March 18, 2025

Hangzhou Laihe Biotech Co., Ltd.
% Ethan Liu
RA Specialist
Shanghai Thinkwell Consulting Co., Ltd.
Xinling Rd., 211/6F
Shanghai, 201100
China

Re: K240287
Trade/Device Name: LYHER® Oral fluid Multi-Drug Test Kit (Cube)
Regulation Number: 21 CFR 862.3610
Regulation Name: Methamphetamine Test System
Regulatory Class: Class II
Product Code: DJC, DIO, DJG, DKZ, LCM, LDJ
Dated: January 24, 2025
Received: February 6, 2025

Dear Ethan 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.

All medical devices, including Class I and unclassified devices and combination product device constituent parts are required to be in compliance with the final Unique Device Identification System rule ("UDI Rule"). The UDI Rule requires, among other things, that a device bear a unique device identifier (UDI) on its label and package (21 CFR 801.20(a)) unless an exception or alternative applies (21 CFR 801.20(b)) and that the dates on the device label be formatted in accordance with 21 CFR 801.18. The UDI Rule (21 CFR 830.300(a) and 830.320(b)) also requires that certain information be submitted to the Global Unique Device Identification Database (GUDID) (21 CFR Part 830 Subpart E). For additional information on these requirements, please see the UDI System webpage at https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/unique-device-identification-system-udi-system.

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,

Marianela Perez-torres -S

Marianela Perez-Torres, Ph.D.
Director
Division of Chemistry and
Toxicology Devices
OHT7: Office of In Vitro Diagnostics
Office of Product Evaluation and Quality
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)*
K240287

Device Name
LYHER® Oral fluid Multi-Drug Test Kit (Cube)

Indications for Use *(Describe)*
The LYHER® Oral fluid Multi-Drug Test Kit (Cube) is a rapid lateral flow immunoassay for the qualitative detection of d-Amphetamine, d-Methamphetamine, Benzoylecgonine, Morphine, Phencyclidine and Delta-9-Tetrahydrocannabinol in human oral fluid. The test cut-off concentrations and the compounds the tests are calibrated to are as follows:

Test	Calibrator	Cut-off (ng/mL)
Opiates(OPI)	Morphine	40
Cocaine (COC)	Benzoylecgonine	20
Amphetamine (AMP)	d-Amphetamine	50
Marijuana (THC)	Delta-9-Tetrahydrocannabinol	40
Methamphetamine (MET)	d-Methamphetamine	50
Phencyclidine (PCP)	Phencyclidine	10

The single or multi-test panels can consist of the above listed analytes in anycombination, up to a maximum of 6 analytes. The tests provide only a preliminary result. A more specific alternate chemical method must be used in order to obtain a confirmed analytical test result. Gas Chromatography/Mass Spectrometry (GC/MS), Liquid Chromatography / Mass Spectrometry (LC/MS) and their tandem mass-spectrometer versions are the preferred confirmatory methods. Careful consideration and judgment should be applied to any drugs of abuse screen test result, particularly when evaluating preliminary positive results.

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.

510(k) Summary

K240287

This summary of 510(k) safety and effectiveness information is being submitted in accordance with requirements of 21 CFR Part 807.92.

1. Submitter

Submitted by:	Hangzhou Laihe Biotech Co., Ltd. Address: Room 401-406, F1-3, Building 1, No.425 Miaohouwang Road, Xixing Street, Binjiang District, Hangzhou, 310051 Zhejiang P.R. China Tel.: +86 571 8765 3090 Fax: +86 571 8665 8000 www.lyher.com
Contact Person:	Ethan Liu Shanghai Thinkwell Consulting Co., Ltd Address:Xinling Rd., 211/6F Shanghai, 201100,P.R. China Phone:0086-15216699240 Email:xtdeepwater@126.com
Date Prepared:	March 6, 2025

2. Device

LYHER® Oral fluid Multi-Drug Test Kit (Cube)

Classification:

Product Code	CFR #	Panel
DJC	862.3610/Methamphetamine test system.	Toxicology
DIO	862.3250/Cocaine test system.	Toxicology
DJG	862.3650/Opiate test system.	Toxicology
DKZ	862.3100/Amphetamine Test System	Toxicology
LCM	Unclassified	Toxicology
LDJ	862.3870/Cannabinoid test system.	Toxicology

3. Predicate Device:

OralTox™ Oral Fluid Drug Test, K171403

4. Device Description

The LYHER® Oral fluid Multi-Drug Test Kit (Cube) is an immunochromatographic assay that uses a lateral flow system for the qualitative detection of d-Amphetamine, d-Methamphetamine, Benzoylecgonine, Morphine, Phencyclidine and Delta-9-Tetrahydrocannabinol in human oral fluid. The LYHER® Oral fluid Multi-Drug Test Kit (Cube) device consists of a cube device, an oral fluid collection swab and a package insert.

5. Intended Use / Indications for Use:

The LYHER® Oral fluid Multi-Drug Test Kit (Cube) is a rapid lateral flow immunoassay for the qualitative detection of d-Amphetamine, d-Methamphetamine, Benzoylecgonine, Morphine, Phencyclidine and Delta-9-Tetrahydrocannabinol in human oral fluid. The test cut-off concentrations and the compounds the tests are calibrated to are as follows:

Test	Calibrator	Cut-off (ng/mL)
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Marijuana (THC)	Delta-9-Tetrahydrocannabinol	40
Methamphetamine (MET)	d-Methamphetamine	50
Phencyclidine (PCP)	Phencyclidine	10

The single or multi-test panels can consist of the above listed analytes in any combination, up to a maximum of 6 analytes.

The tests provide only a preliminary result. A more specific alternate chemical method must be used in order to obtain a confirmed analytical test result. Gas Chromatography/Mass Spectrometry (GC/MS), Liquid Chromatography/Mass Spectrometry (LC/MS) and their tandem mass-spectrometer versions are the preferred confirmatory methods. Careful consideration and judgment should be applied to any drugs of abuse screen test result, particularly when evaluating preliminary positive results.

6. Substantial Equivalence

A summary comparison of features of the LYHER® Oral fluid Multi-Drug Test Kit (Cube) and the predicate devices is provided in following tables.

<table>
<tr><td>Item</td><td>Proposed Device</td><td>Predicate Device-K171403</td></tr>
<tr><td colspan="3">Similarities</td></tr>
<tr><td>Indication(s) for Use</td><td>For the qualitative determination of drugs of abuse in human oral fluid.</td><td>Same</td></tr>
<tr><td>Methodology</td><td>Competitive binding, Lateral flow immunochromatographic assay based on principle of antigen antibody immunochemistry</td><td>Same</td></tr>
<tr><td>Type of Test</td><td>Qualitative</td><td>Same</td></tr>
<tr><td>Specimen Type</td><td>Human oral fluid</td><td>Same</td></tr>
<tr><td>Cut-off Values</td><td><table><tr><td>Test</td><td>Cut-off (ng/mL)</td></tr><tr><td>OPI</td><td>40</td></tr><tr><td>COC</td><td>20</td></tr><tr><td>AMP</td><td>50</td></tr><tr><td>THC</td><td>40</td></tr><tr><td>MET</td><td>50</td></tr><tr><td>PCP</td><td>10</td></tr></table></td><td>Same</td></tr>
<tr><td>Intended Use</td><td>For prescription use.</td><td>Same</td></tr>
<tr><td colspan="3">Differences</td></tr>
<tr><td>Configurations</td><td>Cube</td><td>Cups</td></tr>
</table>

7. Test Principle

Each device employs lateral flow immunochromatographic technology and is based on the principle of competitive binding. Drugs, if present in concentrations below the cutoff level, will not saturate the binding sites of the antibody coated particles on the drug specific test strips. The goat-anti-rabbit IgG antibody-coated particles will then be captured by immobilized drug-specific conjugate. If the level of drug in the oral fluid specimen is below the cutoff concentration, the T line appears as a visible burgundy line. If the level of drug in the oral fluid specimen is above the cutoff, no T line develops. The control line (C line) serves as an internal quality control. The control line should always appear as a burgundy-colored band regardless of the presence of the drug, if enough sample volume has been added to the test and if the sample has correctly migrated up the test strip.

Testing is based on the principle of a competitive immunochemical reaction between a chemically labeled drug (drug-protein conjugate) and the drug or drug metabolites which may be present in the oral fluid sample competing for the limited antibody binding sites.

8. Performance Characteristics

8.1 Analytical Performance

a. Precision-Reproducibility-Cut-Off

Precision-Reproducibility-Cut-Off studies were carried out for samples with concentrations of -100% cut off, -75% cut off, -50% cut off, -25% cut off, cut off, +25% cut off, +50% cut off , +75% cut off and +100% cut off. These samples were prepared by spiking drug in negative oral fluid samples. Each drug concentration was confirmed by LC/MS. All sample aliquots were blindly labeled by the person who prepared the samples and didn't take part in the sample testing. For each concentration, tests were performed two runs per day for 30 days per device lot in a randomized order. The data is summarized below.

Amphetamine

Operator 1									
	-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	0+/60-	0+/60-	0+/60-	5+/55-	48+/12-	54+/6-	60+/0-	60+/0-	60+/0-
Lot 2	0+/60-	0+/60-	0+/60-	5+/55-	47+/13-	55+/5-	60+/0-	60+/0-	60+/0-
Lot 3	0+/60-	0+/60-	0+/60-	5+/55-	47+/13-	55+/5-	60+/0-	60+/0-	60+/0-
Operator 2									
Lot 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	0+/60-	0+/60-	0+/60-	5+/55-	47+/13-	55+/5-	60+/0-	60+/0-	60+/0-
Lot 2	0+/60-	0+/60-	0+/60-	5+/55-	48+/12-	54+/6-	60+/0-	60+/0-	60+/0-
Lot 3	0+/60-	0+/60-	0+/60-	5+/55-	47+/13-	55+/5-	60+/0-	60+/0-	60+/0-
Operator 3									
Lot 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	0+/60-	0+/60-	0+/60-	5+/55-	47+/13-	56+/4-	60+/0-	60+/0-	60+/0-
Lot 2	0+/60-	0+/60-	0+/60-	5+/55-	47+/13-	56+/4-	60+/0-	60+/0-	60+/0-
Lot 3	0+/60-	0+/60-	0+/60-	6+/54-	48+/12-	54+/6-	60+/0-	60+/0-	60+/0-

Cocaine

Operator 1									
Lot 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	0+/60-	0+/60-	0+/60-	6+/54-	48+/12-	56+/4-	60+/0-	60+/0-	60+/0-
Lot 2	0+/60-	0+/60-	0+/60-	5+/55-	48+/12-	56+/4-	60+/0-	60+/0-	60+/0-
Lot 3	0+/60-	0+/60-	0+/60-	6+/54-	49+/11-	55+/5-	60+/0-	60+/0-	60+/0-
Operator 2									
Lot 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	0+/60-	0+/60-	0+/60-	6+/54-	48+/12-	56+/4-	60+/0-	60+/0-	60+/0-
Lot 2	0+/60-	0+/60-	0+/60-	5+/55-	48+/12-	56+/4-	60+/0-	60+/0-	60+/0-
Lot 3	0+/60-	0+/60-	0+/60-	5+/55-	49+/11-	56+/4-	60+/0-	60+/0-	60+/0-
Operator 3									
Lot 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	0+/60-	0+/60-	0+/60-	5+/55-	49+/11-	56+/4-	60+/0-	60+/0-	60+/0-
Lot 2	0+/60-	0+/60-	0+/60-	6+/54-	48+/12-	56+/4-	60+/0-	60+/0-	60+/0-
Lot 3	0+/60-	0+/60-	0+/60-	5+/55-	48+/12-	56+/4-	60+/0-	60+/0-	60+/0-

Methamphetamine

Operator 1									
Lot 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	0+/60-	0+/60-	0+/60-	6+/54-	47+/13-	56+/4-	60+/0-	60+/0-	60+/0-
Lot 2	0+/60-	0+/60-	0+/60-	5+/55-	48+/12-	55+/5-	60+/0-	60+/0-	60+/0-
Lot 3	0+/60-	0+/60-	0+/60-	6+/54-	48+/12-	54+/6-	60+/0-	60+/0-	60+/0-
Operator 2									
Lot 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	0+/60-	0+/60-	0+/60-	6+/54-	48+/12-	56+/4-	60+/0-	60+/0-	60+/0-
Lot 2	0+/60-	0+/60-	0+/60-	5+/55-	47+/13-	56+/4-	60+/0-	60+/0-	60+/0-
Lot 3	0+/60-	0+/60-	0+/60-	6+/54-	48+/12-	55+/5-	60+/0-	60+/0-	60+/0-
Operator 3									
Lot 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	0+/60-	0+/60-	0+/60-	5+/55-	48+/12-	55+/5-	60+/0-	60+/0-	60+/0-
Lot 2	0+/60-	0+/60-	0+/60-	5+/55-	48+/12-	56+/4-	60+/0-	60+/0-	60+/0-
Lot 3	0+/60-	0+/60-	0+/60-	5+/55-	47+/13-	56+/4-	60+/0-	60+/0-	60+/0-

Morphine

Operator 1									
Lot 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	0+/60-	0+/60-	0+/60-	5+/55-	48+/12-	56+/4-	60+/0-	60+/0-	60+/0-
Lot 2	0+/60-	0+/60-	0+/60-	6+/54-	49+/11-	56+/4-	60+/0-	60+/0-	60+/0-
Lot 3	0+/60-	0+/60-	0+/60-	6+/54-	49+/11-	55+/5-	60+/0-	60+/0-	60+/0-
Operator 2									
Lot 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	0+/60-	0+/60-	0+/60-	5+/55-	49+/11-	55+/5-	60+/0-	60+/0-	60+/0-
Lot 2	0+/60-	0+/60-	0+/60-	6+/54-	48+/12-	55+/5-	60+/0-	60+/0-	60+/0-
Lot 3	0+/60-	0+/60-	0+/60-	5+/55-	49+/11-	56+/4-	60+/0-	60+/0-	60+/0-
Operator 3									
Lot 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	0+/60-	0+/60-	0+/60-	6+/54-	49+/11-	56+/4-	60+/0-	60+/0-	60+/0-
Lot 2	0+/60-	0+/60-	0+/60-	5+/55-	49+/11-	55+/5-	60+/0-	60+/0-	60+/0-
Lot 3	0+/60-	0+/60-	0+/60-	5+/55-	48+/12-	55+/5-	60+/0-	60+/0-	60+/0-

Phencyclidine

Operator 1									
Lot 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	0+/60-	0+/60-	0+/60-	6+/54-	48+/12-	55+/5-	60+/0-	60+/0-	60+/0-
Lot 2	0+/60-	0+/60-	0+/60-	6+/54-	48+/12-	54+/6-	60+/0-	60+/0-	60+/0-
Lot 3	0+/60-	0+/60-	0+/60-	5+/55-	48+/12-	56+/4-	60+/0-	60+/0-	60+/0-
Operator 2									
Lot 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	0+/60-	0+/60-	0+/60-	5+/55-	48+/12-	54+/6-	60+/0-	60+/0-	60+/0-
Lot 2	0+/60-	0+/60-	0+/60-	5+/55-	48+/12-	55+/5-	60+/0-	60+/0-	60+/0-
Lot 3	0+/60-	0+/60-	0+/60-	5+/55-	48+/12-	54+/6-	60+/0-	60+/0-	60+/0-
Operator 3									
Lot 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	0+/60-	0+/60-	0+/60-	6+/54-	48+/12-	55+/5-	60+/0-	60+/0-	60+/0-
Lot 2	0+/60-	0+/60-	0+/60-	6+/54-	48+/12-	54+/6-	60+/0-	60+/0-	60+/0-
Lot 3	0+/60-	0+/60-	0+/60-	6+/54-	48+/12-	55+/5-	60+/0-	60+/0-	60+/0-

Marijuana (THC)

Operator 1									
Lot 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	0+/60-	0+/60-	0+/60-	6+/54-	49+/11-	56+/4-	60+/0-	60+/0-	60+/0-
Lot 2	0+/60-	0+/60-	0+/60-	6+/54-	48+/12-	55+/5-	60+/0-	60+/0-	60+/0-
Lot 3	0+/60-	0+/60-	0+/60-	5+/55-	48+/12-	56+/4-	60+/0-	60+/0-	60+/0-
Operator 2									
Lot 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	0+/60-	0+/60-	0+/60-	5+/55-	48+/12-	55+/5-	60+/0-	60+/0-	60+/0-
Lot 2	0+/60-	0+/60-	0+/60-	6+/54-	49+/11-	55+/5-	60+/0-	60+/0-	60+/0-
Lot 3	0+/60-	0+/60-	0+/60-	6+/54-	48+/12-	55+/5-	60+/0-	60+/0-	60+/0-
Operator 3									
Lot 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	0+/60-	0+/60-	0+/60-	6+/54-	48+/12-	55+/5-	60+/0-	60+/0-	60+/0-
Lot 2	0+/60-	0+/60-	0+/60-	6+/54-	48+/12-	55+/5-	60+/0-	60+/0-	60+/0-
Lot 3	0+/60-	0+/60-	0+/60-	6+/54-	49+/11-	56+/4-	60+/0-	60+/0-	60+/0-

The following cut-off values for the candidate devices have been verified.

Calibrator	**Cut-off (ng/mL)**
d-Amphetamine	50
Benzoylecgonine	20
d-Methamphetamine	50
Morphine	40
Phencyclidine	10
Delta-9-Tetrahydrocannabinol	40

b. Linearity
Not applicable.

c. Stability
Device stability has been evaluated through accelerated and real-time studies. The devices are stable at 2-30°C for 24 months based on the real time stability study at room temperature.

d. Interference
Potential interfering substances were added to drug-free oral fluid and target drugs oral fluid with concentrations at 50% below and 50% above cut-off levels. These oral fluid samples were tested using three batches of the device. Compounds that showed no interference for all the six drugs at a concentration of 10 µg/mL are summarized in the following table.

Acetaminophen	Dextromethorphan	Naltrexone
Acetylcodeine	Digoxin	Naproxen
Allobarbital	Dihydrocodeine	Nicotinamide
Alprazolam	diltiazem HCl	Nicotine
Amobarbital	Diphenhydramine HCl	Noscapine
Apomorphine	DL-Propranolol	Omeprazole
Atenolol	Doxylamine	Papaverine
Atropine	Ecgonine methylester	Pentazocine
Baclofen	Estradiol	Phentermine
Benzocaine	Estrone	Phenylpropanolamine
Butabarbital	Fluconazole	Phenytoin
Caffeine	Furosemide	Pioglitazone HCl
Cannabidiol	Hexobarbital	Prednisolone
Carbamazepine	Hydrochlorothiazide	Prednisone
Chlordiazepoxide	Ibuprofen	Procainamide HCl
Chlorpromazine	Imipramine	Procaine HCl
Cimetidine	Lamotrigine	Promethazine
Citalopram HBr	Levetiracetam	Quinine HCl
Clobazam	Lidocaine	R,R(-)-Pseudoephedrine
Clomipramine	Lormetazepam	Salicylic Acid
Clonazepam	L-Thyroxine	Sertraline HCl
Clonidine	Metformin HCl	Simvastin
Clopidogrel bisulfate	Methylphenidate HCl	Theophylline
Cortisol	Metoprolol	Thiamine
Cotinine	Metronidazole	Topiramate
d,l-Salbutamol	Montelukast sodium salt	Valproic Acid
Deoxycorticosterone	Naloxone	Verapamil
Zonisamide		

Food items such as methanol cough drops, cough syrup, cola, mouthwash, coffee, tea, milk, sugar, chewing gum, alcohol, baking soda, salt, cranberry juice, orange juice, food coloring (red, blue, green), toothpaste, tomatoes and MSG were added in either drug-free oral fluid or oral fluid containing the target drug with concentrations of 50% below and 50% above cutoff levels to a concentration of 5%. None of the substances showed interference. Hemoglobin showed no interference at 100 µg/mL. Cigarette smoking showed no interference.

e. Specificity

To test specificity, drug metabolites and other components that are likely to interfere in oral fluid samples were tested using three batches of the device. The following are summaries.

Amphetamine (AMP) (Cut-off=50 ng/mL)	**Result Positive at (ng/mL)**	**% Cross Reactivity**
D-Amphetamine	50	100.00%
L-Amphetamine	4000	1.25%
D,L-Amphetamine	125	40.00%
Methoxyamphetamine	500	10%
Methylenedioxyamphetamine(MDA)	150	33%
Benzodioxolylbutanamine (BDB)	10000	0.5%
3-Hydroxy Tyramine	5000	1%
d,l-p-Chloramphetamine	500	10%
Phenethylamine	4000	1.25%
Hydroxyamphetamine	800	< 6.25%
d,l-Phenylpropanolamine	Negative at 10000	< 0.50%
Phentermine	Negative at 10000	< 0.50%
Methylenedioxyethylamphetamine (MDEA)	Negative at 10000	< 0.50%
Methylenedioxy-methamphetamine (MDMA)	Negative at 10000	< 0.50%
d-Methamphetamine	Negative at 10000	< 0.50%
l-Methamphetamine	Negative at 10000	< 0.50%
Dimethylamylamine (DMAA)	Negative at 10000	< 0.50%
Methylbenzodioxolylbutanamine	Negative at 10000	< 0.50%
para-Methoxymethamphetamine	Negative at 10000	< 0.50%
Phendimetrazine	Negative at 10000	< 0.50%
Phenmetrazine	Negative at 10000	< 0.50%
D-Ephedrine	Negative at 10000	< 0.50%
L-Ephedrine	Negative at 10000	< 0.50%
D,L-Ephedrine	Negative at 10000	< 0.50%
diphenhydramine	Negative at 10000	< 0.50%
d-Pseudoephedrine	Negative at 10000	< 0.50%
Fenfluramine	Negative at 10000	< 0.50%
Isoxsuprine	Negative at 10000	< 0.50%

l-Pseudoephedrine	Negative at 10000	< 0.50%
Mephentermine	Negative at 10000	< 0.50%

COCAINE (COC) (Cut-off=20 ng/mL)	**Result Positive at (ng/mL)**	**% Cross Reactivity**
Cocaine	20	100.00%
Benzoylecgonine	20	100.00%
Cocaethylene	25	80.00%
Ecgonine	1500	1.33%
Ecgonine methyl ester	12500	0.16%
Procaine	Negative at 20000	< 0.10%
Norcocaine	Negative at 20000	< 0.10%

METHAMPHETAMINE (MET) (Cut-off=50 ng/mL)	**Result Positive at (ng/mL)**	**% Cross Reactivity**
D-Methamphetamine	50	100.00%
L-Methamphetamine	3000	1.67%
Methoxymethamphetamine	50	100.00%
Ephedrine	400	12.50%
Phenylephrine	4000	1.25%
Procaine	2000	2.50%
Methylephedrine	400	12.50%
Methylenedioxyethylamphetamine(MDEA)	400	12.50%
3,4-methylenedioxy-methamphetamine(MDMA)	50	100.00%
Amphetamine	Negative at 100000	< 0.05%
D-Amphetamine	Negative at 100000	< 0.05%
L-Amphetamine	Negative at 100000	< 0.05%
3,4-methylenedioxyamphetamine	Negative at 100000	< 0.05%

OPIATES (OPI) (Cut-off=40 ng/mL)	**Result Positive at (ng/mL)**	**% Cross Reactivity**
Morphine	40	100.00%
Acetylmorphine	30	133.33%
Codeine	10	400.00%
Ethylmorphine	30	133.33%
Heroin	50	80.00%
Hydromorphone	100	40.00%
Thebaine	1500	2.67%
Norcodeine	1500	2.67%
Morphine 6-β-glucuronide	50	80.00%

OPIATES (OPI) (Cut-off=40 ng/mL)	Result Positive at (ng/mL)	% Cross Reactivity
Oxycodone	25000	0.16%
Oxymorphone	25000	0.16%
Nalorphine	10000	0.40%
Hydrocodone	100	40.00%
6-Monoacetylmorphine	30	133.33%
Morphine 3-β-glucuronide	50	80.00%

Phencyclidine (PCP) (Cut-off=10 ng/mL)	Result Positive at (ng/mL)	% Cross Reactivity
Phencyclidine	10	100.00%
Hydrocodone	Negative at 30000	< 0.03%
Hydromorphone	Negative at 30000	< 0.03%
Nalorphine	Negative at 30000	< 0.03%
Tenocyclidine (TCP)	2000	0.50%
1-(1-phenylcyclohexyl)morpholine (PCM)	20	50.00%
4-hydroxyphencyclidine	20	50.00%
EDDP	Negative at 100000	< 0.10%
Ketamine	Negative at 100000	< 0.10%
Prazepam	Negative at 100000	< 0.10%
Amitriptyline	Negative at 100000	< 0.10%
(+) Brompheniramine	Negative at 100000	< 0.10%
(+) Chlorphenamine	Negative at 100000	< 0.10%
Desmethylvenlafaxine	Negative at 100000	< 0.10%
Chlorpromazine	Negative at 100000	< 0.10%
Clomipramine	Negative at 100000	< 0.10%
Cyclizine	Negative at 100000	< 0.10%
Cyclobenzaprine	Negative at 100000	< 0.10%
Dexbrompheniramine	Negative at 100000	< 0.10%
Dextromethorphan	Negative at 100000	< 0.10%
Diphenhydramine	Negative at 100000	< 0.10%
Doxepin	Negative at 100000	< 0.10%
Doxylamine	Negative at 100000	< 0.10%
Imipramine	Negative at 100000	< 0.10%
Trioridazine	Negative at 100000	< 0.10%
Venlafaxine	Negative at 100000	<0.10%

MARIJUANA (THC) (Cut-off=40 ng/mL)	Result Positive at (ng/mL)	% Cross Reactivity
Delta-9-Tetrahydrocannabinol	40	100.00%
11-nor-Δ9-THC-9 COOH	12	333.33%
Δ8-Tetrahydrocannabinol	12500	0.32%

MARIJUANA (THC) (Cut-off=40 ng/mL)	Result Positive at (ng/mL)	% Cross Reactivity
11-hydroxy-Δ9-THC	400	10.00%
Cannabinol	12500	0.32%
Cannabidol	Negative at 12500	< 0.32%
11-Nor-Δ9-THC-carboxy-glucuronide	80	50.00%
(-)-11-nor-9-carboxy-Δ9-THC	60	66.67%
11-nor-Δ8-THC-9-COOH	5	800.00%
8-beta- 11-dihydroxy-Δ9-THC	400	10.00%
8-beta-hydroxy-Δ9-THC	300	13.33%
Exo-THC	80	50.00%
l-11-Nor-Δ9-THC-9-Carboxylic Acyl-Glucuronide	15	266.67%
Δ8-THC	6000	0.67%
Δ8-THC Carboxylic Acid	5	800.00%
Δ9-THC Carboxylic Acid	12	333.33%

f. Effect of Oral fluid pH

To investigate the effect of oral fluid pH, oral fluid samples with pH 3 to 9 were spiked with target drugs at 50% below and 50% above cut-off levels. These samples were tested using three lots of the device. Results were all positive for samples at and above +50% cut-off and all negative for samples at and below -50% cut-off.

g. Drug Recovery Study

Negative oral fluid samples in glass bottles were spiked with the drug to concentrations of -50% and +50% of the cutoff. The samples were transferred to the devices and store at room temperature, at -20℃ and at 40℃. Over 90% recoveries were observed for all drugs in the devices. Oral fluid samples can be stored in the device at -20℃ for at least 3 months. Oral fluid samples can be shipped overnight in the device for LC/MS confirmation.

8.2 Comparison Studies

Method comparison studies for the LYHER Oral fluid Multi-Drug Test Kit(Cube) were performed at three testing sites with three operators at each site. Operators tested the samples using the candidate device and the results were compared to LC/MS results. The results are presented in the tables below.

D-Amphetamine

Operator	Test result	Negative oral fluid	<-50% cut off	-50% cut off-cut off	Cut off-+50% cut off	>+50% cut off
Total (all operators and sites)	Negative	360	93	74	9	0
	Positive	0	0	1	180	183

Cocaine

Operator	Test result	Negative oral fluid	<-50% cut off	-50% cut off-cut off	Cut off-+50% cut off	>+50% cut off
Total (all operators and sites)	Negative	360	69	83	8	0
	Positive	0	0	4	172	186

d-Methamphetamine

Operator	Test result	Negative oral fluid	<-50% cut off	-50% cut off-cut off	Cut off-+50% cut off	>+50% cut off
Total (all operators and sites)	Negative	360	63	70	7	0
	Positive	0	0	2	164	189

Morphine

Operator	Test result	Negative oral fluid	<-50% cut off	-50% cut off-cut off	Cut off-+50% cut off	>+50% cut off
Total (all operators and sites)	Negative	360	57	84	6	0
	Positive	0	0	3	183	180

Phencyclidine

Operator	Test result	Negative oral fluid	<-50% cut off	-50% cut off-cut off	Cut off-+50% cut off	>+50% cut off
Total (all operators and sites)	Negative	360	51	109	13	0
	Positive	0	0	5	170	192

Delta-9-Tetrahydrocannabinol

Operator	Test result	Negative oral fluid	<-50% cut off	-50% cut off-cut off	Cut off-+50% cut off	>+50% cut off
Total (all operators and sites)	Negative	360	93	96	8	0
	Positive	0	0	3	172	195

8.3 Clinical Studies
Not Applicable.

9. Conclusion

Based on the test principle and acceptable performance characteristics including precision, interference, specificity, and method comparison studies of the devices, it's concluded that the LYHER Oral fluid Multi-Drug Test Kit(Cube) is substantially equivalent to the predicate.