be combined with clinical observations, patient history and/or epidemiological information. Negative results do not preclude herpes simplex virus type 1, herpes simplex virus type 2, or varicella-zoster virus infection that is not detected by a cutaneous or mucocutaneous lesion swab specimen. Positive results do not rule out co-infection with other organisms. Additional laboratory testing (e.g., viral culture, immunoassay, serology) may be necessary for patient evaluation. Savanna HSV 1+2/VZV Assay is for professional use. The Savanna HSV 1+2/VZV Assay is intended for use only with the Savanna instrument.

Warning: The Savanna HSV 1+2/VZV Assay is not intended for use with the cerebrospinal fluid (CSF) or to aid in the diagnosis of HSV or VZV infections of the central nervous system (CNS). The Savanna HSV 1+2/VZV Assay is not intended for use in prenatal screening.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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510(K) SUMMARY

Submitter
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Date Prepared
July 31, 2023

Proprietary and Established Names
Savanna HSV 1+2/VZV Assay
Savanna HSV 1+2/VZV Control Set
Savanna Instrument

Classification

Product Code	Classification	Regulatory Section	Description
PGI	II	866.3309	Herpes Virus (Vzv, Hsv1, Hsv2), DNA Detection Assay For Cutaneous And Mucocutaneous Lesion Samples

Panel
Microbiology

Predicate Device
Solana HSV 1+2/VZV Assay (K162451)

Intended Use

The Savanna HSV 1+2/VZV Assay is an automated, rapid multianalyte real-time PCR test for the simultaneous qualitative detection and differentiation of herpes simplex virus type 1, herpes simplex virus type 2, and varicella-zoster virus DNA isolated from human cutaneous or mucocutaneous lesion samples obtained from symptomatic patients suspected of active herpes simplex virus 1, herpes simplex virus 2 and/or varicella-zoster infection. This *in vitro* diagnostic test is intended to aid in the diagnosis of patients with signs or symptoms of herpes simplex virus type 1, herpes simplex virus type 2, and varicella-zoster virus infection.

The Savanna HSV 1+2/VZV Assay is intended to aid in the diagnosis of herpes simplex virus 1, herpes

simplex virus 2 and varicella-zoster virus active infections. The results of this test should not be used as the sole basis for diagnosis, treatment or other management decisions and must be combined with clinical observations, patient history and/or epidemiological information. Negative results do not preclude herpes simplex virus type 1, herpes simplex virus type 2, or varicella-zoster virus infection that is not detected by a cutaneous or mucocutaneous lesion swab specimen. Positive results do not rule out co-infection with other organisms. Additional laboratory testing (e.g., viral culture, immunoassay, serology) may be necessary for patient evaluation. Savanna HSV 1+2/VZV Assay is for professional use. The Savanna HSV 1+2/VZV Assay is intended for use only with the Savanna instrument.

Warning: The Savanna HSV 1+2/VZV Assay is not intended for use with the cerebrospinal fluid (CSF) or to aid in the diagnosis of HSV or VZV infections of the central nervous system (CNS). The Savanna HSV 1+2/VZV Assay is not intended for use in prenatal screening.

Device Description

The Savanna HSV 1+2/VZV Assay consists of a single, self-contained assay cartridge employing real-time PCR technology for use with the Savanna instrument to detect and differentiate DNA from herpes simplex virus type 1, herpes simplex virus type 2 and varicella-zoster virus. In approximately 24 minutes, this platform extracts, amplifies and detects DNA present in cutaneous or mucocutaneous lesion swab specimens obtained from symptomatic patients and placed in transport media.

To initiate the assay, a patient cutaneous or mucocutaneous lesion swab specimen in transport medium is transferred via the supplied transfer pipette to the Liquid Sample Port of the Test Cartridge. The user closes the Sample Port and inserts the Test Cartridge into the Savanna instrument, initiating sample processing. The sample containing human DNA is pushed out of the Sample Port by lysis buffer, which then rehydrates the Process Internal Control (IC), and together with the paramagnetic nucleic acid binding particles, are pumped into the extraction chamber. The solution is mixed, and virus and/ or bacteria are further lysed by sonication within the extraction chamber. Specimen and IC DNA are bound to, washed and then eluted off the paramagnetic particles. The purified specimen DNA and IC solution is used to rehydrate four individual lyophilized master mixes. Each master mix is pumped into a PCR chamber and Taq-man® multiplex real-time PCR reactions are carried out under optimized conditions, generating amplicons for the targeted pathogen (if present) and the Process Internal Control (IC).

Each master mix contains primers and dual-labeled probes unique for the pathogen targets and the IC. The probes are labeled with a fluorophore on one end and a quencher on the other end. Target DNA sequences are amplified by pathogen-specific primers and detected by correspondingly specific fluorescence probes. The IC targets are also amplified by specific primers and detected by an IC-specific fluorescence probe. A polymerase included in the master mix cleaves the probes bound to complementary DNA sequences, separating the fluorophore from the quencher. This step generates a signal and if it surpasses multiple defined thresholds, the sample is reported as positive for the detected target sequence.

The Savanna instrument will display the test results (Positive, Negative or Invalid) on the main bay screen.

Comparison with Predicate

Features	Predicate Device Solana HSV 1+2/VZV Assay (K162451)	New Device Savanna HSV 1+2/VZV Assay (K232286)
Intended Use	The Solana HSV 1+2/VZV Assay is an in vitro diagnostic test, using isothermal amplification technology (helicase dependent amplification, HDA), for the qualitative detection and differentiation of herpes simplex virus type 1, herpes simplex virus type 2, and varicella-zoster virus DNA isolated and purified from cutaneous or mucocutaneous lesion samples obtained from symptomatic patients suspected of active herpes simplex virus 1, herpes simplex virus 2 and/or varicella-zoster infection. The Solana HSV 1+2/VZV Assay is intended to aid in the diagnosis of herpes simplex virus 1, herpes simplex virus 2 and varicella-zoster virus active cutaneous or mucocutaneous infections. Negative results do not preclude herpes simplex virus 1, herpes simplex virus 2 and varicella-zoster virus infections and should not be used as the sole basis for diagnosis, treatment, or other management decisions. The Solana HSV 1+2/VZV Assay is intended for use only with the Solana instrument. Warning: The Solana HSV 1 + 2/VZV Assay is not intended for use with cerebrospinal fluid or to aid in the diagnosis of HSV or VZV infections of the central nervous system. The Solana HSV 1 + 2/VZV Assay is not intended for use in prenatal screening.	The Savanna HSV 1+2/VZV Assay is an automated, rapid, multianalyte real-time PCR test for the simultaneous qualitative detection and differentiation of herpes simplex virus type 1, herpes simplex virus type 2, and varicella-zoster virus DNA isolated from human cutaneous or mucocutaneous lesion samples obtained from symptomatic patients suspected of active herpes simplex virus 1, herpes simplex virus 2 and/or varicella-zoster infection. This *in vitro* diagnostic test is intended to aid in the diagnosis of patients with signs or symptoms of herpes simplex virus type 1, herpes simplex virus type 2, and varicella-zoster virus infection. The Savanna HSV 1+2/VZV Assay is intended to aid in the diagnosis of herpes simplex virus 1, herpes simplex virus 2 and varicella-zoster virus active infections. The results of this test should not be used as the sole basis for diagnosis, treatment or other management decisions and must be combined with clinical observations, patient history and/or epidemiological information. Negative results do not preclude herpes simplex virus type 1, herpes simplex virus type 2, or varicella-zoster virus infection that is not detected by a cutaneous or mucocutaneous lesion swab specimen. Positive results do not rule out co-infection with other organisms. Additional laboratory testing (e.g., viral culture, immunoassay, serology) may be necessary for patient evaluation. Savanna HSV 1+2/VZV Assay is for professional use. The Savanna HSV 1+2/VZV Assay is intended for use only with the Savanna instrument. **Warning**: The Savanna HSV 1+2/VZV Assay is not intended for use with the cerebrospinal fluid (CSF) or to aid in the diagnosis of HSV or VZV infections of the central nervous system (CNS). The Savanna HSV 1+2/VZV Assay is not intended for use in prenatal screening.

Features	Predicate Device Solana HSV 1+2/VZV Assay (K162451)	New Device Savanna HSV 1+2/VZV Assay (K232286)
Instrument	Solana	Savanna
Qualitative	Yes	Yes
Analyte	Viral DNA from HSV-1, HSV-2 and VZV	Viral DNA from HSV-1, HSV-2 and VZV
Specimen Types	Cutaneous or mucocutaneous lesion swabs in transport medium	Cutaneous or mucocutaneous lesion swabs in transport medium
Test Principle	Isothermal Helicase-Dependent Amplification (HDA)	PCR
Automated Analysis	Yes	Yes
Development Time	50 min	Within 24 min
Kit Storage	2ºC to 8ºC	2ºC to 30ºC
External Controls	Positive and Negative Controls (Available as a separate kit)	Positive and Negative Controls (Available as a separate kit)
Quality Control Features	Competitive Process Control (PRC)	Process Internal Control (IC)

Performance Data

Numerous studies were undertaken to document the performance characteristics and the substantial equivalence of the test to the predicate device. These studies included the following:

Limit of Detection

The limits of detection (LoD) for the Savanna HSV 1+2/VZV Assay were determined using two types/strains of HSV-1, two types/strains of HSV-2 and two types/strains of VZV, serially diluted in negative matrix. The LoD for each pathogen is listed below in **Table 1**.

Table 1. Savanna HSV 1+2/VZV Limit of Detection

Pathogen	Type/ Strain ID	LoD ($TCID_{50}$/mL)	LoD (cp/mL)
HSV-1	Isolate 2	1.16E+02	6.65E+02
	Macintyre	1.08E-03	2.86E+02
HSV-2	Strain G	2.50E+01	1.27E+04
	MS	8.51E+00	7.64E+01
VZV	Ellen	N/A	3.32E+03
	Strain 82	N/A	1.02E+03

Co-spike Limit of Detection

Co-spike study demonstrated that multi-analyte preparation does not impact the LoD for the Savanna HSV 1+2/VZV Assay as established in Limit of Detection Study. DNA of one strain of each of HSV-1, HSV-2 and VZV were mixed at 1x LoD level and evaluated with three kit lots. The co-spiked multi-analyte sample mix showed ≥95% positivity for each target DNA, verifying that the co-spike does not impact the LoD.

Inclusivity

Inclusivity, or analytical reactivity, for Savanna HSV 1+2/VZV Assay was demonstrated using four additional strains of HSV-1 (Isolate 3, Isolate 7, Isolate 11, Isolate 20), four additional strains of HSV-2 (Isolate 6, Isolate 9, Isolate 10, Isolate 20) and five additional strains of VZV (AV923L, 9939, Isolate B, 275, Isolate D). All pathogens tested were detected by the assay at the following concentrations (**Table 2**).

Table 2. Inclusivity/Reactivity Testing Results

Virus	Type/Strain	Concentration in UTM ($TCID_{50}$/mL)	Concentration in UTM (cp/mL)	Inclusive (Yes/No)
HSV-1	Isolate 3	4.00E+00	8.56E+02	Yes
	Isolate 7	1.72E+01	Not Available	Yes
	Isolate 11	2.53E+01	Not Available	Yes
	Isolate 20	5.45E+01	1.40E+02	Yes
HSV-2	Isolate 6	2.94E+00	2.54E+03	Yes
	Isolate 9	2.94E+00	3.26E+02	Yes
	Isolate 10	2.94E+00	1.34E+02	Yes
	Isolate 20	2.94E+00	Not Available	Yes
VZV	AV923L	Not Available	4.00E+02	Yes
	9939	1.05E+01	1.09E+03	Yes
	Isolate B	Not Available	8.20E+02	Yes
	275	Not Available	2.88E+02	Yes
	Isolate D	Not Available	1.65E+03	Yes

In silico Inclusivity Analysis

Specific nucleic acid sequences used in the Savanna HSV 1+2/VZV Assay target the highly conserved regions of each pathogen. The inclusivity of the assay was established through *in silico* analyses of available HSV-1, HSV-2 and VZV sequences in NCBI databases. The analyses determined that the primer and probe sets for HSV-1, HSV-2 and VZV have high homologies toward their respective target sequences as summarized in **Table 3**.

Table 3. Summary of Savanna HSV 1+2/VZV Assay Oligo Homologies

Analyte	Total # Aligned Sequences (%)	Homology Range
HSV-1	136 (100%)	93.3-100%
HSV-2	284 (100%)	93.33-100%
VZV	181 (100%)	100%

Cross Reactivity/Microbial Interference

The potential cross reactivity and microbial interference of 22 viral isolates and 38 bacterial and fungal microorganisms were evaluated in the Savanna HSV 1+2/VZV Assay. None of the viruses or microorganisms listed below in **Table 4** showed signs of cross reactivity or microbial interference at the concentrations listed, in the presence or absence of the target analytes.

Table 4. Potential-Cross-Reacting and Interfering Viruses and Microorganisms evaluated

Condition Description	Virus/Bacteria/Fungus Concentration	Condition Description	Virus/Bacteria/Fungus Concentration
Acholeplasma laidlawi	1.00E+06 CFU/mL	*Haemophilus influenzae Type B*	1.00E+06 CFU/mL
Acinetobacter calcoaceticus	1.00E+06 CFU/mL	*Hepatitis A virus*	2.70E+05 cp/mL
Acinetobacter lwoffii	1.01E+06 CFU/mL	*Hepatitis B virus*	2.45E+05 cp/mL
Adenovirus 7	1.04E+05 TCID50/mL	*Hepatitis C virus*	4.15E+05 cp/mL
Bacteroides fragilis	1.00E+06 CFU/mL	*HIV-1 Type 1*	1.95E+05 cp/mL
Bordetella bronchiseptica	1.06E+06 CFU/mL	*Human Herpes virus HHV6*	≥ 1.01E+05 TCID50/mL
Bordetella pertussis	1.01E+06 CFU/mL	*Human Herpes virus HHV7*	2.34E+04 TCID50/mL
Candida albicans	1.00E+06 CFU/mL	*Human Herpes virus HHV8*	1.01E+05 TCID50/mL
Candida glabrata	1.03E+06 CFU/mL	*Human Metapneumovirus A1*	1.90E+05 TCID50/mL
Candida krusei	1.14E+06 CFU/mL	*Human papillomavirus HPV-16*	2.85E+05 cp/mL
Candida parapsilosis	1.20E+06 CFU/mL	*Human papillomavirus HPV-18*	2.60E+05 cp/mL
Candida tropicalis	1.04E+06 CFU/mL	*Klebsiella pneumoniae*	1.00E+06 CFU/mL
Chlamydia trachomatis	1.06E+06 CFU/mL	*Lactobacillus acidophilus*	1.04E+06 CFU/mL
Chlamydophila pneumoniae	1.13E+06 CFU/mL	*Measles virus*	1.04E+05 TCID50/mL
Clostridium perfringens	1.00E+06 CFU/mL	*Mobiluncus mulieris*	1.00E+06 CFU/mL
Coronavirus OC43	1.00E+05 TCID50/mL	*Moraxella catarrhalis*	1.34E+06 CFU/mL
Coxsackievirus B1	1.00E+05 TCID50/mL	*Mycoplasma orale*	1.00E+06 CFU/mL
Cutibacterium acnes	1.00E+06 CFU/mL	*Mycoplasma pneumoniae*	1.00E+06 CFU/mL
Cytomegalovirus	1.00E+05 TCID50/mL	*Neisseria gonorrhoeae*	1.00E+06 CFU/mL
Cytomegalovirus Towne	8.00E+04 TCID50/mL	*Neisseria meningitidis*	1.09E+06 CFU/mL
Echovirus 11	1.40E+05 TCID50/mL	*Prevotella melaninogenica*	1.20E+06 CFU/mL
Enterobacter cloacae	1.04E+06 CFU/mL	*Proteus mirabilis*	1.04E+06 CFU/mL
Enterococcus faecalis	1.04E+06 CFU/mL	*Rubella virus; Strain: RA 27/3*	1.00E+05 TCID50/mL
Enterovirus 70	1.00E+05 TCID50/mL	*Staphylococcus aureus*	1.15E+06 CFU/mL
Epstein Barr (EBV)	6.05E+06 cp/mL	*Staphylococcus aureus (MRSA)*	1.03E+06 CFU/mL
Escherichia coli	1.00E+06 CFU/mL	*Staphylococcus saprophyticus*	1.15E+06 CFU/mL
Fusobacterium nucleatum	1.07E+06 CFU/mL	*Streptococcus agalactiae*	1.13E+06 CFU/mL
Gardnerella vaginalis	1.03E+06 CFU/mL	*Streptococcus pneumoniae*	1.20E+06 CFU/mL

Haemophilus ducreyi	1.00E+06 CFU/mL	*Streptococcus pyogenes*	3.17E+06 CFU/mL
Haemophilus influenzae (Type A)	1.00E+06 CFU/mL	*Streptococcus salivarius*	1.00E+06 CFU/mL

Interfering Substances

The performance of Savanna HSV 1+2/VZV Assay was evaluated with potentially interfering substances that may be present in lesion specimens. Several endogenous substances, over the counter (OTC) products, and prescription medications were evaluated with the Savanna HSV 1+2/VZV Assay. None of the substances in **Table 5** interfered with the assay at the levels listed below.

Table 5. Potential Interfering Substances evaluated

Substance	Active Ingredient	Test Concentration
Blood/EDTA	N/A	0.63%
Casein	Casein Bovine Milk	7 mg/mL
Feces	N/A	2.5 mg/mL
Female Urine	Urea	7%
Leukocytes	N/A	$2.5x10^5$ cells/mL
Male Urine	Urea	3.5%
Mucus (Mucin, bovine submaxillary gland, type I-S)	Mucin	5% (w/v)
Seminal fluid	Semen	2%
Abreva Docosanol	Docosanol	3.5% (w/v)
Acetaminophen	Acetominophen	1.75% (w/v)
Anti-itch cream	Benzalkonium chloride	3.5% (w/v)
Balneol Hygienic Cleansing Lotion	N/A	3.5% (w/v)
Carmex Cold Sore Lip Balm	Benzocaine, White Petrolatum	3.5% (w/v)
Chlor-Trimeton	Chlorpheniramine maleate	1.25 mg/mL
Clotrimazole 3 Vaginal Cream	Clotrimazole	3.5% (w/v)
Cornstarch	N/A	1.25 mg/mL
Dextromethorphan hydrobromide (*i.e.* Mucinex)	Dextromethorphan, Guaifenesin, Phenylephrine	5 mg/mL
Douche	Decyl Glucoside; Octoxynol-9	7% (w/v)
K-Y Brand Jelly	Glycerol	7% (w/v)
Lanacane	3% w/w Benzocaine	3.5% (w/v)
Lip Clear Lysine+	Menthol	3.5% (w/v)
Listerine	Thymol	7% (w/v)
Miconazole 1	N/A	7% (w/v)
Miconazole 3	N/A	7% (w/v)
Monistat 1	N/A	7% (w/v)
Monistat 3	N/A	7% (w/v)
Preparation H	Witch Hazel	3.5% (w/v)
Releev	Benzalkonium chloride	3.5% (w/v)
Toothpaste	Sodium Fluoride	7% (w/v)
Triconazole 1	Tioconazole	7% (w/v)

Substance	Active Ingredient	Test Concentration
Vagisil Cream	Benzocaine, Resorcinol	7% (w/v)
YeastGard	Sodium Borate	7% (w/v)
Acyclovir	Acyclogauanosine	7 mg/mL
Cidofovir	Cidofovir Hydrate	2.5 mg/mL
Foscarnet	Foscarnet Sodium	1.25 mg/mL
Ganciclovir	Ganciclovir	2.5 mg/mL

Competitive Interference

A competitive interference study was conducted to evaluate the performance of the Savanna HSV 1+2/VZV Assay using samples containing 2 target analytes at different combination of high and low analyte concentrations. Each sample was prepared with one of the analytes at 3X LoD and the other analytes at 10X, 500X or 1000X LoD in negative buccal matrix. Five replicates per sample were evaluated. When competitive interference was observed (shaded in Table 6), titration of the high-level analyte was done and tested. Results are listed in **Table 6**.

Table 6. Non-Competing Analytes

	Low Analyte	High Analyte	HSV-1 Positivity	HSV-2 Positivity	VZV Positivity
1	HSV-1 (3x LoD)	HSV-2 (1000x LoD)	0.0% (0/5)	100.0% (5/5)	0% (0/5)*
2	HSV-1 (3x LoD)	HSV-2 (500x LoD)	0.0% (0/5)	100.0% (5/5)	0% (0/5)*
3	HSV-1 (3x LoD)	HSV-2 (250x LoD)	20.0% (1/5)	100.0% (5/5)	0% (0/5)*
4	HSV-1 (3x LoD)	HSV-2 (100x LoD)	60.0% (3/5)	100.0% (5/5)	0% (0/5)*
5	HSV-1 (3x LoD)	HSV-2 (10x LoD)	100.0% (5/5)	100.0% (5/5)	0% (0/5)*
6	HSV-1 (3x LoD)	VZV (500x LoD)	100.0% (5/5)	0% (0/5)*	100.0% (5/5)
7	HSV-2 (3x LoD)	HSV-1 (1000x LoD)	100.0% (5/5)	60.0% (3/5)	0% (0/5)*
8	HSV-2 (3x LoD)	HSV-1 (500x LoD)	100.0% (5/5)	100.0% (5/5)	0% (0/5)*
9	HSV-2 (3x LoD)	HSV-1 (250x LoD)	100.0% (5/5)	100.0% (5/5)	0% (0/5)*
10	HSV-2 (3x LoD)	HSV-1 (100x LoD)	100.0% (5/5)	100.0% (5/5)	0% (0/5)*
11	HSV-2 (3x LoD)	HSV-1 (10x LoD)	100.0% (5/5)	100.0% (5/5)	0% (0/5)*
12	HSV-2 (3x LoD)	VZV (500x LoD)	0% (0/5)*	100.0% (5/5)	100.0% (5/5)
13	VZV (3x LoD)	HSV-1 (1000x LoD)	100.0% (5/5)	0% (0/5)*	100.0% (5/5)
14	VZV (3x LoD)	HSV-2 (1000x LoD)	0% (0/5)*	100.0% (5/5)	100.0% (5/5)

*Analyte not present in the sample, the negative results are not due to competitive interference. The negative results are true negative.

Repeatability/ Within-Lab Precision

A 20-day within laboratory precision study was performed with two testing events per day, each testing had two replicates of a three- member test panel on three product lots. The test panel was prepared in negative buccal cell matrix comprised of a negative sample, a co-spiked low positive sample (at LoD for each pathogen), and a co- spiked moderate positive sample (at 4 times the LoD for each pathogen). The negative sample had an overall 99.6% (239/240) expected agreement for HSV-1, 99.6% (239/240) expected agreement for HSV-2 and 100.0% (242/242) expected agreement for VZV across all lots. The

low positive sample had an overall 99.2% (237/239) expected agreement for HSV-1, 100.0% (239/239) expected agreement for HSV- 2 and 99.6% (238/239) expected agreement for VZV across all lots. The moderate positive sample had an overall 99.6% (239/240) expected agreement for HSV-1, 100.0% (240/240) expected agreement for HSV- 2 and 99.6% (240/241) expected agreement for VZV across all lots**.** Results are presented in **Table 7.**

Table 7. Repeatability/Within-Laboratory Precision

Analyte	Sample	Agreement with Expected Results	Detected Mean Ct	Repeatability		Between Runs		Between Days		Between Lot		Total	
				SD	% CV	SD	% CV	SD	% CV	SD	% CV	SD	% CV
	Negative	239/240 (99.6%)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
HSV-1	Low Positive	237/239 (99.2%	36.4	1.50	4.1	0.07	0.2	0.19	0.5	0.50	1.4	1.60	4.4
	Moderate Positive	239/240 (99.6%)	34.3	1.06	3.1	0.70	2.0	0.00	0.0	0.41	1.2	1.33	3.9
	Negative	239/240 (99.6%)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
HSV-2	Low Positive	239/239 (100%)	33.9	0.95	2.8	0.49	1.5	0.05	0.2	0.42	1.3	1.16	3.4
	Moderate Positive	240/240 (100%)	31.9	0.98	3.1	0.46	1.5	0.00	0.0	0.00	0.0	1.09	3.4
	Negative	242/242 (100%)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
VZV	Low Positive	238/239 (99.6%)	35.7	0.77	2.2	0.11	0.3	0.20	0.6	0.19	0.5	0.83	2.3
	Moderate Positive	240/241 (99.6%)	34.1	0.54	1.6	0.00	0.0	0.11	0.3	0.18	0.5	0.58	1.7

Reproducibility

A five-day, multi-site reproducibility study was conducted at three healthcare facilities. Each day, two operators at each site ran two replicates of a three-member test panel prepared in negative buccal cell matrix comprised of a negative sample, a co-spiked low positive sample (at LoD for each pathogen), and a co-spiked moderate positive sample (at 4 times the LoD for each pathogen). The negative sample had an 100% (179/179) expected agreement across all sites for all three analytes. The low positive samples were called positive 99.4% (179/180) of the time for HSV-1, 100% (180/180) of the time for HSV-2 and 100% (180/180) of the time for VZV. The moderate positive samples were called positive 99.4% (179/180) of the time for HSV-1, 100% (180/180) HSV-2 and 99.4% (179/180) for VZV. Results are in **Table 8.**

Table 8. Reproducibility Study Results (3 Sites)

Analyte	Sample	Agreement with Expected Results	Detected Mean Ct	Repeatability		Between Day		Between Site		Between Lot		Between Operator		Reproducibility	
				SD	% CV	SD	% CV	SD	%CV	SD	% CV	SD	% CV	SD	% CV
	Negative	179/179 (100%)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
HSV-1	Low Positive	179/180 (99.4%)	36.22	1.31	3.6	0.35	1.0	0.06	1.36	1.36	0.4	0.00	0.0	1.36	3.8
	Moderate Positive	179/180 (99.4%)	34.38	1.05	3.1	0.00	0.0	0.27	1.23	1.23	1.6	0.14	0.4	1.23	3.6

Analyte	Sample	Agreement with Expected	Detected Mean	Repeatability		Between Day		Between Site		Between Lot		Between Operator		Reproducibility	
	Negative	179/179 (100%)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
HSV-2	Low Positive	180/180 (100%)	33.73	1.19	3.5	0.25	0.7	0.00	1.23	1.23	0.0	0.00	0.0	1.23	3.6
	Moderate Positive	180/180 (100%)	31.86	0.96	3.0	0.00	0.0	0.19	1.10	1.10	0.5	0.14	0.4	1.10	3.5
	Negative	179/179 (100%)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
VZV	Low Positive	180/180 (100%)	35.79	1.29	3.6	0.00	0.0	0.34	1.34	1.34	0.5	0.00	0.0	1.34	3.7
	Moderate Positive	179/180 (99.4%)	33.99	0.52	1.5	0.00	0.0	0.25	0.64	0.64	0.6	0.17	0.5	0.64	1.9

External Control Performance

The Savanna HSV 1+2/VZV External Control Set, comprised of a pouched positive control swab and a negative control, was evaluated with the Savanna HSV 1+2/VZV Assay at 30 replicates each on three device lots for a total of 180 tests. The positive control produced 100% agreement to the expected positive results on all three device lots. The negative control produced 96.8% agreement to the expected results on one device lot and 100% agreement on the other two device lots.

Transport Media and Specimen Stability/Storage

Specimen stability in various Transport Media (Copan UTM, Remel M4RT, Remel M5, Remel M6) was evaluated. The following Co-spike samples were used in the test: Negative, Low Positive (2x LoD), and High Positive (4x LoD). Specimens collected in transport medium are stable when stored according to the conditions specified in **Table 9.**

Table 9. Transport Media Storage Claims

Transport Medium	Room Temperature (15-30ºC)	Refrigerated (4ºC)
Copan UTM	Up to 24 hours	Up to 48 hours
Remel M4RT	Up to 96 hours	Up to 96 hours
Remel M5	Up to 48 hours	Up to 96 hours
Remel M6	Up to 72 hours	Up to 72 hours

Clinical Performance

Performance characteristics of the Savanna HSV 1+2/VZV Assay were established through 2 multi-site clinical studies, testing cutaneous and mucocutaneous lesions from symptomatic individuals, as described below. Clinical Study 1 evaluated assay performance from fresh samples while clinical study 2 evaluated performance after residual samples were stored frozen.

Clinical Study #1

A multi-site study was conducted in the United States to evaluate the Savanna HSV 1+2/VZV Assay using cutaneous or mucocutaneous lesion samples in transport media. Five hundred and ninety (590) residual specimens were randomly selected from subjects with signs and symptoms of HSV-1, HSV-2 or VZV infection that were tested and for whom samples were collected in an all-comers fashion. A single replicate of each specimen was tested with both the candidate assay, Savanna HSV 1+2/VZV Assay and the comparator assay. Testing was split across three clinical sites and 44 Savanna instruments. Savanna HSV 1+2/VZV Control Sets were tested each day by the clinical sites during sample testing. The clinical performance of the Savanna HSV 1+2/VZV Assay was established by comparing to FDA-cleared nucleic acid amplification tests.

The specimens have been categorized as cutaneous (skin lesion, genital), or mucocutaneous (anorectal, genital, nares, ocular, oral and urethral). The gender and age demographics for each category are listed below.

Table 10. Subject Demographics – Clinical Study #1

Specimen	Age	Female	Male	Total
Cutaneous Lesion	<= 5 years	5	10	15
	6 to 21 years	13	10	23
	22 to 59 years	57	39	96
	>= 60 years	50	23	73
	Total	**125**	**82**	**207**
Mucocutaneous Lesion	<= 5 years	8	3	11
	6 to 21 years	50	24	74
	22 to 59 years	185	56	241
	>= 60 years	43	14	57
	Total	**286**	**97**	**383**
Total	<= 5 years	13	13	26
	6 to 21 years	63	34	97
	22 to 59 years	242	95	337
	>= 60 years	93	37	130
	Total	**411**	**179**	**590**

The clinical performance results compared to commercially available RT-PCR comparator method are shown in Tables 11 to 13, for cutaneous and mucocutaneous lesions separately.

Table 11: HSV1 Clinical performance for the Savanna HSV 1+2/VZV Assay in cutaneous and mucocutaneous fresh specimens

		HSV1 Results				
		Cutaneous (N=207)			Mucocutaneous (N=383)	
		Comparator			Comparator	
		Positive	Negative		Positive	Negative
Savanna HSV 1+2/VZV Assay Results	Positive	23	1		81	11
	Negative	2	181		0	291
	Total	25	182		81	302
		PPA= 92.00% (23/25) (75.04% - 97.78%)	NPA= 99.45% (181/182) (96.95% - 99.90%)		PPA= 100.00% (81/81) (95.47% - 100.00%)	NPA= 96.36% (291/302) (93.60% - 97.95%)

Table 12: HSV2 Clinical performance for the Savanna HSV 1+2/VZV Assay in cutaneous and mucocutaneous fresh specimens

		HSV2 Results				
		Cutaneous (N=207)			Mucocutaneous (N=383)	
		Comparator			Comparator	
		Positive	Negative		Positive	Negative
Savanna HSV 1+2/VZV Assay Results	Positive	13	0		50	3
	Negative	1	193		3	327
	Total	14	193		53	330
		PPA= 92.86% (13/14) (68.53% - 98.73%)	NPA= 100.00% (193/193) (98.05% - 100.00%)		PPA= 94.34% (50/53) (84.63% - 98.06%)	NPA= 99.09% (327/330) (97.36% - 99.69%)

Table 13: VZV Clinical performance for the Savanna HSV 1+2/VZV Assay in cutaneous and mucocutaneous fresh specimens

		VZV Results				
		Cutaneous (N=207)			Mucocutaneous (N=383)	
		Comparator			Comparator	
		Positive	Negative		Positive	Negative
Savanna HSV 1+2/VZV Assay Results	Positive	37	1		5	0
	Negative	0	169		0	377
	Total	37	170		5	377
		PPA= 100.00% (37/37) (90.60% - 100.00%)	NPA= 99.41% (169/170) (96.74% - 99.90%)		PPA= 100.00% (5/5) (56.56% - 100.00%)	NPA= 100.00% (377/377) (98.99% - 100.00%)

Clinical Study #2

Analysis of frozen residual cutaneous and mucocutaneous swab samples in transport medium was performed in July 2023 to supplement Clinical Study #1. The samples were residual specimens left over

from patients with signs and symptoms of HSV-1, HSV-2 or VZV infection. The total number of evaluable samples was one hundred fifty-four (154). The clinical study #2 performance results compared to commercially available RT- PCR comparator method(s) are shown in **Tables 14 to 16**.

Table 14: HSV1 Clinical performance for the Savanna HSV 1+2/VZV Assay in cutaneous and mucocutaneous residual frozen specimens

		HSV1 Results			
		Cutaneous (N=90)		Mucocutaneous (N=64)	
		Comparator		Comparator	
		Positive	Negative	Positive	Negative
Savanna HSV 1+2/VZV Assay Results	Positive	27	2	29	0
	Negative	0	61	0	35
	Total	27	63	29	35
		PPA= 100.00% (27/27) (87.55% - 100.00%)	NPA= 96.83% (61/63) (89.14% - 99.13%)	PPA= 100.00% (29/29) (88.31% - 100.00%)	NPA= 100.00% (35/35) (90.11% - 100.00%)

Table 15: HSV2 Clinical performance for the Savanna HSV 1+2/VZV Assay in cutaneous and mucocutaneous residual frozen specimens

		HSV2 Results			
		Cutaneous (N=90)		Mucocutaneous (N=64)	
		Comparator		Comparator	
		Positive	Negative	Positive	Negative
Savanna HSV 1+2/VZV Assay Results	Positive	30	0	15	1
	Negative	0	60	0	48
	Total	30	60	15	49
		PPA= 100.00% (30/30) (88.65% - 100.00%)	NPA= 100.00% (60/60) (93.98% - 100.00%)	PPA= 100.00% (15/15) (79.62% - 100.00%)	NPA= 97.96% (48/49) (89.31% - 99.64%)

Table 16: VZV Clinical performance for the Savanna HSV 1+2/VZV Assay in cutaneous and mucocutaneous residual frozen specimens

		VZV Results			
		Cutaneous (N=90)		Mucocutaneous (N=64)	
		Comparator		Comparator	
		Positive	Negative	Positive	Negative
Savanna HSV 1+2/VZV Assay Results	Positive	17	0	4	0
	Negative	0	73	0	60
	Total	17	73	4	60
		PPA= 100.00% (17/17) (81.57% - 100.00%)	NPA= 100.00% (73/73) (95.00% - 100.00%)	PPA= 100.01% (4/4) (51.02% - 100.01%)	NPA= 100.01% (60/60) (93.98% - 100.00%)

Conclusion

These studies demonstrated equivalent performance of the Savanna HSV 1+2/VZV Assay to the predicate product, the Solana HSV 1+2/VZV Assay.