



# **k153726**

## **Alere Afinion HbA1c Dx Test System**

Clinical Chemistry and Toxicology Panel Meeting  
July 22, 2016

### **FDA Presentation**

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FDA/CDRH/OIR/DCTD

# Purpose of Panel Meeting

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Cleared assay on the market:

## **Afinion HbA1c test system**

Quantitative determination of % HbA1c in capillary and venous blood  
Intended for the long-term metabolic control in patients with diabetes  
( = “[monitoring claim](#)”)



Current 510(k) submission:

The sponsor is seeking a new [diagnostic claim](#) for the Afinion HbA1c

# Presentation Agenda

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- Regulatory History
- HbA1c testing
  - CLIA Complexity
  - Proficiency Testing
- Point-of-Care (POC)
  - Advantages
  - Disadvantages
- **Panel Question 1**
- Monitoring Afinion HbA1c vs. diagnostic Afinion HbA1c Dx
- **Panel Question 2**
- CLIA Waiver by application
- **Panel Question 3**

# Proposed Indications for Use

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## **Afinion HbA1c Dx (diagnostic claim):**

This test is to be used as an aid in the [diagnosis of diabetes](#) and as an aid in identifying patients who may be at [risk for developing diabetes](#). The measurement of % HbA1c is recommended as a marker of long-term metabolic control in persons with diabetes mellitus.

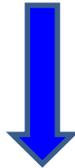
For use in clinical laboratories and [moderately complex] [point-of-care](#) laboratory settings.

# Regulatory History HbA1c

Since before 1976:

For patients already diagnosed with diabetes

Track long-term glycemic control



**Monitoring HbA1c tests**



*Only if acceptable analytical/clinical performance (e.g., accuracy)*

Since 2013:

For patients without diabetes

Diagnose diabetes

Determine the risk of developing diabetes in the future



**Diagnostic HbA1c tests**

# Diagnostic HbA1c tests

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- Performance must be equivalent to the performance of a legally marketed diagnostic HbA1c device
  - Devices must be precise
  - Devices must be accurate: the total error compared to a standardized method cannot exceed 6%
  - Devices must have little to no chance of giving false test results for samples containing common hemoglobin variants (HbC, HbD, HbE, HbA2, HbS)
  - Devices must maintain annual certification with a glycohemoglobin standardization organization (e.g., NGSP)
- Currently, all diagnostic HbA1c devices have been cleared for use in central laboratory settings

# Panel Meeting Focus

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American Diabetes Association 2016 guidelines:

“...use of point-of-care assays for diagnostic purposes is not recommended.”



Panel Discussion



Diagnosis of diabetes using  
HbA1c in moderately complex  
POC settings?

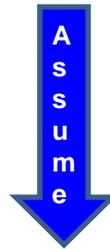
Future CLIA waiver?

# Device Performance

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FDA is still evaluating the performance characteristics of the Afinion HbA1c Dx system (e.g., accuracy, precision)

**Today's discussion focus is on point-of-care (POC)**



Performance of Afinion HbA1c Dx system

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Performance of other diagnostic HbA1c tests on the market

**Note: FDA will not clear this device for marketing unless its performance is substantially equivalent to other cleared diagnostic HbA1c devices**

# HbA1c testing environments



Central laboratories



Physician Office Laboratories

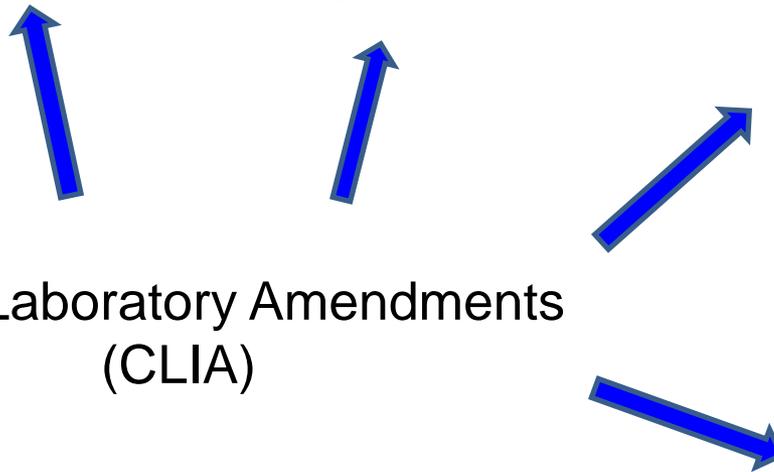


Emergency Departments

Clinical Laboratory Amendments  
(CLIA)



Community Health Clinics



# Clinical Laboratory Improvement Amendments (CLIA)

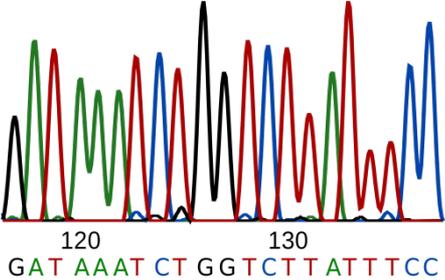
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- Ensure quality laboratory testing
- Any laboratory that performs testing on human specimens (e.g. blood, urine, tissue) for the purpose of diagnosis, prevention, or treatment of disease, or assessment of health, must be certified under the CLIA regulations
- Every *in vitro* diagnostic test falls into one of three CLIA categories:
  - Waived
  - Moderate Complexity
  - High Complexity
- The type of CLIA certificate determines the complexity of tests a lab is allowed to run

# CLIA Complexity - Laboratories

	Certificate of Waiver	Moderate Complexity	High Complexity
<b>Example</b>	 <p>Community Health Clinics</p>	 <p>Community Hospital Labs</p>	 <p>University Hospital Labs</p>
<b>Proficiency Testing</b>	Not required	Required (3 times/year)	Required (3 times/year)
<b>Personnel requirements</b>	None	Yes	Yes
<b>QC/QA requirements</b>	Follow manufacturer's QC instructions	Yes	Yes
<b>CMS Inspection Frequency</b>	On-site visits for ~ 2% of laboratories each year	On-site visits every 2 years	On-site visits every 2 years

# CLIA Complexity - Tests

	Waived	Moderate Complexity	High Complexity
<b>Definition</b>	<p>Simple tests with low likelihood of erroneous result</p> <p>Over-the-counter, CLIA waiver by application</p>	<p>Tests with several steps (i.e., sample separation into serum/plasma)</p>	<p>Complex tests with manual steps or extensive troubleshooting</p> <p>Any tests not categorized or cleared tests modified by lab</p>
<b>Example</b>	 <p>Urine pregnancy test</p>	 <p>Automated immunoassay to detect Vitamin D in serum</p>	 <p>DNA sequencing</p>

# Proficiency Testing for HbA1c...

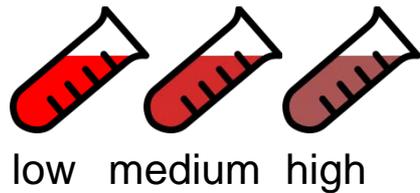
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- ... determines and compares the performance (e.g., accuracy, precision) of individual laboratories on unknown test samples provided by a proficiency testing program (e.g., the CAP survey)
- ... is designed to ensure ongoing quality of test results
- ... evaluates test performance in a realistic clinical environment
- ... should be performed at least 2x per year to verify test accuracy
- ... is only required in moderate and high complexity labs

Note: Proficiency testing results for HbA1c typically only reflect the use of venous blood samples, not capillary fingerstick blood samples

# CAP\* proficiency testing survey for HbA1c

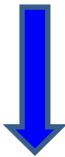
\*College of American Pathologists



low medium high

%HbA1c

Pooled, fresh venous whole blood samples  
(target values assigned by mean of all standardized reference labs in NGSP network)

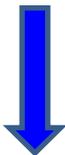


Samples



Analysis = patient sample

Clinical Lab



Results

CAP survey

Reports accuracy and inter-lab precision for each method tested

To pass CAP survey:  
2 out of 3 samples  
must have accuracy within  
 $\pm 6\%$  of sample target value

# Point-of-Care (POC) testing



Physician Office Laboratories



Emergency Departments  
Intensive Care Units

**Near patient testing**



Operating Rooms



Community Health Screenings  
Diabetes Clinics

# Advantages of POC testing for HbA1c

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↑ Access / patient engagement



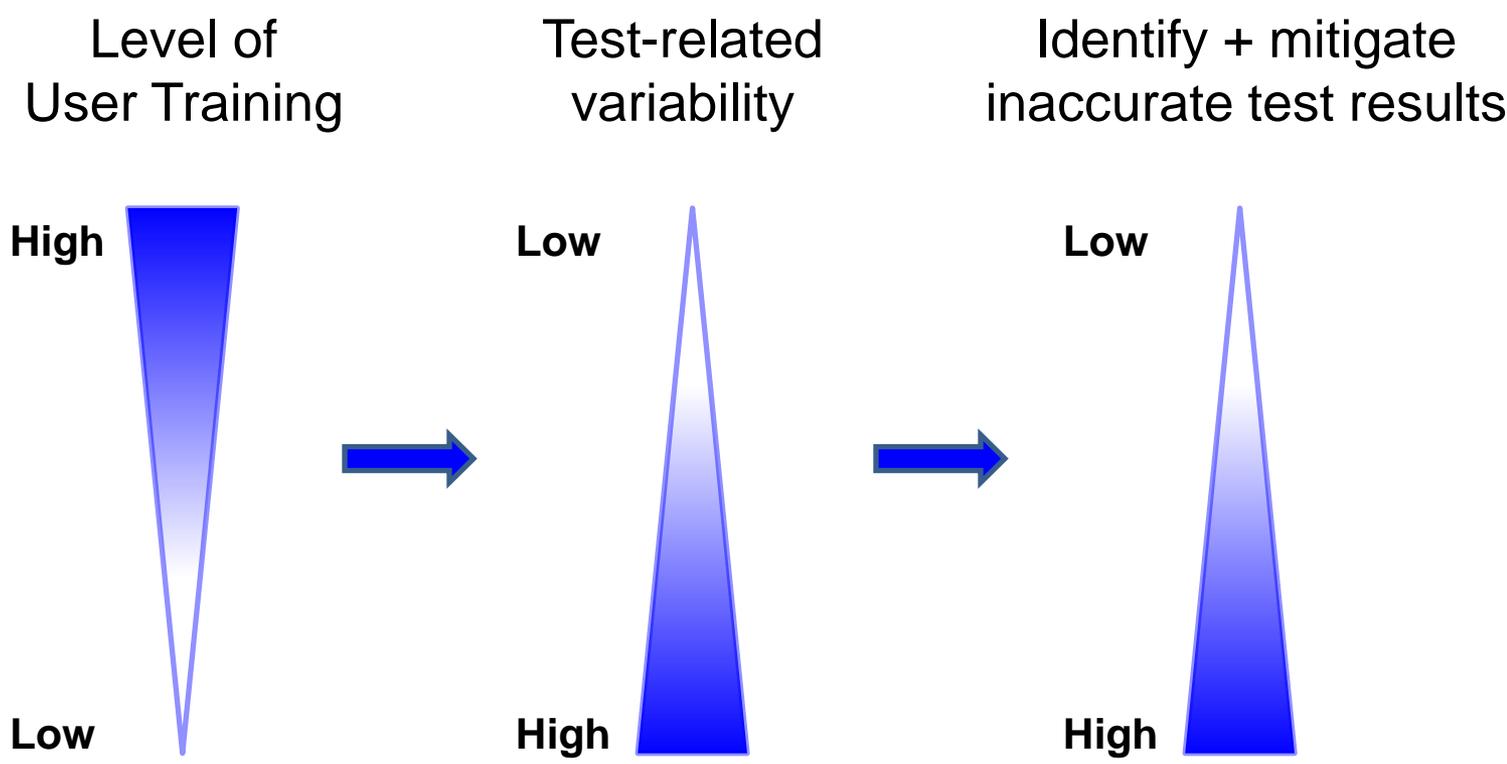
↑ Timely treatment decisions



↑ Glycemic control

# Disadvantages of POC testing in general

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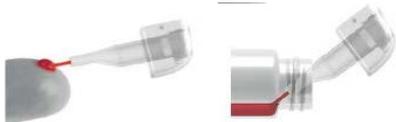
# Panel Questions

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1. In their “Standards of Medical Care in Diabetes” practice guidelines, the American Diabetes Association (ADA) recommends against the use of POC HbA1c tests for the diagnosis of diabetes.
  - a. Does the panel have any concerns about risks to health regarding the use of POC HbA1c devices in general for the diagnosis of diabetes? If so, please describe these concerns.
  - b. Does the Afinion HbA1c Dx test system, with an intended use in moderate complexity POC settings, raise any new concerns about risks to health? If so, please describe these concerns.
  - c. If the panel has concerns about risks to health for a or b above, what mitigations, if any, may be implemented to address those concerns?

# Afinion HbA1c (waived) vs. Afinion HbA1c Dx

- The Afinion HbA1c (waived) test has been in clinical use since 2005

	Afinion HbA1c (waived)	Afinion HbA1c Dx
	Sample type and collection (capillary, venous blood)	SAME
	Assay reagents	SAME
	Analyzer <ul style="list-style-type: none"> <li>Name</li> <li>Sample processing</li> <li>%HbA1c calculation algorithm</li> <li>QC control lockout to restrict operators and tests</li> <li>User manual</li> </ul>	SAME

# Afinion HbA1c (waived) vs. Afinion HbA1c Dx

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- Differences:
  - Reagent cartridge:
    - Name and catalog number
    - Barcode
    - Package insert
  - Analyzer:

CLIA waived version	Moderate complexity version
At start up, screen displays "CLIA waived"	N/A
Restricted to run only CLIA-waived Afinion HbA1c reagent cartridge	Runs all Afinion tests
CLIA-waived quick guide	Moderate complexity quick guide
Results display 1 decimal point	Results display 2 decimal points

## Panel Questions

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2. The sponsor has proposed a number of ways to separate their current CLIA waived monitoring HbA1c test from their proposed moderately complex diagnostic HbA1c test. However, laboratories in the clinical community will be aware that the Afinion HbA1c diagnostic test and the current Afinion HbA1c monitoring test are the same test with two different names.

Is the sponsor's proposed strategy to differentiate the current CLIA waived monitoring Afinion HbA1c test system from the proposed Afinion HbA1c diagnostic test system adequate to address concerns about the use of [POC monitoring HbA1c tests to diagnose diabetes in CLIA waived settings by untrained personnel?](#)

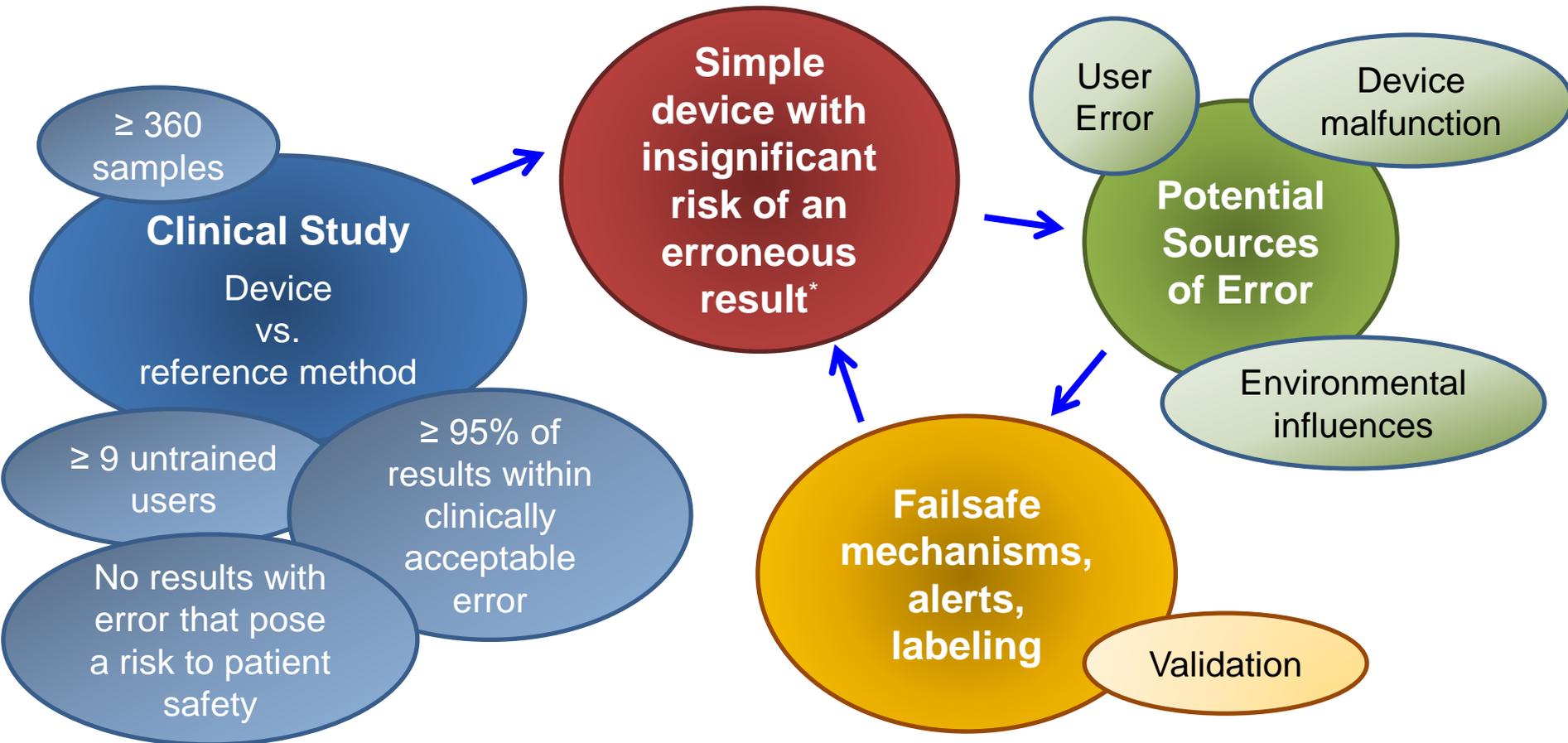
# CLIA Waiver

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- The currently marketed monitoring Afinion HbA1c test system was CLIA waived by application in 2006 and is primarily used in CLIA waived POC sites
- Afinion HbA1c Dx as described in this 510(k) is intended for use in moderate complexity laboratories

**The sponsor has indicated that they might apply for a CLIA waiver for the Afinion HbA1c Dx in the future**

# How to obtain a CLIA Waiver by application



\*FDA Guidance "Recommendations for Clinical Laboratory Improvement Amendments of 1988 (CLIA) Waiver Applications for Manufacturers of In Vitro Diagnostic Devices"

# Panel Questions

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3. Based on the design of the Afinion HbA1c Dx test system:
  - a. Please discuss the potential advantages and disadvantages of using this test as an aid in the diagnosis of diabetes and as an aid in identifying patients who may be at risk for developing diabetes in CLIA waived point-of-care settings?
  - b. If there are any risks to health associated with the use of this device in CLIA waived point-of-care settings, are there potential mitigations that may be employed by the manufacturer that are adequate to address these risks to health?

# Thank you!

## American Diabetes Association 2016 guidelines:

“...use of point-of-care assays for diagnostic purposes is not recommended.”



Diagnosis of diabetes using HbA1c in moderately complex POC settings?



Future CLIA waiver for diagnostic HbA1c POC devices?

# References

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