

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

A. 510(k) Number:

k110239

B. Purpose for Submission:

New device

C. Measurand:

Cannabinoids

D. Type of Test:

Qualitative and semi-quantitative immunoassay

E. Applicant:

Lin-Zhi International, Inc.

F. Proprietary and Established Names:

LZI Cannabinoids (cTHC) Enzyme Immunoassay

LZI Cannabinoids (cTHC) Drugs of Abuse (DAU) Calibrators

LZI Cannabinoids (cTHC) Drugs of Abuse (DAU) Controls

G. Regulatory Information:

| Product Code | Classification | Regulation Section | Panel |
|--------------|-------------------|--|---------------|
| LDJ | Class II | 21 CFR § 862.3870, Enzyme Immunoassay, Cannabinoids | 91-Toxicology |
| DLJ | Class II | 21 CFR § 862.3200, Calibrators, Drug specific | 91-Toxicology |
| LAS | Class I, reserved | 21 CFR 862.3280 Clinical Toxicology control material | 91-Toxicology |

H. Intended Use:

1. Intended use(s):

See Indications for use, below.

2. Indication(s) for use:

The LZI Cannabinoids (cTHC) Enzyme Immunoassay is intended for the qualitative and semi-quantitative determination of Cannabinoids in human urine using 11-nor- Δ^9 -THC-9-COOH (the major metabolite of THC

referred to here as cTHC) as calibrator at the cutoff values of 25, 50, or 100 ng/mL. The assay is designed for prescription use with a number of automated clinical chemistry analyzers.

The semi-quantitative mode is for purposes of

- (1) enabling laboratories to determine an appropriate dilution of the specimen for confirmation by a confirmatory method such as GCMS
- or
- (2) permitting laboratories to establish quality control procedures.

The Cannabinoids (cTHC) Drugs of Abuse (DOA) Calibrators are for use as calibrators in the qualitative and semi-quantitative calibration of the LZI Cannabinoids (cTHC) Enzyme Immunoassay.

The Cannabinoids (cTHC) Drugs of Abuse (DOA) Controls are for use as assayed quality control materials to monitor the precision of the LZI Cannabinoids (cTHC) Enzyme Immunoassay.

The assay provides only a preliminary analytical result. A more specific alternative chemical method must be used in order to obtain a confirmed analytical result. Gas or liquid chromatography/mass spectrometry (GC/MS or LC/MS) is the preferred confirmatory methods. Clinical consideration and professional judgment should be exercised with any drug of abuse test result, particularly when the preliminary test result is positive.

3. Special conditions for use statement(s):
The assay is for *in vitro* prescription use only.
4. Special instrument requirements:
Performance data was provided for Hitachi 717 analyzer.

I. Device Description:

The LZI Cannabinoids (cTHC) Enzyme Immunoassay consists of two separately packaged reagents (R1 and R2):

| Reagent | Description |
|---------|--|
| R1 | Contains mouse monoclonal anti-cannabinoid antibody, glucose-6-phosphate (G6P), nicotinamide adenine dinucleotide (NAD), and sodium azide as a preservative. |
| R2 | Contains cannabinoid derivative–labeled glucose-6-phosphate dehydrogenase (G6PDH) in buffer with sodium azide as a preservative. |

The calibrators and controls are ready to use human urine-based liquid.

J. Substantial Equivalence Information:

1. Predicate device names
Homogeneous enzyme immunoassay for the determination of cannabinoids (THC) level in urine
Cannabinoid Calibrators and Controls
2. Predicate 510(k) number(s):
k021887
k021449
3. Comparison with predicate:

| | | |
|-----------------|---|--|
| ITEM | The LZI Cannabinoids (cTHC) Enzyme Immunoassay LZI Cannabinoids (cTHC) Drugs of Abuse (DAU) Calibrators LZI Cannabinoids (cTHC) Drugs of Abuse (DAU) Controls | Homogeneous enzyme immunoassay for the determination of cannabinoids (THC) level in urine (021887) Cannabinoid Calibrators (021449) |
| Cutoff | 25, 50, and 100 ng/ml | 20, 50 and 100 |
| Intended Use | Qualitative and semi-quantitative analysis of cannabinoids in human urine | Same |
| Sample type | Human urine | Same |
| Type of reagent | Liquid ready to use Two reagent assay | Same |
| Calibrators | Liquid ready to use (5 levels) THC 25 : 0, 12.5, 25, 37.5, and 50 ng/mL THC 50: 0, 25, 50, 75 and 100 ng/mL THC 100: 0, 50, 100, 150, 200 ng/mL) | Liquid ready to use (5 levels) |
| Controls | Liquid ready to use (2 levels) THC 25: 18.75, 31.25 ng/mL THC 50: 37.5, 62.5 ng/mL THC 100: 75, 125 ng/mL | Liquid ready to use (2 levels) |

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

- CLSI Protocol EP5-A2: *Evaluation of Precision Performance of Quantitative Method-Second Edition*

L. Test Principle:

The LZI Cannabinoids (cTHC) is an immunoassay with ready-to-use liquid reagent. The assay is based on competition between drug in the sample and drug labeled with the enzyme glucose-6-phosphate dehydrogenase (G6PDH) for a fixed amount of antibody in the reagent. In the absence of drug in the sample, the antibody binds the conjugated 11-nor- Δ^9 -THC-9-COOH -labeled G6PDH. When free drug is present in the sample, the antibody will bind to the free drug and the unbound 11-nor- Δ^9 -THC-9-COOH -labeled G6PDH exhibits its maximal enzyme activity. The G6PDH activity is measured spectrophotometrically at 340 nm because of conversion of NAD to NADH.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Precision was performed and evaluated according to the CLSI Document EP5-A2, *Evaluation of Precision Performance of Quantitative Measurement Methods*. The sponsor conducted precision studies on the Hitachi 717 analyzer using samples containing 11-nor- Δ^9 -THC-9-COOH. Samples were prepared by spiking a negative human urine pool with 11-nor- Δ^9 -THC-9-COOH for all three cutoff values. Samples were tested in 2 replicates per run, 2 runs per day for 22 days, total N=88. The qualitative and semi-quantitative results confirmed by GC/MS for the cutoff values of 25 (THC 25), 50 (THC 50), or 100 ng/mL (THC 100) are presented below:

Qualitative Precision Data

| 25 ng/mL Cutoff Result (THC 25): | | Within Run | | Total Precision | |
|----------------------------------|-------------|-------------------------|--------------------|-------------------------|--------------------|
| Sample concentration (ng/mL) | % of Cutoff | Number of Determination | Immunoassay Result | Number of Determination | Immunoassay Result |
| 0 | negative | 22 | 22 Negative | 88 | 88 Negative |
| 6.25 | -75% | 22 | 22 Negative | 88 | 88 Negative |
| 12.50 | -50% | 22 | 22 Negative | 88 | 88 Negative |
| 18.75 | -25% | 22 | 22 Negative | 88 | 88 Negative |
| 25.00 | Cutoff | 22 | 11 Pos/11 Neg | 88 | 48 Pos/40 Neg |
| 31.25 | 25% | 22 | 22 Positive | 88 | 88 Positive |
| 37.50 | 50% | 22 | 22 Positive | 88 | 88 Positive |
| 43.75 | 75% | 22 | 22 Positive | 88 | 88 Positive |
| 50.00 | 200% | 22 | 22 Positive | 88 | 88 Positive |

Semi-Quantitative Precision Data

| 25 ng/mL Cutoff Result (THC 25): | | Within Run | | Total Precision | |
|---|--------------------|--------------------------------|---------------------------|--------------------------------|---------------------------|
| Sample concentration (ng/mL) | % of Cutoff | Number of Determination | Immunoassay Result | Number of Determination | Immunoassay Result |
| 0 | negative | 22 | 22 Negative | 88 | 88 Negative |
| 6.25 | -75% | 22 | 22 Negative | 88 | 88 Negative |
| 12.50 | -50% | 22 | 22 Negative | 88 | 88 Negative |
| 18.75 | -25% | 22 | 22 Negative | 88 | 88 Negative |
| 25.00 | Cutoff | 22 | 3 Pos/19 Neg | 88 | 19 Pos/69 Neg |
| 31.25 | 25% | 22 | 22 Positive | 88 | 88 Positive |
| 37.50 | 50% | 22 | 22 Positive | 88 | 88 Positive |
| 43.75 | 75% | 22 | 22 Positive | 88 | 88 Positive |
| 50.00 | 200% | 22 | 22 Positive | 88 | 88 Positive |

Qualitative Precision Data

| 50 ng/mL Cutoff Result (THC 50): | | Within Run | | Total Precision | |
|---|--------------------|--------------------------------|---------------------------|--------------------------------|---------------------------|
| Sample concentration (ng/mL) | % of Cutoff | Number of Determination | Immunoassay Result | Number of Determination | Immunoassay Result |
| 0 | negative | 22 | 22 Negative | 88 | 88 Negative |
| 12.5 | -75% | 22 | 22 Negative | 88 | 88 Negative |
| 25.0 | -50% | 22 | 22 Negative | 88 | 88 Negative |
| 37.5 | -25% | 22 | 22 Negative | 88 | 88 Negative |
| 50.0 | Cutoff | 22 | 5 Pos/17 Neg | 88 | 32 Pos/56 Neg |
| 62.5 | 25% | 22 | 22 Positive | 88 | 88 Positive |
| 75.0 | 50% | 22 | 22 Positive | 88 | 88 Positive |
| 87.5 | 75% | 22 | 22 Positive | 88 | 88 Positive |
| 100.0 | 200% | 22 | 22 Positive | 88 | 88 Positive |

Semi-Quantitative Precision Data

| 50 ng/mL Cutoff Result (THC 50): | | Within Run | | Total Precision | |
|---|--------------------|--------------------------------|---------------------------|--------------------------------|---------------------------|
| Sample concentration (ng/mL) | % of Cutoff | Number of Determination | Immunoassay Result | Number of Determination | Immunoassay Result |
| 0 | negative | 22 | 22 Negative | 88 | 88 Negative |
| 12.5 | -75% | 22 | 22 Negative | 88 | 88 Negative |
| 25.0 | -50% | 22 | 22 Negative | 88 | 88 Negative |
| 37.5 | -25% | 22 | 22 Negative | 88 | 88 Negative |
| 50.0 | Cutoff | 22 | 11 Pos/11 Neg | 88 | 38 Pos/50 Neg |

| | | | | | |
|-------|------|----|-------------|----|-------------|
| 62.5 | 25% | 22 | 22 Positive | 88 | 88 Positive |
| 75.0 | 50% | 22 | 22 Positive | 88 | 88 Positive |
| 87.5 | 75% | 22 | 22 Positive | 88 | 88 Positive |
| 100.0 | 200% | 22 | 22 Positive | 88 | 88 Positive |

Qualitative Precision Data

| 100 ng/mL Cutoff Result (THC 100): | | Within Run | | Total Precision | |
|---|--------------------|--------------------------------|---------------------------|--------------------------------|---------------------------|
| Sample concentration (ng/mL) | % of Cutoff | Number of Determination | Immunoassay Result | Number of Determination | Immunoassay Result |
| 0 | negative | 22 | 22 Negative | 88 | 88 Negative |
| 25 | -75% | 22 | 22 Negative | 88 | 88 Negative |
| 50 | -50% | 22 | 22 Negative | 88 | 88 Negative |
| 75 | -25% | 22 | 22 Negative | 88 | 88 Negative |
| 100 | Cutoff | 22 | 16 Pos/6 Neg | 88 | 53 Pos/35 Neg |
| 125 | 25% | 22 | 22 Positive | 88 | 88 Positive |
| 150 | 50% | 22 | 22 Positive | 88 | 88 Positive |
| 175 | 75% | 22 | 22 Positive | 88 | 88 Positive |
| 200 | 200% | 22 | 22 Positive | 88 | 88 Positive |

Semi-Quantitative Precision Data

| 100 ng/mL Cutoff Result (THC 100): | | Within Run | | Total Precision | |
|---|--------------------|--------------------------------|---------------------------|--------------------------------|---------------------------|
| Sample concentration (ng/mL) | % of Cutoff | Number of Determination | Immunoassay Result | Number of Determination | Immunoassay Result |
| 0 | negative | 22 | 22 Negative | 88 | 88 Negative |
| 25 | -75% | 22 | 22 Negative | 88 | 88 Negative |
| 50 | -50% | 22 | 22 Negative | 88 | 88 Negative |
| 75 | -25% | 22 | 22 Negative | 88 | 88 Negative |
| 100 | Cutoff | 22 | 22 Negative | 88 | 10 Pos/78 Neg |
| 125 | 25% | 22 | 22 Positive | 88 | 88 Positive |
| 150 | 50% | 22 | 22 Positive | 88 | 88 Positive |
| 175 | 75% | 22 | 22 Positive | 88 | 88 Positive |
| 200 | 200% | 22 | 22 Positive | 88 | 88 Positive |

b. Linearity/assay reportable range:

The sponsor performed recovery studies by serially diluting a spiked urine pool containing 11-nor- Δ^9 -THC-9-COOH for all three cutoff concentrations (THC 25, THC 50 and THC 100 ng/mL). Each sample from these studies was run in 10 replicates on the Hitachi 717 analyzer. The results were averaged and compared

to the expected result and the percent recovery was calculated. The linearity results are presented below:

THC 25

| Expected Concentration (ng/mL) | Observed Concentration (ng/mL) | % Recovery (Observed/Expected x 100) |
|--------------------------------|--------------------------------|--------------------------------------|
| 0 | 0.9 | Not applicable |
| 5 | 5.4 | 108.78 |
| 10 | 9.6 | 95.61 |
| 15 | 13.4 | 89.34 |
| 20 | 18.0 | 90.08 |
| 25 | 23.3 | 93.35 |
| 30 | 28.0 | 93.47 |
| 35 | 33.4 | 95.32 |
| 40 | 38.9 | 97.28 |
| 45 | 44.3 | 98.53 |
| 50 | 47.6 | 95.12 |

THC 50

| Expected Concentration (ng/mL) | Observed Concentration (ng/mL) | % Recovery (Observed/Expected x 100) |
|--------------------------------|--------------------------------|--------------------------------------|
| 0 | 0.4 | Not applicable |
| 10 | 11.3 | 112.9 |
| 20 | 20.2 | 101.1 |
| 30 | 29.6 | 98.5 |
| 40 | 39.2 | 98.0 |
| 50 | 51.6 | 103.2 |
| 60 | 62.2 | 103.7 |
| 70 | 74.0 | 105.7 |
| 80 | 82.7 | 103.4 |
| 90 | 92.9 | 103.3 |
| 100 | 101.6 | 101.6 |

THC 100

| Expected Concentration (ng/mL) | Observed Concentration (ng/mL) | % Recovery (Observed/Expected x 100) |
|--------------------------------|--------------------------------|--------------------------------------|
| 0 | 1.93 | Not applicable |
| 15 | 21.5 | 143.20 |
| 40 | 44.8 | 111.95 |
| 60 | 62.4 | 104.02 |
| 80 | 80.0 | 99.96 |
| 100 | 103.2 | 103.21 |

| | | |
|-----|-------|--------|
| 120 | 128.1 | 106.71 |
| 140 | 137.5 | 98.21 |
| 160 | 157.3 | 98.33 |
| 180 | 181.3 | 100.74 |
| 200 | 195.2 | 97.60 |

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

Traceability and value assignment

Stability

A stock solution of 1000 µg/mL 11-nor- Δ^9 -THC-9-COOH purchased from a commercial source is spiked into the calibrator and controls to the desired concentration. The concentration of the calibrator and controls are confirmed by GC/MS. Purity determination and gravimetric preparation using balances calibrated with NIST traceable weights ensure the accuracy of the stock standard solution. The sponsor claimed open-recapped and closed stability of 18 months at 2 to 8°C for the calibrator and control bottles. After the calibrator and control bottles are initially opened, the screw-on caps can be resealed. The study protocols, summary of the results and acceptance criteria were reviewed and found to be adequate.

d. Detection limit:

Performance at low drug concentrations in the semi-quantitative assay was characterized by determination of recovery (see section b above).

e. Analytical specificity:

The sponsor performed studies to evaluate effect of different substances on the performance of the assay for all three cutoff concentrations. These studies were performed by spiking structurally related and unrelated compounds into drug-free and drug-containing urine samples. Drug-containing urine samples were tested at two different concentrations, +25% and -25% of the cut-off concentration of 25, 50 and 100 ng/mL. Drug-free urine samples were used as controls. % cross-reactivity was calculated using the cross-reactant concentration that gives a reaction absorbance which matches the reaction absorbance obtained by the cut-off calibrator. The cut-off calibrator concentration divided by the cross-reactant concentration that achieved the matching reactant absorbance x 100% gives the % cross reactivity. The percent cross-reactivity of the tested compounds is summarized below:

Structurally related compounds:

THC 25

| Compound | Target concentration (ng/mL) | Cross-reactivity (%) |
|----------|------------------------------|----------------------|
| | | |

| | | |
|---|-------|--------|
| 11-nor- Δ^9 -THC-9-COOH | 25 | 100% |
| 8- β -hydroxy- Δ^9 -THC | 40 | 65.45% |
| 8- β -dihydroxy- Δ^9 -THC | 40 | 50.54% |
| Cannabidiol | 4,500 | 0.48% |
| Cannabinol | 120 | 23.51% |
| exo - THC | 50 | 57.53% |
| <i>l</i> -11-Hydroxy- Δ^9 -THC | 40 | 93.99% |
| <i>l</i> -11-Nor- Δ^9 -THC-Carboxylic Acid | 25 | 97.30% |
| <i>l</i> -11-Nor- Δ^9 -THC-Carboxylic acil-Glucuronide | 1,500 | 1.42% |
| Δ^8 -THC | 50 | 63.59% |
| Δ^9 -THC | 100 | 35.79% |

THC 50

| Compound | Target concentration (ng/mL) | Cross-reactivity (%) |
|---|------------------------------|----------------------|
| 11-nor- Δ^9 -THC-9-COOH | 50 | 100% |
| 8- β -hydroxy- Δ^9 -THC | 80 | 58.00% |
| 8- β -dihydroxy- Δ^9 -THC | 90 | 45.44% |
| Cannabidiol | 9,000 | 0.51% |
| Cannabinol | 220 | 21.07% |
| exo - THC | 90 | 52.00% |
| <i>l</i> -11-Hydroxy- Δ^9 -THC | 55 | 96.00% |
| <i>l</i> -11-Nor- Δ^9 -THC-Carboxylic Acid | 50 | 98.80% |
| <i>l</i> -11-Nor- Δ^9 -THC-Carboxylic acil-Glucuronide | 5,000 | 1.41% |
| Δ^8 -THC | 90 | 51.78% |
| Δ^9 -THC | 140 | 33.11% |

THC 100

| Compound | Target concentration (ng/mL) | Cross-reactivity (%) |
|---|------------------------------|----------------------|
| 11-nor- Δ^9 -THC-9-COOH | 100 | 100% |
| 8- β -hydroxy- Δ^9 -THC | 140 | 60.68% |
| 8- β -dihydroxy- Δ^9 -THC | 160 | 44.81% |
| Cannabidiol | 16,000 | 0.53% |
| Cannabinol | 400 | 24.50% |
| exo - THC | 160 | 60.00% |
| <i>l</i> -11-Hydroxy- Δ^9 -THC | 100 | 101.50% |
| <i>l</i> -11-Nor- Δ^9 -THC-Carboxylic Acid | 100 | 97.40% |

| | | |
|---|-------|--------|
| <i>l</i> -11-Nor- Δ^9 -THC-Carboxylic acid-Glucuronide | 6,000 | 1.50% |
| Δ^8 -THC | 160 | 61.59% |
| Δ^9 -THC | 260 | 36.48% |

Structurally unrelated compounds:

THC 25

| Compound | Tested Concentration (ng/mL) | -25% 11-nor- Δ^9 -THC-9-COOH (18.75 ng/mL) | +25% 11-nor- Δ^9 -THC-9-COOH (31.25 ng/mL) |
|--|------------------------------|---|---|
| Acetaminophen | 500,000 | Negative | Positive |
| Acetylsalicylic acid | 500,000 | Negative | Positive |
| Amitriptyline | 100,000 | Negative | Positive |
| Amobarbital | 500,000 | Negative | Positive |
| Amphetamine | 500,000 | Negative | Positive |
| Benzoylcegonine | 500,000 | Negative | Positive |
| Burpropion | 500,000 | Negative | Positive |
| Caffeine | 500,000 | Negative | Positive |
| Chlorpheniramine | 500,000 | Negative | Positive |
| Chlorpromazine | 100,000 | Negative | Positive |
| Cocaine | 500,000 | Negative | Positive |
| Codeine | 500,000 | Negative | Positive |
| Dextromethorphan | 100,000 | Negative | Positive |
| Ecgonine methyl ester | 500,000 | Negative | Positive |
| d,l-Ephedrine | 500,000 | Negative | Positive |
| Imipramine | 100,000 | Negative | Positive |
| JWH-018(1-pentyl-3(1-naphthoyl)indole) | 500,000 | Negative | Positive |
| JWH-073(1-butyl-3(1-naphthoyl)indole) | 500,000 | Negative | Positive |
| Lidocaine | 500,000 | Negative | Positive |
| Meperidine | 500,000 | Negative | Positive |
| Methadone | 500,000 | Negative | Positive |
| Methamphetamine | 500,000 | Negative | Positive |
| Methaqualone | 500,000 | Negative | Positive |
| Morpine | 500,000 | Negative | Positive |
| Nortriptyline | 100,000 | Negative | Positive |
| Oxazepam | 500,000 | Negative | Positive |
| Phencyclidine | 500,000 | Negative | Positive |
| Phentobarbital | 500,000 | Negative | Positive |
| Promethazine | 100,000 | Negative | Positive |
| Propoxyphene | 500,000 | Negative | Positive |
| Ranitidine | 500,000 | Negative | Positive |

| | | | |
|---------------|---------|----------|----------|
| Secobarbital | 500,000 | Negative | Positive |
| Valproic acid | 500,000 | Negative | Positive |

THC 50

| Compound | Tested Concentration (ng/mL) | -25% 11-nor- Δ^9 -THC-9-COOH (37.5 ng/mL) | +25% 11-nor- Δ^9 -THC-9-COOH (62.5 ng/mL) |
|--|------------------------------|--|--|
| Acetaminophen | 500,000 | Negative | Positive |
| Acetylsalicylic acid | 500,000 | Negative | Positive |
| Amitriptyline | 500,000 | Negative | Positive |
| Amobarbital | 500,000 | Negative | Positive |
| Amphetamine | 500,000 | Negative | Positive |
| Benzoylcegonine | 500,000 | Negative | Positive |
| Burpropion | 500,000 | Negative | Positive |
| Caffeine | 500,000 | Negative | Positive |
| Chlorpheniramine | 500,000 | Negative | Positive |
| Chlorpromazine | 500,000 | Negative | Positive |
| Cocaine | 500,000 | Negative | Positive |
| Codeine | 500,000 | Negative | Positive |
| Dextromethorphan | 100,000 | Negative | Positive |
| Ecgonine methyl ester | 500,000 | Negative | Positive |
| d,l-Ephedrine | 500,000 | Negative | Positive |
| Imipramine | 500,000 | Negative | Positive |
| JWH-018(1-pentyl-3(1-naphthoyl)indole) | 500,000 | Negative | Positive |
| JWH-073(1-butyl-3(1-naphthoyl)indole) | 500,000 | Negative | Positive |
| Lidocaine | 500,000 | Negative | Positive |
| Meperidine | 500,000 | Negative | Positive |
| Methadone | 500,000 | Negative | Positive |
| Methamphetamine | 500,000 | Negative | Positive |
| Methaqualone | 500,000 | Negative | Positive |
| Morphine | 500,000 | Negative | Positive |
| Nortriptyline | 500,000 | Negative | Positive |
| Oxazepam | 500,000 | Negative | Positive |
| Phencyclidine | 500,000 | Negative | Positive |
| Phentobarbital | 500,000 | Negative | Positive |
| Promethazine | 100,000 | Negative | Positive |
| Propoxyphene | 500,000 | Negative | Positive |
| Ranitidine | 500,000 | Negative | Positive |
| Secobarbital | 500,000 | Negative | Positive |
| Valproic acid | 500,000 | Negative | Positive |

THC 100

| Compound | Tested Concentration (ng/mL) | -25% 11-nor- Δ^9 -THC-9-COOH (75 ng/mL) | +25% 11-nor- Δ^9 -THC-9-COOH (125 ng/mL) |
|--|------------------------------|--|---|
| Acetaminophen | 500,000 | Negative | Positive |
| Acetylsalicylic acid | 500,000 | Negative | Positive |
| Amitriptyline | 500,000 | Negative | Positive |
| Amobarbital | 500,000 | Negative | Positive |
| Amphetamine | 500,000 | Negative | Positive |
| Benzoylcegonine | 500,000 | Negative | Positive |
| Burpropion | 500,000 | Negative | Positive |
| Caffeine | 500,000 | Negative | Positive |
| Chlorpheniramine | 500,000 | Negative | Positive |
| Chlorpromazine | 500,000 | Negative | Positive |
| Cocaine | 500,000 | Negative | Positive |
| Codeine | 500,000 | Negative | Positive |
| Dextromethorphan | 100,000 | Negative | Positive |
| Ecgonine methyl ester | 500,000 | Negative | Positive |
| d,l-Ephedrine | 500,000 | Negative | Positive |
| Imipramine | 500,000 | Negative | Positive |
| JWH-018(1-pentyl-3(1-naphthoyl)indole) | 500,000 | Negative | Positive |
| JWH-073(1-butyl-3(1-naphthoyl)indole) | 500,000 | Negative | Positive |
| Lidocaine | 500,000 | Negative | Positive |
| Meperidine | 500,000 | Negative | Positive |
| Methadone | 500,000 | Negative | Positive |
| Methamphetamine | 500,000 | Negative | Positive |
| Methaqualone | 500,000 | Negative | Positive |
| Morphine | 500,000 | Negative | Positive |
| Nortriptyline | 500,000 | Negative | Positive |
| Oxazepam | 500,000 | Negative | Positive |
| Phencyclidine | 500,000 | Negative | Positive |
| Phentobarbital | 500,000 | Negative | Positive |
| Promethazine | 100,000 | Negative | Positive |
| Propoxyphene | 500,000 | Negative | Positive |
| Ranitidine | 500,000 | Negative | Positive |
| Secobarbital | 500,000 | Negative | Positive |
| Valproic acid | 500,000 | Negative | Positive |

Endogenous compounds:

The following endogenous compounds were added into drug-free urine and drug containing urine sample at the concentrations of $\pm 25\%$ surrounding all three cutoff concentrations. The substances listed in the table below were determined not to interfere at the concentration shown:

THC 25, THC 50 and THC 100

| Compound | Tested Concentration (mg/dL) |
|---------------------|-----------------------------------|
| Acetone | 1000 |
| Ascorbic acid | 500 |
| Creatinine | 500 |
| Ethanol | 1000 |
| Galactose | 10 |
| γ -Globulin | 500 |
| Glucose | 1500 |
| Hemoglobin | 300 |
| Human Serum Albumin | 500 |
| Oxalic acid | 100 |
| Riboflavin | 0.25 (THC25) 0.65 (THC50, THC100) |
| Sodium chloride | 2000 |
| Urea | 2000 |

In addition, pH levels of 3 to 11 had no effect on the performance of the assay. Further, variations in specific gravity between 1.002 and 1.024 had no effect on results.

The package insert includes the complete list of all structurally related and unrelated compounds and metabolites tested.

f. Assay cut-off:

Analytical performance of the device around the claimed cutoff is described in precision section (1 a.) above.

2. Comparison studies:

a. Method comparison with predicate device:

THC 25:

Forty-four (44) positive and forty-three (43) negative unaltered clinical urine samples were evaluated by the LZI Cannabinoids (cTHC) Enzyme Immunoassay and compared to GC/MS or LC/MS for 11-nor- Δ^9 -THC-9-COOH concentration. Results from the study are presented below:

THC 25 - Qualitative

| THC 25 | Negative | < 50% of the cutoff | Near Cutoff Negative (between 50% below the cutoff and the cutoff) | Near Cutoff Positive (concentration between 50% above the cutoff and the cutoff) | High Positive > 50% above the cutoff | % Agreement |
|----------|----------|---------------------|--|--|--------------------------------------|-------------|
| Positive | 0 | 1 | 7 | 15 | 29 | 100.00% |
| Negative | 12 | 16 | 7 | 0 | 0 | 83.72% |

THC 25 - Semi-quantitative

| THC 25 | Negative | < 50% of the cutoff | Near Cutoff Negative (between 50% below the cutoff and the cutoff) | Near Cutoff Positive (concentration between 50% above the cutoff and the cutoff) | > 50% above the cutoff | % Agreement |
|----------|----------|---------------------|--|--|------------------------|-------------|
| Positive | 0 | 1 | 7 | 15 | 29 | 100.00% |
| Negative | 12 | 16 | 7 | 0 | 0 | 83.72% |

Summary of Discordant Results in Qualitative/Semi-Quantitative mode:

| Discordant Cut-off | LZI Cannabinoid Assay (POS/NEG) | Drug/Metabolite GC/MS value (ng/mL) |
|--------------------|---------------------------------|-------------------------------------|
| THC 25 | | |
| 25 ng/mL | POS | 7 |
| | POS | 19 |
| | POS | 20 |
| | POS | 21 |
| | POS | 23 |
| | POS | 23 |
| | POS | 24 |
| | POS | 24 |

A new study with additional unaltered patient samples (eleven (11) positive and twelve (12) negative)) was performed to support method comparison. Results from the additional study are presented below:

THC 25 – Qualitative mode

| THC 50 | Negative | < 50% of the cutoff | Near Cutoff Negative (between 50% below the cutoff and the cutoff) | Near Cutoff Positive (concentration between 50% above the cutoff and the cutoff) | High Positive > 50% above the cutoff | % Agreement |
|----------|----------|---------------------|--|--|--------------------------------------|-------------|
| Positive | 0 | 0 | 1 | 3 | 8 | 100.00% |
| Negative | 2 | 7 | 2 | 0 | 0 | 91.67% |

THC 25 – Semi-quantitative mode

| THC 50 | Negative | < 50% of the cutoff | Near Cutoff Negative (between 50% below the cutoff and the cutoff) | Near Cutoff Positive (concentration between 50% above the cutoff and the cutoff) | High Positive > 50% above the cutoff | % Agreement |
|----------|----------|---------------------|--|--|--------------------------------------|-------------|
| Positive | 0 | 0 | 1 | 3 | 8 | 100.00% |
| Negative | 2 | 7 | 2 | 0 | 0 | 91.67% |

| Discordant Cut-off | LZI Cannabinoid Assay (POS/NEG) | Drug/Metabolite GC/MS value (ng/mL) |
|--------------------|---------------------------------|-------------------------------------|
| THC 50 | | |
| 50 ng/mL | POS | 16 |

THC 50:

Forty-three (43) positive and forty-three (43) negative unaltered clinical urine samples were evaluated by the LZI Cannabinoids (cTHC) Enzyme Immunoassay and compared to GC/MS or LC/MS for 11-nor- Δ^9 -THC-9-COOH concentration. Results from the study are presented below:

THC 50 – Qualitative mode

| THC 50 | Negative | < 50% of the cutoff | Near Cutoff Negative (between 50% below the cutoff and the cutoff) | Near Cutoff Positive (concentration between 50% above the cutoff and the cutoff) | High Positive > 50% above the cutoff | % Agreement |
|----------|----------|---------------------|--|--|--------------------------------------|-------------|
| Positive | 0 | 1 | 5 | 15 | 28 | 100.00% |
| Negative | 11 | 17 | 9 | 0 | 0 | 86.00% |

THC 50 – Semi-quantitative mode

| THC 50 | Negative | < 50% of the cutoff | Near Cutoff Negative (between 50% below the cutoff and the cutoff) | Near Cutoff Positive (concentration between 50% above the cutoff and the cutoff) | > 50% above the cutoff | % Agreement |
|----------|----------|---------------------|--|--|------------------------|-------------|
| Positive | 0 | 0 | 3 | 15 | 28 | 100.00% |
| Negative | 11 | 17 | 12 | 0 | 0 | 93% |

Summary of Discordant Results in Qualitative mode:

| Discordant Cut-off | LZI Cannabinoid Assay (POS/NEG) | Drug/Metabolite GC/MS value (ng/mL) |
|--------------------|---------------------------------|-------------------------------------|
| THC 50 | | |
| 50 ng/mL | POS | 7 |
| | POS | 27 |
| | POS | 36 |
| | POS | 37 |
| | POS | 46 |
| | POS | 48 |

Summary of Discordant Results in Semi-Quantitative mode:

| Discordant Cut-off | LZI Cannabinoid Assay (POS/NEG) | Drug/Metabolite GC/MS value (ng/mL) |
|--------------------|---------------------------------|-------------------------------------|
| THC 50 | | |
| 50 ng/mL | POS | 36 |
| | POS | 46 |
| | POS | 48 |

A new study with additional unaltered patient samples (twenty-two (22) positive and

twenty-five (25) negative)) was performed to support method comparison. Results from the additional study are presented below:

THC 50 – Qualitative mode

| THC 50 | Negative | < 50% of the cutoff | Near Cutoff Negative (between 50% below the cutoff and the cutoff) | Near Cutoff Positive (concentration between 50% above the cutoff and the cutoff) | High Positive > 50% above the cutoff | % Agreement |
|----------|----------|---------------------|--|--|--------------------------------------|-------------|
| Positive | 0 | 0 | 3 | 0 | 22 | 100.00% |
| Negative | 0 | 19 | 3 | 0 | 0 | 92.00% |

THC 50 – Semi-quantitative mode

| THC 50 | Negative | < 50% of the cutoff | Near Cutoff Negative (between 50% below the cutoff and the cutoff) | Near Cutoff Positive (concentration between 50% above the cutoff and the cutoff) | > 50% above the cutoff | % Agreement |
|----------|----------|---------------------|--|--|------------------------|-------------|
| Positive | 0 | 0 | 2 | 0 | 22 | 100.00% |
| Negative | 0 | 19 | 4 | 0 | 0 | 92.00% |

Summary of Discordant Results in Qualitative mode:

| Discordant Cut-off | LZI Cannabinoid Assay (POS/NEG) | Drug/Metabolite GC/MS value (ng/mL) |
|--------------------|---------------------------------|-------------------------------------|
| THC 50 50 ng/mL | POS | 44.7 |
| | POS | 48 |
| | POS | 49.3 |

Summary of Discordant Results in Quantitative mode:

| Discordant Cut-off | LZI Cannabinoid Assay (POS/NEG) | Drug/Metabolite GC/MS value (ng/mL) |
|--------------------|---------------------------------|-------------------------------------|
| THC 50 50 ng/mL | POS | 44.7 |
| | POS | 48 |

THC 100:

Forty (40) positive and forty-two (42) negative unaltered clinical urine

samples were evaluated by the LZI Cannabinoids (cTHC) Enzyme Immunoassay and compared to GC/MS or LC/MS for 11-nor- Δ^9 -THC-9-COOH concentration. Results from the study are presented below:

THC 100 – Qualitative mode

| THC 100 | Negative | < 50% of the cutoff | Near Cutoff Negative (between 50% below the cutoff and the cutoff) | Near Cutoff Positive (concentration between 50% above the cutoff and the cutoff) | High Positive > 50% above the cutoff | % Agreement |
|----------|----------|---------------------|--|--|--------------------------------------|-------------|
| Positive | 0 | 0 | 4 | 15 | 25 | 100.00% |
| Negative | 2 | 30 | 6 | 0 | 0 | 90.48% |

THC 100 – Semi-quantitative mode

| THC 100 | Negative | < 50% of the cutoff | Near Cutoff Negative (between 50% below the cutoff and the cutoff) | Near Cutoff Positive (concentration between 50% above the cutoff and the cutoff) | > 50% above the cutoff | % Agreement |
|----------|----------|---------------------|--|--|------------------------|-------------|
| Positive | 0 | 0 | 4 | 15 | 25 | 100.00% |
| Negative | 2 | 30 | 6 | 0 | 0 | 90.48% |

Summary of Discordant Results in Qualitative/Semi-Quantitative mode:

| Discordant Cut-off | LZI Cannabinoid Assay (POS/NEG) | Drug/Metabolite GC/MS value (ng/mL) |
|--------------------|---------------------------------|-------------------------------------|
| THC 100 | | |
| 100 ng/mL | POS | 83 |
| | POS | 83 |
| | POS | 85 |
| | POS | 96 |

b. *Matrix comparison:*

Not applicable. The test is only for urine specimens.

3. Clinical studies:

a. *Clinical Sensitivity:*

Not applicable. Not reviewed for this device type.

b. Clinical specificity:

Not applicable. Not reviewed for this device type.

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:

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.