

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION  
DECISION SUMMARY  
ASSAY AND INSTRUMENT**

**I Background Information:**

**A 510(k) Number**

K183648

**B Applicant**

Clever Culture Systems AG

**C Proprietary and Established Names**

APAS Independence

**D Regulatory Information**

Product Code(s)	Classification	Regulation Section	Panel
PPU	Class II	<a href="#">21 CFR 866.2190</a> - Automated Image Assessment System For Microbial Colonies On Solid Culture Media	IM - Immunology & MI - Microbiology

**II Submission/Device Overview:**

**A Purpose for Submission:**

To obtain a substantial equivalence determination for the APAS Independence.

**B Measurand:**

Digital images of microbial colonies cultured on blood and MacConkey agar plates.

### C Type of Test:

The APAS Independence when using its Urine Analysis Module is an *in vitro* diagnostic test system for automated assessment and enumeration of microbial colonies on solid culture media. The system is for use on urine cultures from suspected cases of urinary tract infection (UTI).

### III Intended Use/Indications for Use:

#### A Intended Use(s):

The APAS Independence is an *in vitro* diagnostic system comprised of an instrument and software analysis module(s) for specific indications that are used to automate imaging and interpretation of microbial colonies on plates of solid culture media.

#### B Indication(s) for Use:

The APAS Independence is an *in vitro* diagnostic system comprised of an instrument for automated imaging of agar culture plates and a software analysis module for the following use:

The APAS Independence, when using its urine analysis module, automates urine culture plate imaging and interpretation to detect the presence or absence of microbial growth on sheep blood and MacConkey agar culture plates that are inoculated with a 1µL sample volume. The APAS Independence, when using its urine analysis module, provides a semi-quantitative assessment of colony counts that are used as an aid in the diagnosis of urinary tract infection. All urine culture plates that are identified as positive for growth by the APAS Independence, when using its urine analysis module, must be reviewed by a trained microbiologist.

#### C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

The performance of the APAS Independence with Urine Analysis Module has not been evaluated with urine samples from pregnant women. The APAS Independence with Urine Analysis Module will detect colonies of GBS if they are present but should not be used for primary screening for Group B *Streptococcus* (GBS) carriers. Follow recommended guidelines for identification of pregnant women who are colonized with GBS. <sup>1</sup>

The performance of the APAS Independence with Urine Analysis Module has not been evaluated with urine samples from suspected cases of complicated urinary tract infection e.g., those with underlying urinary tract pathology, suspected cases of persistent urinary tract infection, urine collected by invasive procedures or urine samples from immunocompromised subjects.

Slow growing organisms such as *Corynebacterium* spp. and *Gardnerella vaginalis* may not exhibit detectable growth within 18-22 hours. If infection with a slow growing species is suspected, extension of the incubation time may be required, followed by manual interpretation

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<sup>1</sup> Revised Guidelines from CDC: Prevention of Perinatal Group B Streptococcal Disease. MMWR 2010 59: RR-10.

of the culture result. The APAS Independence with Urine Analysis Module should not be used to interpret cultures incubated for greater than 22 hours.

The APAS Independence with Urine Analysis Module is for use with the following culture plates manufactured by Remel: Tryptic Soy Sheep Blood Agar (R01202A) and MacConkey Agar with Crystal Violet (R01552A).

APAS Independence has been designed and validated for use only with whole plates. Bi-plates have not been evaluated and should not be used.

#### **D Special Instrument Requirements:**

APAS Independence

### **IV Device/System Characteristics:**

#### **A Device Description:**

The APAS Independence with Urine Analysis Module is an automated system that for screening of urine culture plates for the presence of microbial growth. The device comprises a plate handling system that moves culture plates loaded by the operator into and out of an imaging station where digital images of the plates are captured, as well as software for image analysis, determination of the presence/absence of microbial growth and enumeration of colonies (if present). A list of the major sub-components of the APAS Compact is depicted in [Table 1](#). The Urine Analysis Module software is compatible with the following types of culture media:

Tryptic Soy Sheep Blood Agar  
MacConkey Agar with Crystal Violet

Both the optical hardware for image acquisition and the Urine Analysis Module software used by the APAS Independence to analyze and interpret the digital images are the same as those used by the predicate APAS Compact with Urine Analysis Module ([DEN150059](#)).

**Table 1.** Sub-components of the APAS Independence

<b>Component</b>	<b>Function</b>
Imaging Station	LED illumination of culture plates and image capture using a CCD camera
Plate Handling System	Movement, positioning and sorting of culture plates within the instrument
APAS Controller PC	Image capture, storage and analysis
Plate Controller PC	Controls movement of culture plates between the input carriers, imaging station and output carriers or stacks
Instrument Controller PC	Provides the user interface for operation of the APAS Independence and coordinates the functions of the APAS and Plate Controller PCs
Urine Analysis Module Software	Installed on the APAS Controller PC to provide the configuration and instructions for image capture and analysis
LIMS Interface Software	Installed on the Instrument Controller PC to import other diagnostic information, such as microscopy or chemistry results, and provide context for interpretation of urine culture results  Imported information may be applied to the system:  “LIMS Force Flag”: automatically forces an APAS result to “Review” irrespective of the growth characteristics observed  “LIMS Complementary Test Flag”: automatically changes a “Negative” designation to “Review” based on user defined rules applied to additional diagnostic information
Color Calibration Tool	Multicolored disk for calibration/checking of system optics
System Check	Simulated culture plates used to confirm instrument function

CCD: Charge Coupled Device LED: Light Emitting Diode; LIMS: Laboratory Information Management System; PC: Personal Computer

## **B Principle of Operation:**

The APAS Independence with Urine Analysis Module is designed for the assessment of microbial colonies on urine culture plates. The instrument comprises an imaging station for

capture of images of urine culture plates, a plate handling system that moves plates between the input carriers, imaging station and output carriers or stacks, together with software for analysis of the images, assessment and enumeration of microbial colonies (if present) and result designation. Plates with growth are designated as either “Positive” or “Review” depending on the number of colonies present and their morphologic characteristics. All plates that exhibit growth therefore require follow up according to standard laboratory practice by a trained microbiologist. Those plates that are designated by the APAS Independence to have no growth may be discarded without further review.

The APAS Independence with Urine Analysis Module is indicated for screening paired sheep blood and MacConkey agar plates that are each inoculated with 1µL of urine and which are incubated at  $35 \pm 2^{\circ}\text{C}$  for 18 to 22 hours. The system takes digital images of each plate that are analyzed automatically to determine the number of colonies present and their associated morphologies. For each plate, the APAS Independence performs the following tasks:

- a) Differentiates between areas of growth (colonies) and no growth (e.g., agar, labels, handwriting);
- b) Differentiates areas that are required for interpretation of colony morphology (e.g.,  $\alpha$ - and  $\beta$ -hemolysis);
- c) Assigns to each area of growth a code that corresponds to a morphology type;
- d) Estimates the number of colonies present, converts this number to an organism concentration in the original urine sample and reports this value in terms of colony forming units per milliliter (CFU/mL).
- e) Generates a growth report including the sample and patient identifiers, type of growth present (if any), the colony count and any additional information pertaining to the patient that is obtained from the Laboratory Information Management System (LIMS).

The colony morphologies reported by the APAS Independence with Urine Analysis Module are shown in [Table 2](#) for sheep blood agar and [Table 3](#) for MacConkey agar. A “significant organism” at  $10^3$  CFU/mL on the plate will trigger designation of that plate as “Positive,” as opposed to “Review.” Plates that are designated as “Positive” or “Review” are required to undergo further evaluation by a clinical microbiologist.

**Table 2.** Colony morphologies on sheep blood agar identified by APAS Independence with Urine Analysis Module

Morphology Name	Description
Coliform <sup>1</sup>	Gram-negative and coliform-like colonies
Cream-white	<i>Staphylococcus</i> and related species
Granular	Granular morphologies (e.g., <i>Pseudomonas</i> spp.)
Small	<i>Enterococcus</i> spp. and related species
Small $\alpha$ -hemolytic	Small colonies with $\alpha$ -hemolysis or very small colonies
Small $\beta$ -hemolytic <sup>1</sup>	Small colonies with $\beta$ -hemolysis
Swarming organism	<i>Proteus</i> spp. and related, high-motility species

<sup>1</sup> “Significant organism;” refer to [Table 4](#)

**Table 3.** Colony morphologies on MacConkey agar identified by APAS Independence with Urine Analysis Module

Morphology Name	Description
Lactose fermenter <sup>1</sup>	Pink/red colonies
Non-fermenter	Colonies without red/pink pigment
Non-fermenter with green pigment	<i>Pseudomonas</i> spp.
Red pigmented colonies	Pigmented <i>Serratia marcescens</i>

<sup>1</sup> “Significant organism;” refer to [Table 4](#)

The interpretation of the growth follows a decision tree that combines information regarding the number of colonies present with their morphological characteristics to designate each plate as either “Positive”, “Review”, “Negative” or “Indeterminate,” as shown in [Table 4](#).

**Table 4.** Result interpretation for APAS Independence with Urine Analysis Module

Colony Count (CFU/mL)	Morphology	APAS Compact Designation
Indeterminate	Swarming organism	Positive
$\geq 10^4$	Any	
$10^3$	Significant organism <sup>1</sup>	Review
$10^3$	No significant organism	
0	Not Applicable	Negative

<sup>1</sup> Defined as growth of coliform-like colonies or small colonies with  $\beta$ -hemolysis on blood agar, or colonies of lactose fermenting bacteria on MacConkey agar

**C Instrument Description Information:**

<b>Modes of Operation</b>	<b>Yes</b>	<b>No</b>
Does the applicant's device contain the ability to transmit data to a computer, webserver, or mobile device?	<input checked="" type="checkbox"/>	<input type="checkbox"/>
Does the applicant's device transmit data to a computer, webserver, or mobile device using wireless transmission?	<input type="checkbox"/>	<input checked="" type="checkbox"/>
<b>Software</b>		
FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types.	<input checked="" type="checkbox"/>	<input type="checkbox"/>

1. Instrument Name:

APAS Independence

2. Specimen Identification:

Plates are identified using an integrated barcode scanner within the Imaging Module of the APAS Independence. The identity of each plate is displayed on the results screen and transmitted automatically to the LIS.

3. Specimen Sampling and Handling:

The operator loads carriers containing culture plates into the Input Module of the APAS Independence from which they are moved automatically, one plate at a time, to the Imaging Module where the barcode is read, the lid is removed and images of the agar surface are captured. Upon completion of image capture and analysis, the plate lid is replaced and the system automatically sorts each plate based on its designation into the appropriate carrier in the Output Module.

4. Calibration:

The APAS Independence requires daily color calibration prior to use. Calibration is performed using the Color Calibration Tool provided with the instrument. Instructions for calibration are included in the APAS Independence User Manual.

5. Quality Control:

In addition to daily calibration, a System Check must be performed using the manufacturer-supplied Part 1 and Part 2 plate tools prior to analysis of urine culture plates. If the System Check fails, the instrument should be locked to prevent processing of additional culture plates until has been service has been performed.

Instructions for daily Quality Control testing using reference culture plates inoculated with *Enterococcus faecalis* and *Escherichia coli* are provided in the User Manual for the APAS Independence with Urine Analysis Module. Both the appropriate colony morphology and colony count must be obtained for the results of the Quality Control testing to be considered acceptable.

In the event of a failure, Quality Control testing should be repeated. If the repeated failure occurs, the instrument should not be used until it has been serviced.

**V Substantial Equivalence Information:**

**A Predicate Device Name(s):**

APAS Compact with Urine Analysis Module

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

[DEN150059](#)

**C Comparison with Predicate(s):**

<b>Device &amp; Predicate Device(s):</b>	<b><a href="#">K183648</a></b>	<b><a href="#">DEN150059</a></b>
Device Trade Name	<b>APAS Independence with Urine Analysis Module</b>	<b>APAS Compact with Urine Analysis Module</b>
<b>General Device Characteristic Similarities</b>		
Intended Use	The APAS Independence is an <i>in vitro</i> diagnostic system comprised of an instrument and software analysis module(s) for specific indications that are used to automate imaging and interpretation of microbial colonies on plates of solid culture media.	The APAS Compact is an <i>in vitro</i> diagnostic system comprised of an instrument and software analysis module(s) for specific indications that are used to automate imaging and interpretation of microbial colonies on plates of solid culture media.
Indications For Use	The APAS Independence is an <i>in vitro</i> diagnostic system comprised of an instrument for automated imaging of agar culture plates and a software analysis module for the following use:  The APAS Independence, when	The APAS Compact is an <i>in vitro</i> diagnostic system comprised of an instrument for automated imaging of agar culture plates and a software analysis module for the following use:  The APAS Compact, when using its urine analysis module,



<b>Device &amp; Predicate Device(s):</b>	<b><u>K183648</u></b>	<b><u>DEN150059</u></b>
	<p>using its urine analysis module, automates urine culture plate imaging and interpretation to detect the presence or absence of microbial growth on sheep blood and MacConkey agar culture plates that are inoculated with a 1µL sample volume. The APAS Independence, when using its urine analysis module, provides a semiquantitative assessment of colony counts that are used as an aid in the diagnosis of urinary tract infection. All urine culture plates that are identified as positive for growth by the APAS Independence, when using its urine analysis module, must be reviewed by a trained microbiologist.</p>	<p>automates urine culture plate imaging and interpretation to detect the presence or absence of microbial growth on sheep blood and MacConkey agar culture plates that are inoculated with a 1µL sample volume. The APAS Compact, when using its urine analysis module, provides a semi-quantitative assessment of colony counts that are used as an aid in the diagnosis of urinary tract infection. All urine culture plates that are identified as positive for growth by the APAS Compact, when using its urine analysis module, must be reviewed by a trained microbiologist.</p>
Imaging Station	Light Emitting Diode (LED) illumination of culture plates and image capture using a Charged Coupled Device (CCD) camera	Same
APAS Controller PC	Controls image capture, analysis, report generation and result storage	Same
Urine Analysis Module	Installed on the APAS Controller PC to provide the configuration and instructions for image	Same

<b>Device &amp; Predicate Device(s):</b>	<b><u>K183648</u></b>	<b><u>DEN150059</u></b>
	capture and analysis	
Calibration	Performed daily using a manufacturer-provided Color Calibration Tool	Same
Biological Quality Control	Performed daily using standardized suspensions of <i>Escherichia coli</i> and <i>Enterococcus faecalis</i>	Same
<b>General Device Characteristic Differences</b>		
Plate Handling	Automated	Manual
Instrument Controller PC	Provides the user interface for the APAS Independence and controls plate movement	Provides the user interface for the APAS Compact
Laboratory Information System (LIS) data import	Instrument Controller PC interfaces with an external LIS server	LIS simulator installed on the Instrument Controller PC
System Check	Performed daily using the manufacturer-provided System Check Tools to verify instrument and software functionality	None
Result Report	Separate report for each culture plate	Results for blood and MacConkey agar plates combined to provide a summary report for the sample

## VI Standards/Guidance Documents Referenced:

ISO 14971 Medical devices - Application of Risk Management to Medical Devices; 2007.

IEC 61010-1: Safety requirements for electrical equipment for measurement, control and laboratory use - Part 1: General requirements; 2010, 3<sup>rd</sup> edition.

IEC 62304: Medical device software - Software life cycle processes; 2006.

IEC 62366-1: Medical devices – Part 1: Application of usability engineering to medical devices; 2015.

IEC 61326-1: Electrical equipment for measurement, control and laboratory use - EMC Requirements – Part 1: General requirements; 2012.

IEC 61326-2-6: Electrical equipment for measurement, control and laboratory use - EMC Requirements - Part 2-6: Particular Requirements - *In vitro* diagnostic (IVD) medical Equipment; 2012.

CISPR 11 Ed. 5.1: Industrial, scientific and medical equipment - Radio frequency disturbance characteristics - Limits and methods of measurement; 2010.

## VII Performance Characteristics (if/when applicable):

### A Analytical Performance:

#### 1. Precision/Reproducibility:

The precision and reproducibility of colony counts obtained with the APAS Independence with Urine Analysis Module was evaluated with three different instruments using dilutions of representative uropathogenic bacterial species (*Escherichia coli*, *Streptococcus agalactiae* and *Enterococcus faecalis*) grown on blood and MacConkey agar. Each dilution of organisms was plated in triplicate and incubated at  $35 \pm 2^\circ\text{C}$  for 18 hours. Plates from three dilutions that exhibited 0 to >100 colonies plate were included in the study. Five images of each plate were captured on each APAS Independence instrument in each of three different orientations (0, 120 and 270°). The mean, standard deviation and percent coefficient of variation of colony counts obtained for each organism dilution on each instrument and overall is presented in **Tables 5** and **6**, for blood and MacConkey agar respectively. The results of the study demonstrated that the precision and reproducibility of colony counts within and between instruments was acceptable.

**Table 5.** Precision and reproducibility of colony counts on blood agar obtained with the APAS Independence with Urine Analysis Module

<i>Escherichia coli</i>											
Dilution (Nominal CFU/plate)			2 (>100)			3 (10-99)			5 (1-9)		
Plate			1	2	3	1	2	3	1	2	3
CFU	APAS 1 (by plate)	Mean	72.6	113.0	123.1	70.7	47.5	50.1	1.7	9.9	3.3
		SD	1.6	2.4	1.1	2.7	0.6	0.9	0.5	0.4	0.5
		%CV	2.3	2.1	0.9	3.8	1.3	1.8	26.4	3.6	14.0
	APAS 2 (by plate)	Mean	74.1	116.7	123.0	66.3	45.8	46.4	1.1	8.0	3.3
		SD	8.0	9.3	6.2	2.0	1.8	1.0	0.5	0.7	0.5
		%CV	10.8	8.0	5.0	3.1	3.9	2.1	45.6	8.2	14.0
	APAS 3 (by plate)	Mean	77.0	116.3	125.6	83.9	48.9	52.5	1.9	10.5	3.8
		SD	2.5	2.3	0.8	4.6	0.7	1.1	0.3	0.6	0.4
		%CV	3.3	2.0	0.7	5.4	1.4	2.0	13.4	6.1	10.9
	All APAS (by plate)	Mean	74.6	115.3	123.9	73.6	47.4	49.6	1.6	9.5	3.4
		SD	5.2	5.8	3.8	8.2	1.7	2.7	0.5	1.2	0.5
		%CV	6.9	5.0	3.0	11.1	3.6	5.4	33.7	12.9	14.6
	All APAS (by dilution)	Mean	<b>104.6</b>			<b>56.9</b>			<b>4.8</b>		
		SD	<b>22.2</b>			<b>12.9</b>			<b>3.5</b>		
		%CV	<b>21.2</b>			<b>22.7</b>			<b>71.7</b>		

<i>Escherichia coli/Streptococcus agalactiae (mixed growth)</i>											
Dilution (Nominal CFU/plate)			2 (>100)			3 (10-99)			5 (1-9)		
Replicate (Plate)			1	2	3	1	2	3	1	2	3
CFU	APAS 1 (by plate)	Mean	218.5	184.7	159.2	78.9	59.8	80.6	9.9	8.7	18.1
		SD	7.8	9.6	8.5	4.1	4.4	4.4	2.7	1.8	3.7
		%CV	3.6	5.2	5.4	5.1	7.4	5.4	27.6	20.1	20.2
	APAS 2 (by plate)	Mean	179.1	174.9	147.9	83.7	54.5	73.2	13.1	6.1	18.3
		SD	5.5	5.4	7.2	4.1	4.1	4.6	2.7	2.4	3.4
		%CV	3.1	3.1	4.9	4.9	7.5	6.2	21.0	39.6	18.3
	APAS 3 (by plate)	Mean	193.7	155.4	174.8	96.0	56.1	77.6	15.2	6.1	14.9
		SD	20.9	6.5	22.2	15.3	13.6	6.8	2.0	3.0	2.0
		%CV	10.8	4.2	12.7	15.9	24.3	8.8	13.4	48.5	13.3
	All APAS (by plate)	Mean	197.1	171.7	160.6	86.2	56.8	77.1	12.7	7.0	17.1
		SD	20.9	14.3	17.9	11.7	8.7	6.1	3.3	2.7	3.4
		%CV	10.6	8.3	11.1	13.6	15.3	7.9	26.1	38.5	19.9
	All APAS (by dilution)	Mean	<b>176.5</b>			<b>73.4</b>			<b>12.3</b>		
		SD	<b>23.5</b>			<b>15.3</b>			<b>5.2</b>		
		%CV	<b>13.3</b>			<b>20.9</b>			<b>42.5</b>		

<i>Enterococcus faecalis</i>											
Dilution (Nominal CFU/plate)		2 (>100)			3 (10-99)			5 (1-9)			
Replicate (Plate)		1	2	3	1	2	3	1	2	3	
CFU	APAS 1 (by plate)	Mean	458.8	705.1	526.9	150.7	119.1	138.7	11.3	8.4	5.6
		SD	44.7	27.7	18.0	13.3	5.9	11.9	1.8	1.6	1.8
		%CV	9.7	3.9	3.4	8.8	4.9	8.6	15.9	19.0	32.2
	APAS 2 (by plate)	Mean	504.1	721.0	531.1	137.3	134.7	152.3	12.3	5.7	4.7
		SD	8.6	54.8	14.7	7.5	9.6	7.7	1.5	1.2	1.2
		%CV	1.7	7.6	2.8	5.4	7.1	5.0	12.5	20.7	24.6
	APAS 3 (by plate)	Mean	591.3	793.6	543.5	183.7	143.9	172.1	9.4	9.8	5.9
		SD	17.0	7.1	15.1	13.3	6.8	7.4	2.7	2.1	1.9
		%CV	2.9	0.9	2.8	7.2	4.7	4.3	29.2	21.5	32.1
	All APAS (by plate)	Mean	518.0	739.9	533.9	157.2	132.6	154.4	11.0	8.0	5.4
		SD	62.0	52.3	17.2	22.8	12.8	16.5	2.4	2.4	1.7
		%CV	12.0	7.1	3.2	14.5	9.6	10.7	21.7	30.0	31.3
	All APA	Mean	<b>597.3</b>			<b>148.1</b>			<b>8.1</b>		
		SD	<b>112.0</b>			<b>20.9</b>			<b>3.2</b>		
		%CV	<b>18.8</b>			<b>14.1</b>			<b>38.8</b>		

CFU: Colony Forming Units; %CV: Percent Coefficient of variation; SD: Standard Deviation

**Note:** No colonies were detected by any of the APAS Independence Instruments on blood agar plates inoculated with saline (i.e., Mean CFU and SD = 0, in all cases).

**Table 6.** Precision and reproducibility of colony counts on MacConkey agar obtained with the APAS Independence with Urine Analysis Module

<i>Escherichia coli</i>											
Dilution (Nominal CFU/plate)		2 (>100)			3 (10-99)			5 (1-9)			
Plate		1	2	3	1	2	3	1	2	3	
CFU	APAS 1 (by plate)	Mean	174.5	127.1	152.9	55.9	65.4	50.7	4.7	2.0	1.6
		SD	5.7	7.0	6.6	4.3	2.1	2.8	0.5	0.0	0.5
		%CV	3.3	5.5	4.3	7.7	3.2	5.5	10.5	0.0	31.7
	APAS 2 (by plate)	Mean	163.7	121.2	142.0	54.8	70.3	46.5	4.0	2.2	2.3
		SD	3.7	1.9	2.4	1.1	1.6	2.2	0.7	0.4	0.9
		%CV	2.3	1.6	1.7	2.0	2.3	4.7	16.4	18.8	38.6
	APAS 3 (by plate)	Mean	186.8	139.0	171.9	56.7	70.7	50.9	4.5	2.0	1.7
		SD	3.9	4.1	6.8	1.3	2.1	4.2	0.5	0.0	0.5
		%CV	2.1	3.0	4.0	2.3	2.9	8.3	11.4	0.0	29.3
	All APAS (by plate)	Mean	175.0	129.1	155.6	55.8	68.8	49.4	4.4	2.1	1.9
		SD	10.5	8.8	13.7	2.7	3.1	3.7	0.6	0.3	0.7
		%CV	6.0	6.8	8.8	4.8	4.5	7.6	14.0	12.2	38.9
	All APAS (by dilution)	Mean	<b>153.2</b>			<b>58.0</b>			<b>2.8</b>		
		SD	<b>21.9</b>			<b>8.7</b>			<b>1.3</b>		
		%CV	<b>14.3</b>			<b>15.1</b>			<b>46.3</b>		

CFU: Colony Forming Units; %CV: Percent Coefficient of variation; SD: Standard Deviation

**Note:** No colonies were detected by any of the APAS Independence Instruments on MacConkey agar plates inoculated with saline (i.e., Mean CFU and SD = 0, in all cases).

2. Linearity:

Agreement between manual colony counts and those obtained with the predicate APAS Compact with Urine Analysis Module was demonstrated under [DEN150059](#). Because the APAS Independence with Urine Analysis Module uses the same hardware and software for image acquisition and analysis as the APAS Compact, additional testing to characterize the accuracy and linearity of colony counts was not needed. Please refer to the Decision Summary for [DEN150059](#) for additional information.

3. Analytical Specificity/Interference:

The analytical specificity of the predicate APAS Compact with Urine Analysis Module was demonstrated under [DEN150059](#). Because the APAS Independence with Urine Analysis Module uses the same hardware and software for image acquisition and analysis as the APAS Compact, additional testing to characterize the analytical specificity of the system was not needed. Please refer to the Decision Summary for [DEN150059](#) for additional information.

4. Assay Reportable Range:

Refer to [Table 4](#) and to [Section VII A\(2\)](#).

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

The device labeling indicates that the APAS Independence with Urine Analysis Module should not be used unless the system has passed the appropriate daily Quality Control (QC) checks. These include Color Calibration and a System Check using the optical tools that are provided with each instrument, as well as biological QC with standardized cultures of *Enterococcus faecalis* and *Escherichia coli*. Please refer to the Decision Summary for [DEN150059](#) for information regarding the performance of the biological Quality Controls.

6. Detection Limit:

The limit of detection of the predicate APAS Compact with Urine Analysis Module was demonstrated under [DEN150059](#). Because the APAS Independence with Urine Analysis Module uses the same hardware and software for image acquisition and analysis as the APAS Compact, additional testing to characterize the analytical sensitivity of the system was not needed. Please refer to the Decision Summary for [DEN150059](#) for additional information.

7. Assay Cut-Off:

Not applicable.

8. Accuracy (Instrument):

Not applicable.

9. Carry-Over:

Not applicable.

## B Comparison Studies:

### 1. Method Comparison with Predicate Device:

A Method Comparison Study was performed to demonstrate that the predicate APAS Compact ([DEN150059](#)) and APAS Independence exhibit similar performance with clinical specimens. In brief, residual clinical urine specimens that had originally been submitted for urinalysis, were inoculated onto bar code-labeled blood and MacConkey agar plates according to the instructions for use for the APAS Urine Analysis Module (1µL inoculum volume). The plates were incubated for 18 hours at 35 ± 2°C and images of each plate were then captured using one APAS Independence and one APAS Compact instrument system, each equipped with the Urine Analysis Module software. The images on each instrument were taken within 4 hours of completion of the specified incubation period.

A total of 550 urine specimens were initially enrolled in the study. Of these, the first 200 were excluded from the analysis of performance because the plate incubator exceeded the specified temperature. The results from the remaining 350 specimens were included in the analysis. A summary of the plate designations assigned by each instrument is shown on [Table 7](#) and [8](#). In general, there was a high level of agreement (~99%) for plates designated as “Positive” by the two systems and there was a tendency for APAS Independence to designate more plates as “Positive” or “Review” than APAS Compact. This is also reflected in the tendency for higher colony counts to be reported by APAS Independence than by APAS Compact ([Tables 9](#) and [10](#)) and is considered acceptable without additional risk mitigation because both these designations require follow-up by a trained microbiologist.

**Table 7.** Summary of agreement in blood agar plate designation using the Urine Analysis Module software on the APAS Compact (predicate) and APAS Independence

Blood Agar Plate Designation		APAS Compact (predicate)			
		Positive	Review	Negative	Total
APAS Independence	Positive	232	5	1	<b>238</b>
	Review	3	32	15	<b>50</b>
	Negative	0	0	62	<b>62</b>
	<b>Total</b>	<b>235</b>	<b>37</b>	<b>78</b>	<b>350</b>
Designation Agreement (95% Confidence Interval)		232/235 <b>98.7%</b> (96.3-99.6%)	32/37 <b>86.5%</b> (72.0-94.1%)	62/78 <b>79.5%</b> (69.2-87.0%)	
		272/272 <b>100%<sup>1</sup></b> (98.6-100%)			

<sup>1</sup> “Positive” and “Review” designations combined

**Table 8.** Summary of agreement in MacConkey agar plate designation using the Urine Analysis Module software on the APAS Compact (predicate) and APAS Independence

MacConkey Agar Plate Designation		APAS Compact (predicate)			
		Positive	Review	Negative	Total
APAS Independence	Positive	133	1	8	<b>142</b>
	Review	0	4	15	<b>19</b>
	Negative	1	0	188	<b>189</b>
	<b>Total</b>	<b>134</b>	<b>5</b>	<b>211</b>	<b>350</b>
Designation Agreement (95% Confidence Interval)		133/134 <b>99.3%</b> (95.9-99.9%)	4/5 <b>80.0%</b> (37.6-96.4%)	188/211 <b>89.1%</b> (84.2-92.6%)	
		137/139 <b>98.6%</b> <sup>1</sup> (94.9-99.6%)			

<sup>1</sup> "Positive" and "Review" designations combined

**Table 9.** Summary of colony counts on blood agar obtained with the Urine Analysis Module software using the APAS Compact (predicate) and APAS Independence

Colony Counts on Blood Agar		APAS Compact CFU/mL (predicate)					Total
		0	10 <sup>3</sup>	10 <sup>4</sup>	10 <sup>5</sup>	IND	
APAS Independence CFU/mL	0	62	0	0	0	0	<b>62</b>
	10 <sup>3</sup>	15	47	0	0	0	<b>62</b>
	10 <sup>4</sup>	1	5	67	1	0	<b>74</b>
	10 <sup>5</sup>	0	0	7	132	0	<b>139</b>
	IND	0	0	0	0	13	<b>13</b>
	<b>Total</b>	<b>78</b>	<b>52</b>	<b>74</b>	<b>133</b>	<b>13</b>	<b>350</b>
% Independence < Compact		NA	0	0	0.8	NA	
% Independence = Compact		79.5	90.4	90.5	99.2	100	
% Independence > Compact		20.5	9.6	9.5	NA	NA	

IND: Indeterminate (swarming organism); NA: Not applicable



**Table 10.** Summary of colony counts on MacConkey agar obtained with the Urine Analysis Module software using the APAS Compact (predicate) and APAS Independence

Colony Counts on MacConkey Agar		APAS Compact CFU/mL (predicate)				
		0	10 <sup>3</sup>	10 <sup>4</sup>	10 <sup>5</sup>	Total
APAS Independence CFU/mL	0	188	1 <sup>1</sup>	0	0	189
	10 <sup>3</sup>	15	26	0	0	41
	10 <sup>4</sup>	8	2	21	0	31
	10 <sup>5</sup>	0	0	3	86	89
	<b>Total</b>	<b>211</b>	<b>29</b>	<b>24</b>	<b>86</b>	<b>350</b>
% Independence < Compact		NA	3.4	0	0	
% Independence = Compact		89.1	89.7	87.5	100	
% Independence > Compact		10.9	6.9	12.5	NA	

NA: Not applicable

<sup>1</sup> APAS Compact detected a single lactose fermenting colony that was not identified by APAS Independence

Tables [11](#) and [12](#) show a comparison of the colony morphology designations assigned to each plate by the APAS Compact and APAS Independence using the Urine Analysis Module. Although the positive and negative agreement differed for each colony morphology, these designations are provided to the operator for informational purposes and are not used in disposition of the plates as “Positive”, “Review” or “Negative” and the performance was therefore determined to be acceptable without the need for additional risk mitigation.

**Table 11.** Comparison of colony morphologies on blood agar designated by the Urine Analysis Module using the APAS Compact (predicate) and APAS Independence

Alpha Hemolysis		APAS Compact (predicate)		
		Positive	Negative	Total
APAS Independence	Positive	61	43	104
	Negative	10	236	246
	Total	71	279	350
Agreement (95% Confidence Interval)		61/71 85.9% (76.0-92.2%)	236/279 84.6% (79.9-88.4%)	
Beta Hemolysis		APAS Compact (predicate)		
		Positive	Negative	Total
APAS Independence	Positive	106	38	144
	Negative	13	193	206
	Total	119	231	350
Agreement (95% Confidence Interval)		106/119 89.1% (82.2-93.5%)	193/231 83.5% (78.2-87.8%)	
Coliform		APAS Compact (predicate)		
		Positive	Negative	Total
APAS Independence	Positive	165	13	178
	Negative	4	168	172
	Total	169	181	350
Agreement (95% Confidence Interval)		165/169 97.6% (94.1-99.1%)	168/181 92.8% (88.1-95.8%)	
Swarming		APAS Compact (predicate)		
		Positive	Negative	Total
APAS Independence	Positive	13	0	13
	Negative	0	337	337
	Total	13	337	350
Agreement (95% Confidence Interval)		13/13 100% (77.2-100%)	337/337 100% (98.9-100%)	
Granular		APAS Compact (predicate)		
		Positive	Negative	Total
APAS Independence	Positive	18	1	19
	Negative	1	330	331
	Total	19	331	350
Agreement (95% Confidence Interval)		18/19 94.7% (75.4-99.1%)	330/331 99.7% (98.3-99.9%)	
Cream White		APAS Compact (predicate)		
		Positive	Negative	Total
APAS Independence	Positive	176	12	188
	Negative	17	145	162
	Total	193	157	350
Agreement (95% Confidence Interval)		176/193 91.2% (86.3-94.4%)	145/157 92.4% (87.1-95.6%)	
Small		APAS Compact (predicate)		
		Positive	Negative	Total
APAS Independence	Positive	195	44	239
	Negative	6	105	111
	Total	201	149	350
Agreement (95% Confidence Interval)		195/201 97.0% (93.6-98.6%)	105/149 70.5% (62.7-77.2%)	

**Table 12.** Comparison of colony morphologies on MacConkey agar designated by the Urine Analysis Module using the APAS Compact (predicate) and APAS Independence

Lactose Fermenter		APAS Compact (predicate)		
		Positive	Negative	Total
APAS Independence	Positive	110	1	111
	Negative	3	236	239
	<b>Total</b>	<b>113</b>	<b>237</b>	<b>350</b>
Agreement (95% Confidence Interval)		110/113 <b>97.3%</b> (92.5-99.1%)	236/237 <b>99.6%</b> (97.6-99.9%)	
Non-Fermenter		APAS Compact (predicate)		
		Positive	Negative	Total
APAS Independence	Positive	51	33	84
	Negative	2	264	266
	<b>Total</b>	<b>53</b>	<b>297</b>	<b>350</b>
Agreement (95% Confidence Interval)		51/53 <b>96.2%</b> (87.2-99.0%)	264/297 <b>88.9%</b> (84.8-92.0%)	
Non-pigmented		APAS Compact (predicate)		
		Positive	Negative	Total
APAS Independence	Positive	1	0	1
	Negative	0	349	349
	<b>Total</b>	<b>1</b>	<b>349</b>	<b>350</b>
Agreement (95% Confidence Interval)		1/1 <b>100%</b> (20.7-100%)	349/349 <b>100%</b> (98.9-100%)	
Red-Pink		APAS Compact (predicate)		
		Positive	Negative	Total
APAS Independence	Positive	7	13	20
	Negative	0	330	330
	<b>Total</b>	<b>7</b>	<b>343</b>	<b>350</b>
Agreement (95% Confidence Interval)		7/7 <b>100%</b> (64.6-100%)	330/343 <b>96.2%</b> (93.6-97.8%)	

2. Matrix Comparison:

Not applicable.

**C Clinical Studies:**

1. Clinical Sensitivity:

The clinical performance of the predicate APAS Compact with Urine Analysis Module was evaluated under [DEN150059](#). Because the APAS Independence with Urine Analysis Module uses the same hardware and software for image acquisition and analysis as the APAS Compact, additional testing to evaluate the sensitivity and specificity of the system was not needed. Please refer to the Decision Summary for [DEN150059](#) for additional information.

2. Clinical Specificity:

Refer to [Section VII C\(1\)](#), above.

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

Not applicable.

**D Clinical Cut-Off:**

Not applicable.

**E Expected Values/Reference Range:**

Refer to [Section VII C\(1\)](#), above.

**F Other Supportive Instrument Performance Characteristics Data:**

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.