510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K231978

B Applicant

VivaChek Biotech (Hangzhou) Co., Ltd

C Proprietary and Established Names

BioSieve™ Marijuana Test Panel 50; BioSieve™ Marijuana Test Strip 50; BioSieve™ Dx Marijuana Test Strip 20; BioSieve™ Dx Marijuana Test Strip 50; BioSieve™ Dx Marijuana Test Panel 20; BioSieve™ Dx Marijuana Test Panel 50

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
NFW	Class II	21 CFR 862.3870 - Cannabinoid Test System	TX - Clinical Toxicology

II Submission/Device Overview:

A Purpose for Submission:

New Device

B Measurand:

Marijuana (11-Nor-Δ^9-THC-9-COOH)

C Type of Test:

Qualitative lateral flow immunochromatographic assay

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

BioSieve™ Dx Marijuana Test Panel 20 is competitive binding, lateral flow immunochromatographic assay for qualitative detection of Marijuana in human urine at the cutoff concentrations of 20 ng/mL.

The test provides only preliminary test results. A more specific alternative chemical method must be used in order to obtain a confirmed analytical result. GC/MS or LC/MS is the preferred confirmatory method.

For in vitro diagnostic use only.

BioSieve™ Dx Marijuana Test Strip 20 is competitive binding, lateral flow immunochromatographic assay for qualitative detection of Marijuana in human urine at the cutoff concentrations of 20 ng/mL.

The test provides only preliminary test results. A more specific alternative chemical method must be used in order to obtain a confirmed analytical result. GC/MS or LC/MS is the preferred confirmatory method.

For in vitro diagnostic use only.

BioSieve™ Dx Marijuana Test Panel 50 is competitive binding, lateral flow immunochromatographic assay for qualitative detection of Marijuana in human urine at the cutoff concentrations of 50 ng/mL.

The test provides only preliminary test results. A more specific alternative chemical method must be used in order to obtain a confirmed analytical result. GC/MS or LC/MS is the preferred confirmatory method.

For in vitro diagnostic use only.

BioSieve™ Dx Marijuana Test Strip 50 is competitive binding, lateral flow immunochromatographic assay for qualitative detection of Marijuana in human urine at the cutoff concentrations of 50 ng/mL.

The test provides only preliminary test results. A more specific alternative chemical method must be used in order to obtain a confirmed analytical result. GC/MS or LC/MS is the preferred confirmatory method.

For in vitro diagnostic use only.

BioSieve™ Marijuana Test Panel 50 is competitive binding, lateral flow immunochromatographic assay for qualitative detection of Marijuana in human urine at the cutoff concentrations of 50 ng/mL.

The test provides only preliminary test results. A more specific alternative chemical method must be used in order to obtain a confirmed analytical result. GC/MS or LC/MS is the preferred confirmatory method.

For in vitro diagnostic use only.

BioSieve™ Marijuana Test Strip 50 is competitive binding, lateral flow immunochromatographic assay for qualitative detection of Marijuana in human urine at the cutoff concentrations of 50 ng/mL.

The test provides only preliminary test results. A more specific alternative chemical method must be used in order to obtain a confirmed analytical result. GC/MS or LC/MS is the preferred confirmatory method.

For in vitro diagnostic use only.

C Special Conditions for Use Statement(s):
Rx and OTC

OTC: BioSieve™ Marijuana Test Panel 50; BioSieve™ Marijuana Test Strip 50

Rx: BioSieve™ Dx Marijuana Test Strip 20; BioSieve™ Dx Marijuana Test Strip 50; BioSieve™ Dx Marijuana Test Panel 20; BioSieve™ Dx Marijuana Test Panel 50

D Special Instrument Requirements:

None

IV Device/System Characteristics:

A Device Description:

The BioSieve™ Marijuana Test Panel (Strip) and the BioSieve™ Dx Marijuana Test Panel (Strip) tests are immunochromatographic assays that use a lateral flow system for the qualitative detection of Marijuana in human urine. The products are single-use in vitro diagnostic devices. Each test kit contains a Test Device and a package insert. Each test device is sealed with a desiccant in an aluminum pouch.

B Principle of Operation:

The BioSieve™ Marijuana Test Panel and the BioSieve™ Marijuana Test Strip tests are rapid tests for the qualitative detection of marijuana in urine samples. They are lateral flow chromatographic immunoassays. When urine sample is added to the device, urine is absorbed into the test strip and migrates upwards by capillary action. If the concentration of target drug

presented in the urine sample is below the cutoff level, the target drug will not saturate the binding sites of its specific monoclonal antibody-coated particles. The antibody-coated particles will then be captured by immobilized drug-conjugate and a visible colored band will be formed on the test line region. If the concentration of target is beyond the cutoff level, the target drug will saturate the binding sites of its specific monoclonal antibody-particles, thus the antibody-coated particles will not be captured by immobilized drug-conjugate hence no colored band will be formed on the test line region. A band should be formed on the control line region regardless of the presence of target drug or metabolite in the sample to indicate that the tests have been performed properly.

V Substantial Equivalence Information:

A Predicate Device Name(s):
BIOEASY Marijuana Test Dip Card, BIOEASY Marijuana Test Strip

B Predicate 510(k) Number(s):
K192301

C Comparison with Predicate(s):

Device & Predicate Device(s):	K231978	K192301
Device Trade Name	BioSieve™ Marijuana Test Panel 50; BioSieve™ Marijuana Test Strip 50; BioSieve™ Dx Marijuana Test Strip 20; BioSieve™ Dx Marijuana Test Strip 50; BioSieve™ Dx Marijuana Test Panel 20; BioSieve™ Dx Marijuana Test Panel 50	BIOEASY Marijuana Test Dip Card, BIOEASY Marijuana Test Strip
General Device Characteristic Similarities		
Intended Use/Indications For Use	For the qualitative determination of marijuana in human urine.	Same
Methodology	Competitive binding, lateral flow immunochromatographic assay based on antigen-antibody reaction	Same
Type of Test	Qualitative	Same
Specimen Type	Human urine	Same
Calibrator	11-Nor-$\triangle^9$-THC-9-COOH	Same
General Device		

Characteristic Differences		
Type of Use	Prescription Use and over-the-counter use	Over-the-counter use
Cutoff Values	20 ng/mL or 50 ng/mL	50 ng/mL

VI Standards/Guidance Documents Referenced:

None Referenced.

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:
Precision studies were carried out for samples with concentrations of -100% cut off, -75% cut off, - 50% cut off, -25% cut off, cutoff, +25% cut off, +50% cut off, +75% cut off and +100% cut off at three different testing sites. Samples with concentration of -100% cutoff were drug-free urine samples. Other samples were prepared by spiking 11-Nor-Δ^9-THC-9-COOH in drug-free urine samples. Each 11-Nor-Δ^9-THC-9-COOH concentration was confirmed by LC/MS. For each concentration, tests were performed on two runs per day at each site for each lot for 10 days. The results obtained are summarized in the following tables:

For Strip Format of 20 ng/mL Cut-off:

Result / drug	-100% cut off	-75% cut off	-50% cut off	-25% cut off	cut off	+25% cut off	+50% cut off	+75% cut off	+100% cut off
Lot 1	60-/0+	60-/0+	60-/0+	42-/18+	32+/28-	46+/14-	60+/0-	60+/0-	60+/0-
Lot 2	60-/0+	60-/0+	60-/0+	43-/17+	35+/25-	42+/18-	60+/0-	60+/0-	60+/0-
Lot 3	60-/0+	60-/0+	60-/0+	41-/19+	33+/27-	45+/15-	60+/0-	60+/0-	60+/0-

For Panel Format of 20 ng/mL Cut-off:

Result / drug	-100% cut off	-75% cut off	-50% cut off	-25% cut off	cut off	+25% cut off	+50% cut off	+75% cut off	+100% cut off
Lot 1	60-/0+	60-/0+	60-/0+	43-/17+	34+/26-	44+/16-	60+/0-	60+/0-	60+/0-
Lot 2	60-/0+	60-/0+	60-/0+	44-/16+	35+/25-	46+/14-	60+/0-	60+/0-	60+/0-
Lot 3	60-/0+	60-/0+	60-/0+	43-/17+	37+/23-	45+/15-	60+/0-	60+/0-	60+/0-

For Strip Format of 50 ng/mL Cut-off:

Result / drug	-100% cut off	-75% cut off	-50% cut off	-25% cut off	cut off	+25% cut off	+50% cut off	+75% cut off	+100% cut off
Lot 1	60-/0+	60-/0+	60-/0+	60-/0+	24-/36+	60+/0-	60+/0-	60+/0-	60+/0-
Lot 2	60-/0+	60-/0+	60-/0+	60-/0+	22-/38+	60+/0-	60+/0-	60+/0-	60+/0-
Lot 3	60-/0+	60-/0+	60-/0+	60-/0+	23-/37+	60+/0-	60+/0-	60+/0-	60+/0-

For Panel Format of 50 ng/mL Cut-off:

Result / drug	-100% cut off	-75% cut off	-50% cut off	-25% cut off	cut off	+25% cut off	+50% cut off	+75% cut off	+100% cut off
Lot 1	60-/0+	60-/0+	60-/0+	60-/0+	30-/30+	60+/0-	60+/0-	60+/0-	60+/0-
Lot 2	60-/0+	60-/0+	60-/0+	60-/0+	26-/34+	60+/0-	60+/0-	60+/0-	60+/0-
Lot 3	60-/0+	60-/0+	60-/0+	60-/0+	28-/32+	60+/0-	60+/0-	60+/0-	60+/0-

2. Linearity:
   Not applicable. Devices are intended for qualitative determination only.

3. Analytical Specificity/Interference:

a) Specificity Study

To test the specificity, drug metabolites and other components that are likely to cross-react in urine samples were spiked into drug-free urine. These urine samples were tested using three lots of each format of the BioSieve™ Marijuana Test Panel and the BioSieve™ Marijuana Test Strip. Percent cross-reactivity, provided in the below table, was calculated as the cutoff concentration divided by the concentration of analyte tested that yielded a positive result, multiplied by 100; compounds that did not yield a positive result at the highest concentration tested have relative cross reactivity results represented by a dash in the table below:

THC(Cannabinoids) (11-nor-Δ^9-THC-9-COOH, Cut-off = 20 ng/mL)	**Result**	**% Cross-Reactivity**
11-nor-Δ^9-THC-9-COOH	20	100%
11-Hydroxy-Δ^9-Tetrahydrocannabinol	2000	1%
11-Nor-Δ^8-Tetrahydrocannabinol-9-COOH	20	100%
Cannabinol	100000	--
Δ^8-Tetrahydrocannabinol	6000	0.5%
Δ^9-Tetrahydrocannabinol	6000	0.5%
Cannabidiol	100000	--
11-Nor-Δ^9-THC-carboxy glucuronide	40	50%
(-)-11-nor-9-carboxy-Δ^9-THC	20	100%

THC(Cannabinoids) (11-nor-Δ^9-THC-9-COOH, Cut-off = 50 ng/mL)	**Result**	**% Cross-Reactivity**
11-nor-Δ^9-THC-9-COOH	50	100%
11-Hydroxy-Δ^9-Tetrahydrocannabinol	5000	1%
11-Nor-Δ^8-Tetrahydrocannabinol-9-COOH	50	100%
Cannabinol	100,000	--
Δ^8-Tetrahydrocannabinol	15,000	0.5%
Δ^9-Tetrahydrocannabinol	15,000	0.5%
Cannabidiol	100,000	--
11-Nor-Δ^9-THC-carboxy glucuronide	100	50%
(-)-11-nor-9-carboxy-Δ^9-THC	50	100%

b) Interfering substances study

Potential interfering substances were added to drug-free urine sample and samples with target drugs at -25% cutoff and +25% cutoff levels and tested with both the 50ng/mL cut-off strip and panel devices. Potential interfering substances were added to drug-free urine sample and samples with target drugs at -50% cutoff and +50% cutoff levels and tested with both the 20ng/mL cut-off strip and panel devices. Compounds that show no interference at a concentration of 100µg/mL (albumin was tested at 100 mg/dL and ethanol was tested at 1%) are listed below.

Acetaminophen, Acetophenetidin, N-Acetylprocainamide, Acetylsalicylic acid, Albumin (100mg/dL), Aminopyrine, Amoxicillin, Ampicillin, Apomorphine, Ascorbic acid, Aspartame, Atropine, Benzilic acid, Benzoic acid, Bilirubin, Chloral hydrate, Chloramphenicol, Chlorothiazide, Chlorpromazine, Cholesterol, Clonidine, Cortisone, (-)-Cotinine, Creatinine, Deoxycorticosterone, Dextromethorphan, Diclofenac, Diflunisal, Digoxin, Diphenhydramine, Ecgonine methyl ester, β-Estradiol, Erythromycin, Ethanol (1%v/v), Fenoprofen, Furosemide, Gentisic acid, Hemoglobin, Hydralazine, Hydrochlorothiazide, Hydrocortisone, O-Hydroxyhippuric acid, 3-Hydroxytyramine, Ibuprofen, Isoproterenol, Isoxsuprine, Ketamine, Ketoprofen, Labetalol, Loperamide, Meperidine, Meprobamate, Methoxyphenamine, Nalidixic acid, Naloxone, Naltrexone, Naproxen, Niacinamide, Nifedipine, Norethindrone, Noscapine, (±)-Octopamine, Oxalic acid, Oxolinic acid, Oxymetazoline, Papaverine, Penicillin G, Perphenazine, Phenelzine, Prednisone, (±)-Propranolol, Pseudoephedrine, Quinine, Ranitidine, Salicylic acid, Serotonin (5-, Hydroxytyramine), Sulfamethazine, Sulindac, Tetrahydrocortisone 3-(β-, Dglucuronide), Tetrahydrocortisone 3-, acetate, Tetrahydrozoline, Thiamine, Thioridazine, Triamterene, Trifluoperazine, Trimethoprim, DL-Tryptophan, Tyramine, DL-Tyrosine, Uric acid, Verapamil, Zomepirac

c) Effect of Urine Density

To investigate the effect of urine specific gravity, urine samples with specific gravity from 1.000 to 1.035 were spiked with target drug at +25% cutoff and -25% cutoff levels for the 50 ng/mL cut-off test strip and test panel devices. And the same urine specific gravity samples were spiked with target drug at +50% cutoff and -50% cutoff levels for the 20 ng/mL cutoff test strip and test panel devices. Three operators tested each sample using test devices from three different lots. The results were all positive for samples at +25% cutoff or +50% cutoff and all negative for samples at -25% cutoff or -50% cutoff, indicating that urine specific gravity between 1.000 and 1.035 does not interfere with device performance.

d) Effect of Urine pH

To investigate the effect of urine pH, urine samples with pH value from 4 to 9 were spiked with target drug at +25% cutoff and -25% cutoff levels for the 50 ng/mL cut-off test strip and test panel devices. And the same urine pH samples were spiked with target drug at +50% cut-off and -50% cutoff levels for the 20 ng/mL cut-off test strip and test panel devices. Three operators tested each sample using test devices from three different lots. The results were all positive for samples at +25% or +50% cutoff and all negative for samples at -25% or -50%

cut-off, indicating that urine pH values between 4.0 and 9.0 do not interfere with device performance.

4. Assay Reportable Range:

   Not applicable. The devices are intended for qualitative determinations only.

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):

   The devices are traceable to a commercial reference standard material.

6. Detection Limit:

   Not applicable.

7. Assay Cut-Off:

   For characterization of how the device performs analytically around the claimed cutoff concentrations, please refer to section VII.A.1 and VII. B.1.

B Comparison Studies:

1. Method Comparison with Predicate Device:

   The method comparison studies for all device configurations were performed with six operators at 3 sites. Operators ran 80 (40 negative and 40 positive) unaltered urine samples. Three different lots of devices were used for both the strip and panel format, one for each site. Two different operators at each site used either the strip or panel format. The samples were blind labeled and compared to LC/MS results. The results are presented in the table below:

BioSieve™ Dx Marijuana Test Strip 20

		Drug-Free	Low Negative by LC-MS/MS (less than -50%)	Near Cutoff Negative by LC-MS/MS (Between -50% and the Cutoff)	Near Cutoff Positive by LC-MS/MS (Between the cutoff and +50%)	High Positive by LC-MS/MS (greater than +50%)
Operator A	Positive	0	0	1	17	22
	Negative	10	16	13	1	0
Operator B	Positive	0	0	2	16	22
	Negative	10	16	12	2	0
Operator C	Positive	0	0	2	16	22
	Negative	10	16	12	2	0

Discordant Results:

Operator	Sample Number	LC/MS Result (ng/mL)	BioSieve™ Result
Operator A	22181	19.6	+
Operator B	22181	19.6	+
Operator B	22042	19.5	+
Operator C	22005	19.3	+
Operator C	22181	19.6	+
Operator A	22006	21.5	-
Operator B	22241	23.1	-
Operator B	22279	23.7	-
Operator C	22006	21.5	-
Operator C	22161	23.2	-

BioSieve™ Dx Marijuana Test Panel 20

		Drug-Free	Low Negative by LC-MS/MS (less than -50%)	Near Cutoff Negative by LC-MS/MS (Between -50% and the Cutoff)	Near Cutoff Positive by LC-MS/MS (Between the cutoff and +50%)	High Positive by LC-MS/MS (greater than +50%)
Operator A	Positive	0	0	2	16	22
	Negative	10	16	12	2	0
Operator B	Positive	0	0	2	17	22
	Negative	10	16	12	1	0
Operator C	Positive	0	0	1	16	22
	Negative	10	16	13	2	0

Discordant Results:

Operator	Sample Number	LC/MS Result (ng/mL)	BioSieve™ Result
Operator D	22071	19.3	+
Operator D	22073	19.6	+
Operator E	22071	19.3	+
Operator E	22204	19.5	+
Operator F	22073	19.6	+
Operator D	22205	23.7	-
Operator D	22302	21.5	-
Operator E	22302	21.5	-
Operator F	22016	23.2	-
Operator F	22302	21.5	-

BioSieve™ Marijuana Test Strip 50

		Drug-Free	Low Negative by LC-MS/MS (less than -50%)	Near Cutoff Negative by LC-MS/MS (Between -50% and the Cutoff)	Near Cutoff Positive by LC-MS/MS (Between the cutoff and +50%)	High Positive by LC-MS/MS (greater than +50%)
Operator A	Positive	0	0	2	16	22
	Negative	10	16	12	2	0
Operator B	Positive	0	0	2	16	22
	Negative	10	16	12	2	0
Operator C	Positive	0	0	1	16	22
	Negative	10	16	13	2	0

Discordant Results:

Operator	Sample Number	LC/MS Result (ng/mL)	BioSieve™ Result
Operator A	22172	49.2	+
Operator A	22318	46.8	+
Operator B	22115	47.8	+
Operator B	22172	49.2	+
Operator C	22172	49.2	+
Operator A	22013	50.5	-
Operator A	22237	50.9	-
Operator B	22237	50.9	-
Operator B	22284	53.9	-
Operator C	22013	50.5	-
Operator C	22237	50.9	-

BioSieve™ Marijuana Test Panel 50

		Drug-Free	Low Negative by LC-MS/MS (less than -50%)	Near Cutoff Negative by LC-MS/MS (Between -50% and the Cutoff)	Near Cutoff Positive by LC-MS/MS (Between the cutoff and +50%)	High Positive by LC-MS/MS (greater than +50%)
Operator A	Positive	0	0	1	16	22
	Negative	10	16	13	2	0
Operator B	Positive	0	0	1	16	22
	Negative	10	16	13	2	0

Operator C	Positive	0	0	2	16	22
	Negative	10	16	12	2	0

Discordant Results:

Operator	Sample Number	LC/MS Result (ng/mL)	BioSieve™ Result
Operator D	22217	46.8	+
Operator E	22206	49.2	+
Operator F	22017	47.8	+
Operator F	22206	49.2	+
Operator D	22137	50.9	-
Operator D	22152	53.9	-
Operator E	22103	50.5	-
Operator E	22137	50.9	-
Operator F	22103	50.5	-
Operator F	22152	53.9	-

2. Matrix Comparison:

   Not Applicable.

C Clinical Studies:

1. Clinical Sensitivity:

   Not applicable.

2. Clinical Specificity:

   Not applicable.

3. Other Clinical Supportive Data (When 1. and 2. Are Not Applicable):

   Read Time

   To investigate the effect of read time, urine samples were spiked with target drug at -100% cutoff, -50% cutoff, -25% cutoff, +25% cutoff, and +50% cutoff and were sampled at different reading times of 3, 4, 5, 10, 15, 20 minutes for the 50 ng/mL cut-off test panel and test strip devices. For the 20ng/mL cut-off test panel and test strip devices, urine samples were spiked with target drug at -100% cutoff, -50% cutoff, and +50% cutoff and were sampled at different reading times of 3, 4, 5, 10, 15, 20 minutes. Three operators tested each sample using test devices from three different lots. The results were all negative at -100% cutoff, -50% cutoff, -25% cutoff and all positive at +25% cutoff, and +50% cutoff levels for all read times evaluated.

Lay-user study:

A lay user study was performed at three sites (2 Health Service Centers, 1 Hospital) with 280 lay persons. The 280 aliquots were equally distributed to the three testing sites where one person tested one sample. The lay users had diverse educational and professional backgrounds and ranged in age from 18 to > 50 years. Urine samples were prepared at the following concentrations; negative, +/-75%, +/-50%, +/-25% of the 50 ng/mL cutoff by spiking 11-Nor-$\triangle^9$-THC-9-COOH into drug free-pooled urine specimens. The concentrations of the samples were confirmed by LC/MS. Each sample was aliquoted into individual containers and blind-labeled. Each participant was provided with the package insert, 1 blind labeled sample and a device. Summary results are shown below.

The results summary for strip format:

% of Cutoff	Number of samples	Drug Concentration by LC/MS/MS(ng/mL)	Lay person Results		The percentage of correct results (%)
			No. of Positive	No. of Negative	
-100% Cutoff	20	0	0	20	100
-75% Cutoff	20	12	0	20	100
-50% Cutoff	20	24.5	0	20	100
-25% Cutoff	20	36.2	1	19	95
+25% Cutoff	20	60.9	20	0	100
+50% Cutoff	20	76.2	20	0	100
+75% Cutoff	20	90.5	20	0	100

The results summary for panel format:

% of Cutoff	Number of samples	Drug Concentration by LC/MS/MS(ng/mL)	Lay person Results		The percentage of correct results (%)
			No. of Positive	No. of Negative	
-100% Cutoff	20	0	0	20	100
-75% Cutoff	20	12	0	20	100
-50% Cutoff	20	24.5	0	20	100
-25% Cutoff	20	36.2	1	19	95
+25% Cutoff	20	60.9	19	1	95
+50% Cutoff	20	76.2	20	0	100

+75% Cutoff	20	90.5	20	0	100

Participants were given surveys on the ease of understanding the instruction for use. All participants indicated that the device instruction is easy to understand and follow. A Flesch-Kincaid reading analysis was performed on each package insert and the scores revealed a reading Grade Level of 7.

D Clinical Cut-Off:

Not applicable.

E Expected Values/Reference Range:

Not applicable.

VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

IX Conclusion:

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