

# Evaluation of the ARK Fentanyl II Assay across Siemens Healthineers Platforms

[siemens-healthineers.com](https://www.siemens-healthineers.com)

For use  
outside  
the U.S.

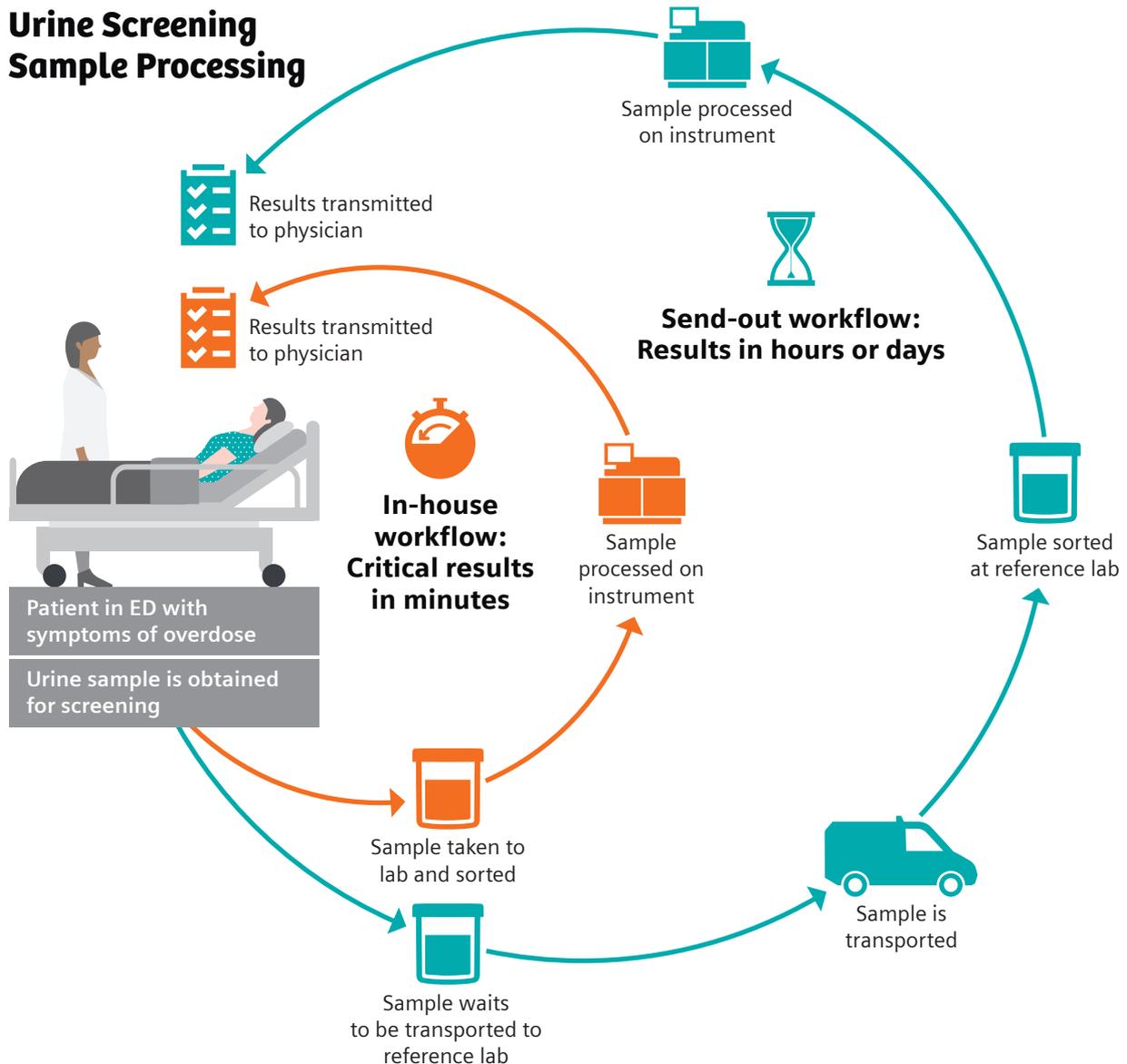
## Introduction

The drug addiction epidemic worldwide continues to grow. The misuse and addiction to opioids—including prescription pain relievers, heroin, and synthetic opioids such as fentanyl—is a serious global crisis that affects public health as well as social and economic welfare.<sup>1</sup> Worldwide, about 0.5 million deaths are attributed to drug use. More than 70% of these deaths are related to opioids, with more than 30% of those deaths caused by overdose.<sup>2</sup>

The number of opioid overdoses has increased in recent years in several countries, in part due to the increased use of opioids in the management of chronic pain and increasing use of highly potent opioids appearing on the

illicit drug market.<sup>2</sup> In the first four months of 2020, drug overdose deaths increased more than 11% compared to 2019.<sup>3</sup> These numbers suggest a correlation between the COVID-19 pandemic and the disruption in life to so many already struggling with drug addiction.

With the influx of illegal fentanyl and fentanyl-laced drugs, patients often do not know which drug they have taken. Lab testing becomes exceedingly challenging, yet critically important when someone is going through a fentanyl overdose. In addition, many labs do not test for fentanyl and must send out for screening and confirmation testing, which increases the time to result.



## Pharmacology<sup>4</sup>

Fentanyl [N-(1-(2-phenylethyl)-4-piperidyl)-N-phenylpropanamide] is a synthetic opioid narcotic analgesic similar to morphine but 50-100 times more potent. The primary metabolism of fentanyl leads to the time-dependent urinary excretion of fentanyl and norfentanyl. The half-life of fentanyl may range 3–12 hours. Fentanyl is exclusively metabolized by N-dealkylation and hydroxylation. More than 90% of the dose is eliminated as norfentanyl and hydroxylated metabolites. Less than 7% of the dose is excreted unchanged in the urine.

Fentanyl is prescribed for patients with chronic pain and is used to manage pain after surgery or for treatment of breakthrough pain in cancer patients. Routes of administration include injection (intravenous, intramuscular, or epidural), transdermal patch, and orally (transmucosal lozenge or film). Similar to other opioid agonists, legal or illicit, Fentanyl can be abused in all forms. All patients receiving opioids should be routinely monitored for signs of misuse and addiction. Fentanyl is abused for its intense euphoric effects. Because of its high potency and short duration of action, it is very dangerous when substituted illicitly for other opioids. Overdoses can lead to respiratory depression and death.

## ARK Fentanyl II Assay Intended Use and Crossreactivity

The ARK Fentanyl II Assay detects fentanyl in human urine. The test is not intended to differentiate between abuse and legitimate prescription use of fentanyl. There are no uniformly recognized drug levels for fentanyl in urine.

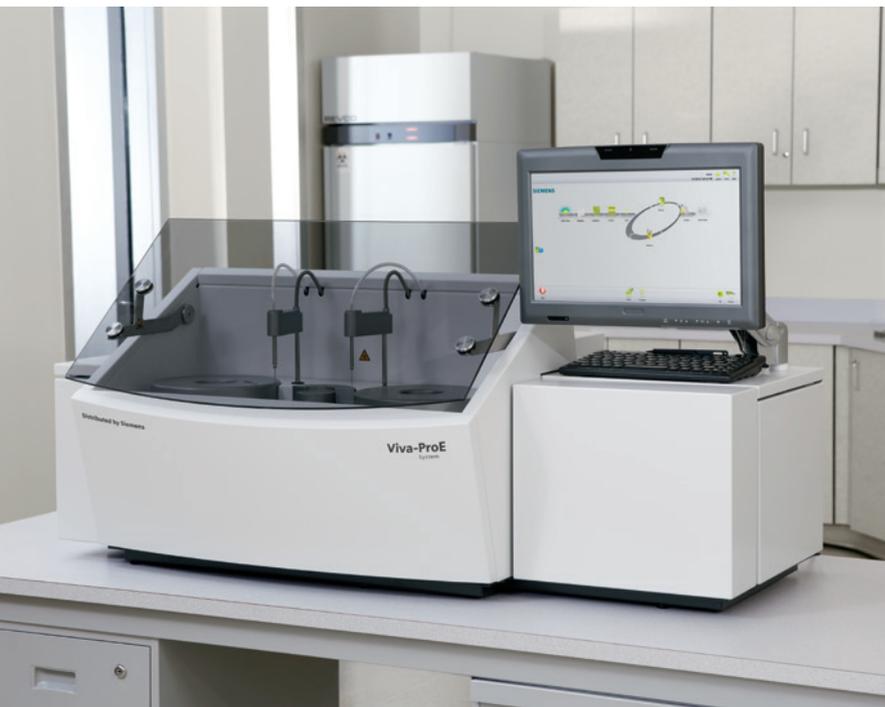
### Cross-reactivity

Norfentanyl (Major Metabolite)

Compound	Concentration Approximately Equivalent to the Cutoff (ng/mL)
Norfentanyl	15

### Other Metabolites and Structural Analogs of Fentanyl

Compound	Concentration Approximately Equivalent to the Cutoff (ng/mL)	Percent Cross-reactivity (%)
Acetyl fentanyl	1.1	90.91
Isobutyryl fentanyl	1.1	90.91
$\omega$ -1-Hydroxyfentanyl	1.2	83.33
Acrylfentanyl	1.3	76.92
Butyryl fentanyl	1.4	71.43
Furanyl fentanyl	1.5	66.67
Para-fluoro fentanyl	1.5	66.67
Ocfentanil	1.6	62.50
4-Fluoro-isobutyryl fentanyl	1.9	52.63
Para-fluorobutyryl fentanyl (p-FBF)	1.9	52.63
Valeryl fentanyl	2.3	43.48
$\beta$ -hydroxyfentanyl	9.5	10.53
Acetyl norfentanyl	12.1	8.26
( $\pm$ ) $\beta$ -hydroxythiofentanyl	32.7	3.06
( $\pm$ )-3-cis-methyl fentanyl	144.1	0.69
Carfentanil	448.2	0.22
Despropionyl fentanyl (4-ANPP)	471.8	0.21
Sufentanil	2,362	0.04
Norcarfentanil	>10,000	<0.01
Remifentanil	>10,000	<0.01
Alfentanil	>100,000	<0.001



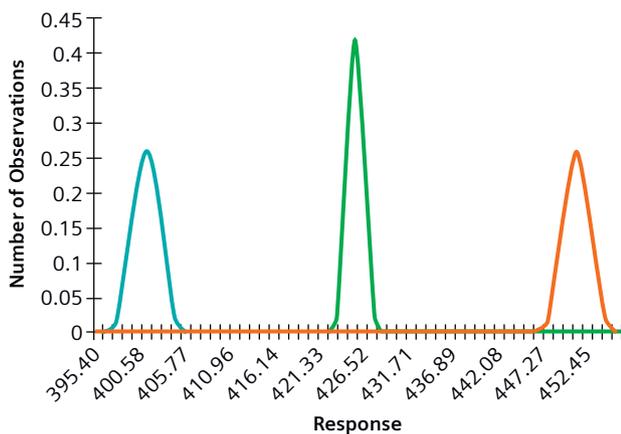
### Performance of the ARK Fentanyl II Assay on the Viva-ProE System

The Viva-ProE® System with EMIT® technology provides proven performance in a reliable, next-generation bench-top system. It delivers big performance without big inconvenience.

- Streamlined workflow with results in as little as 10 minutes.
- Comprehensive testing platform with semi-continuous sample loading and true random-access capability for routine and STAT samples.
- Innovative technologies and a consolidated drug-testing menu for drugs-of-abuse and validity testing, serum toxicology, and therapeutic and immunosuppressant drug monitoring.

#### Theoretical Distribution of Data Assuming Normality

Overlap was performed at the cutoff, -50% of the cutoff, and +50% of the cutoff



Characteristics	Results
Cutoff	1.0 ng/mL
Reagent Onboard stability	29 days
Calibration Stability	29 days
Sample volume	14 µL
Kit yield	245 tests (28 mL Reagent Kit) 1000 tests (115 mL Reagent Kit)

Method Comparison	ARK Fentanyl II Assay Result on AU680	
	(+)	(-)
ARK Fentanyl II Assay Result on Viva-ProE (+)	50	0
ARK Fentanyl II Assay Result on Viva-ProE (-)	0	50

## Performance of the ARK Fentanyl II Assay on the Dimension Series of Analyzers

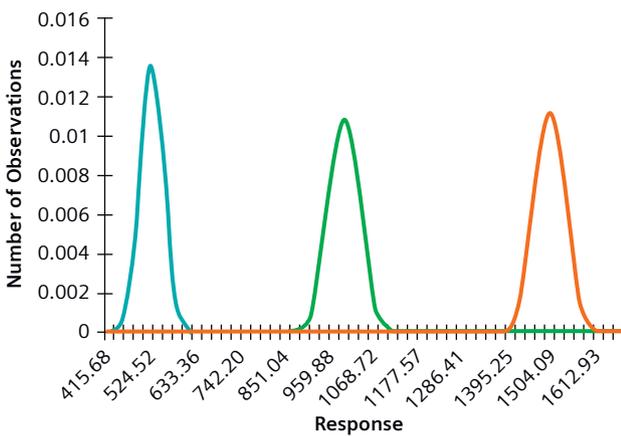
Dimension® EXL™ Integrated Chemistry Systems offer fast, easy-to-use versatility and proven outcomes.

- Deliver fast and reliable results using trusted, proven technologies including LOCI® advanced chemiluminescence.
- Free up your staff with automated, productivity-enhancing features, including proactive alerts, STAT sample loading in any position, and single-tube simultaneous sampling for both chemistry and immunoassays.
- Provide a comprehensive menu with many critical laboratory assays.



### Theoretical Distribution of Data Assuming Normality

Overlap was performed at the cutoff, -50% of the cutoff, and +50% of the cutoff



Characteristics	Results
Cutoff	1.0 ng/mL
Taped flex stability	7 days
Open well reagent stability	48 hours
Calibration stability	14 days
Sample volume	20 µL
Kit yield	140 tests (28 mL Reagent Kit) 620 tests (115 mL Reagent Kit)

Method Comparison		ARK Fentanyl II Assay Result on AU680	
		(+)	(-)
ARK Fentanyl II Assay Result on Dimension	(+)	50	0
	(-)	0	50



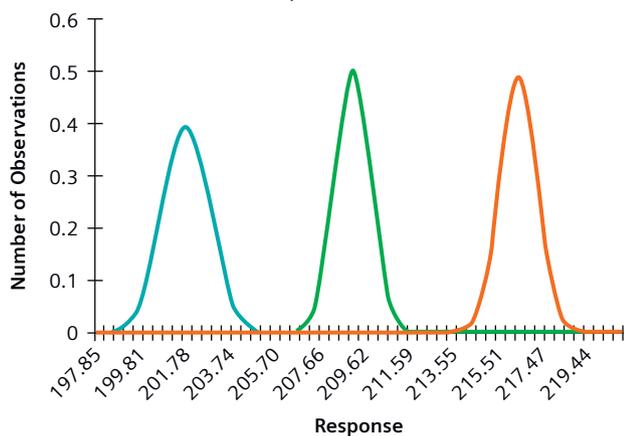
## Performance of the ARK Fentanyl II Assay on the Dimension Vista Series of Analyzers

The Dimension Vista® Intelligent Lab Systems provide intelligent analytics in which sample-centric design, unique integration of four technologies including LOCI® advanced chemiluminescence technology, and customer-driven engineering all come together for a more efficient workflow.

- Incorporate Lean principles with a sample-centric design for simplified, consolidated sample processing.
- Unique integration of four technologies to allow simultaneous processing of tests for multiple disease states on a single platform from a single tube.
- Eliminate many manual tasks with customer-driven engineering, freeing up technical time to address critical issues throughout the lab.

### Theoretical Distribution of Data Assuming Normality

Overlap was performed at the cutoff, -50% of the cutoff, and +50% of the cutoff



Characteristics	Results
Cutoff	1.0 ng/mL
Taped flex Stability	7 days
Open well Reagent Stability	24 hours
Calibration Stability	14 days
Sample Volume	7.5 µL
Kit Yield	340 tests (28 mL Reagent Kit) 1420 tests (115 mL Reagent Kit)

Method Comparison		ARK Fentanyl II Assay Result on AU680	
		(+)	(-)
ARK Fentanyl II Assay Result on Dimension Vista	(+)	50	0
	(-)	0	50

## Performance of the ARK Fentanyl II Assay on the Atellica® CH Analyzer

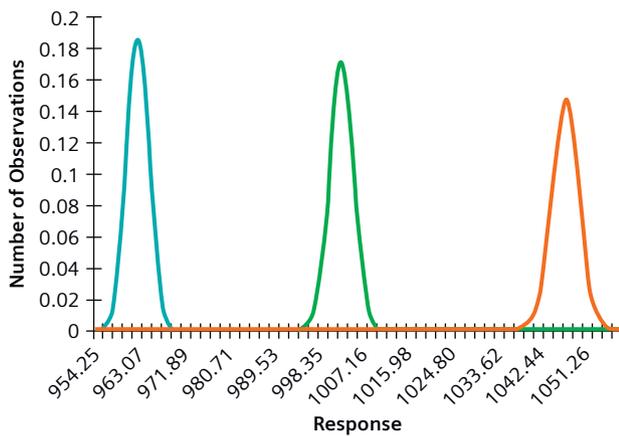
The Atellica Solution provides a broad and expanding menu to help your lab drive better clinical and business outcomes. The Atellica® CH Analyzer combines the proven technologies of IMT, Emit, PETINIA, and photometry, delivering a menu of over 90 chemistry assays.

- Provides confidence in results with assays that are highly specific for the target drugs, reproducible, and demonstrate consistent lot-to-lot stability.
- Simplifies your workflow and saves technicians' time with ready-to-use liquid reagents and calibrators with extended calibration stability.
- Identifies patients that are at risk and may need addiction treatment services.



### Theoretical Distribution of Data Assuming Normality

Overlap was performed at the cutoff, -50% of the cutoff, and +50% of the cutoff



Characteristics	Results
Cutoff	1.0 ng/mL
Reagent stability	60 days
Calibration stability	14 days
Sample volume	23 µL
Kit yield	260 tests (28 mL Reagent Kit) 1300 tests (115 mL Reagent Kit)

Method Comparison	ARK Fentanyl II Assay Result on AU680	
	(+)	(-)
ARK Fentanyl II Assay Result on Atellica CH (+)	50	0
ARK Fentanyl II Assay Result on Atellica CH (-)	0	49



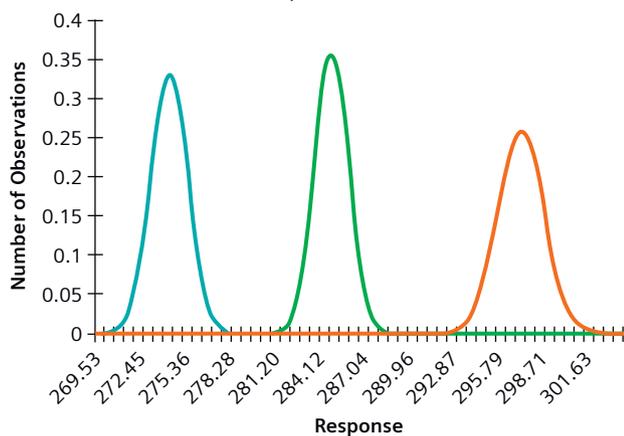
### Performance of the ARK Fentanyl II Assay on the ADVIA Chemistry System

ADVIA® Chemistry Systems offer simple, continuous operation; timely, reliable results; and powerful, seamless connectivity to keep pace with expanding laboratory demands.

- Deliver fast, predictable TAT and parallel processing through unique sample management and system verification technologies.
- Reduce blood-draw requirements and increase walkaway time with microvolume technology that enables over 100,000 tests onboard and uses a single 30 µL sample for up to 15 tests.
- Provide a comprehensive menu that includes general and specialty chemistry, drugs-of-abuse testing (DAT), therapeutic drug monitoring (TDM), and specific proteins.

#### Theoretical Distribution of Data Assuming Normality

Overlap was performed at the cutoff, -50% of the cutoff, and +50% of the cutoff



Characteristics	Results
Cutoff	1.0 ng/mL
Reagent Onboard stability	60 days
Calibration Stability	14 days
Sample volume	23 µL
Kit yield	318 tests (30 mL Reagent Kit) 1306 tests (115 mL Reagent Kit)

Method Comparison	ARK Fentanyl II Assay Result on AU680	
	(+)	(-)
ARK Fentanyl II Assay Result on ADVIA (+)	50	0
ARK Fentanyl II Assay Result on ADVIA (-)	0	50



## Competitive Comparison to Immunalysis SEFRIA

ARK Diagnostics, Inc. performed a comparison study of the ARK™ Fentanyl II Assay vs. Immunalysis SEFRIA Fentanyl Assay on the Beckman Coulter AU680® system. The ARK™ Fentanyl II Assay and Immunalysis SEFRIA™ Fentanyl Assay are intended for the qualitative detection of fentanyl in human urine at a cutoff concentration 1.0 ng/mL. Precision, method comparison, and cross-reactivity profiles were all evaluated.

Precision was evaluated for both assays using their respective controls. A single calibration was generated, and 20 replicates each for low and high controls and cutoff were assayed in qualitative mode.

### ARK Fentanyl II Assay System Check Precision

ARK	Mean*	SD	%CV	N
LOW 0.5 ng/mL	42.4	3.8	8.9	20
Cutoff 1.0 ng/mL	93.5	3.2	3.4	20
HIGH 1.5 ng/mL	147.5	3.4	2.3	20

\*Qualitative units are relative to 1.0 ng/mL normalized as 100 Units

### Immunalysis SEFRIA Fentanyl Assay System Check Precision

Immunalysis SEFRIA	Mean*	SD	%CV	N
LOW 0.5 ng/mL	65.0	4.0	6.1	20
Cutoff 1.0 ng/mL	101.8	5.9	5.8	20
HIGH 1.5 ng/mL	169.8	5.6	3.3	20

\*Qualitative units are relative to 1.0 ng/mL normalized as 100 Units

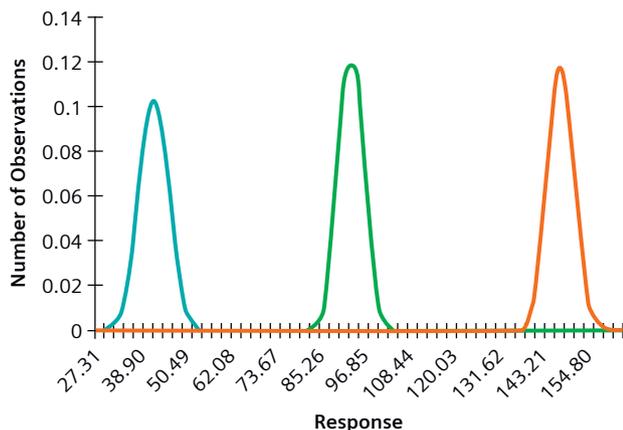
When comparing precision at the cutoff for both assays, the ARK Fentanyl II Assay demonstrates a smaller %CV when compared to the SEFRIA assay. Both assays have slightly higher %CVs at the low end, which is typical performance.

### Histogram (Overlap Chart)

This data highlights performance of each assay with controls run at the cutoff, -50% of the cutoff, and +50% of the cutoff. This demonstrates how an assay performs near the cutoff. In the study performed by ARK Diagnostics, results meet the specification of less than 5% chance of controls overlapping with cutoff.

#### Theoretical Distribution of Data Assuming Normality

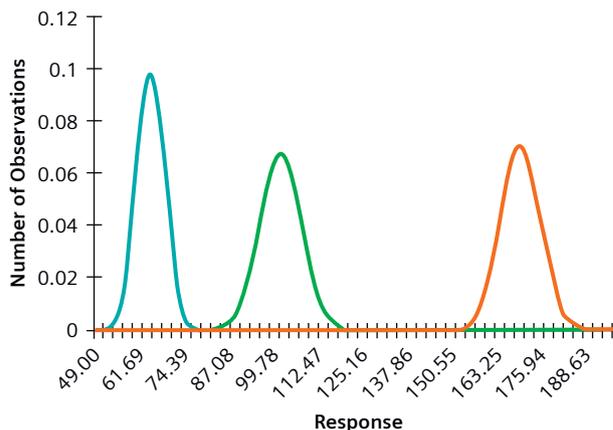
Overlap was performed at the cutoff, -50% of the cutoff, and +50% of the cutoff



ARK Fentanyl II Histogram

#### Theoretical Distribution of Data Assuming Normality

Overlap was performed at the cutoff, -50% of the cutoff, and +50% of the cutoff



Immunalysis SEFRIA Fentanyl Histogram

The ARK Fentanyl II Assay results show a greater separation between the low and high controls in relation to the cutoff when compared to the Immunalysis SEFRIA results.

### Method Comparison

Relative to the 1 ng/mL cutoff, the results show that both the ARK assay and Immunalysis SEFRIA assay distinguished 95 samples as positive and 50 samples as negative. The percent agreement of samples between the ARK assay and Immunalysis SEFRIA assay for the 1 ng/mL cutoff is 100%.

1 ng/mL Cutoff		ARK Fentanyl II Assay	
		(+)	(-)
Immunalysis SEFRIA Fentanyl Assay	(+)	95	0
	(-)	0	50

### Cross-reactivity

The major metabolite, norfentanyl, was spiked into negative pooled urine and evaluated relative to the 1 ng/mL cutoff by both assays. The results are summarized in the table to the right.

Sample	ARK	SEFRIA
	Concentration (ng/mL)	
Norfentanyl	15	12,333

SEFRIA IFU claims 20,000 ng/mL creates a norfentanyl positive

The primary metabolism of fentanyl leads to the time-dependent urinary excretion of fentanyl and norfentanyl. The half-life of fentanyl may range from 3–12 hours. More than 90% of the dose is eliminated as norfentanyl and hydroxylated metabolites. Less than 7% of the dose is excreted unchanged in the urine.<sup>3</sup>

In general, one may expect to find urine norfentanyl concentrations 3–4 times higher than those of fentanyl.<sup>5</sup> Because of this rapid metabolism of fentanyl to norfentanyl, it is imperative for assays to pick up norfentanyl. If there is no cross-reactivity with norfentanyl, there is risk of false-negative results.

The table to the right illustrates the assay response in mixtures of fentanyl and norfentanyl spiked at varying concentrations in negative human urine. In the design of the ARK assay, antibodies were selected to detect both fentanyl and norfentanyl so that samples that have fentanyl concentrations below the 1.0 ng/mL fentanyl cutoff could screen positive if norfentanyl was also present in the sample. Thus, as seen in the table above, fentanyl concentrations below the 1.0 ng/mL fentanyl cutoff could screen positive by the ARK assay if norfentanyl is present in the sample.

### ARK vs. Immunalysis SEFRIA Norfentanyl Mixture Cross-reactivity

		Norfentanyl (ng/mL)				
		0.0	5.0	10.0	25.0	
ARK	Fentanyl (ng/mL)	0.0	NEG	NEG	NEG	POS
		0.5	NEG	NEG	POS	POS
		1.0	POS	POS	POS	POS
SEFRIA	Fentanyl (ng/mL)	0.0	NEG	NEG	NEG	NEG
		0.5	NEG	NEG	NEG	NEG
		1.0	POS	POS	POS	POS

The cross-reactivity of haloperidol, labetalol, risperidone, and trazodone were determined by spiking each compound into negative pooled urine to trigger the cutoff calibrator. The results are summarized in the table to the right and are expressed as the minimum concentration required to produce a response approximately equivalent to the cutoff of the assay. What can be noted from the table above is that these four commonly prescribed drugs do not cause a false positive in the ARK Fentanyl until levels that are very high. Conversely in the Immunalysis SEFRIA Fentanyl Assay, these four drugs will illicit a positive (false positive) result with as little as 1,700 ng/mL of Haloperidol in the sample.

### ARK vs. Immunalysis SEFRIA Cross-reactivity

Sample	ARK	SEFRIA
	Concentration (ng/mL)	
Haloperidol	56,400	1,700
Labetalol	>100,000	14,700
Risperidone	>100,000	6,600
Trazodone	>100,000	5,600

## Summary

The ARK Fentanyl II Assay is available across the entire Siemens Healthineers chemistry portfolio of instruments, making it easy to implement into any drug-testing panel in the laboratory. Through an exclusive partnership arrangement, ARK Diagnostics and Siemens Healthineers can work together in creating Alliance Applications that are optimized to perform on Siemens Healthineers instruments.

Siemens Healthineers offers a comprehensive portfolio of drugs-of-abuse assays to assist laboratories in customizing their screening panels that better enable physicians to identify, treat, and support their community of addicted patients. The opioid epidemic does not discriminate. Treatment starts with a test.



## Ordering Information

SMN	ARK Catalog Number	Description
11554027	5069-0001-00	ARK Fentanyl II Assay, 28 mL R1 (Antibody/Substrate) 28 mL R2 (Enzyme)
11554028	5069-0001-01	ARK Fentanyl II Assay, 115 mL R1 and 115 mL R2
11554029	5069-0001-02	ARK Fentanyl II Assay, 500 mL R1 and 500 mL R2
11354475	5031-0002-01	ARK Fentanyl Calibrator A (Negative) 0 ng/mL fentanyl in human urine
11354476	5031-0002-02	ARK Fentanyl Calibrator B (Cutoff) 1.0 ng/mL fentanyl in human urine
11354477	5031-0003-00	ARK Fentanyl Control, low (0.5 ng/mL fentanyl) and high (1.5 ng/mL) in human urine

### References:

1. <https://www.drugabuse.gov/drug-topics/opioids/opioid-overdose-crisis>
2. <https://www.who.int/news-room/fact-sheets/detail/opioid-overdose>
3. <https://www.aamc.org/news-insights/covid-19-and-opioid-crisis-when-pandemic-and-epidemic-collide>
4. ARK Package Insert for Fentanyl II 1600-1032-00 Rev 01
5. <https://www.ncbi.nlm.nih.gov/pubmed/15516290>





At Siemens Healthineers, our purpose is to enable healthcare providers to increase value by empowering them on their journey toward expanding precision medicine, transforming care delivery, and improving patient experience, all made possible by digitalizing healthcare.

An estimated 5 million patients globally benefit every day from our innovative technologies and services in the areas of diagnostic and therapeutic imaging, laboratory diagnostics, and molecular medicine, as well as digital health and enterprise services.

We are a leading medical technology company with over 120 years of experience and 18,000 patents globally. Through the dedication of more than 50,000 colleagues in 75 countries, we will continue to innovate and shape the future of healthcare.

Atellica, Dimension, Dimension Vista, EMIT, EXL, LOCI, Viva-ProE, and all associated marks are trademarks of Siemens Healthcare Diagnostics Inc., or its affiliates. All other trademarks and brands are the property of their respective owners.

Product availability may vary from country to country and is subject to varying regulatory requirements. Please contact your local representative for availability.

---

**Siemens Healthineers Headquarters**

Siemens Healthcare GmbH  
Henkestr. 127  
91052 Erlangen, Germany  
Phone: +49 9131 84-0  
siemens-healthineers.com

**Published by**

Siemens Healthcare Diagnostics Inc.  
Laboratory Diagnostics  
511 Benedict Avenue  
Tarrytown, NY 10591-5005  
USA  
Phone: +1 914-631-8000