Successful Submissions for Point-of Care (POC) IVDs

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Disclaimers

- This presentation is intended for informational purposes only and does not constitute legal or regulatory advice.

- Examples used in this presentation are for educational purposes and do not represent in any way FDA endorsement to any specific POC device.

Outline

- What is POC testing
- Claims for POC devices
- Performance Studies to support POC
  - Sites and Operators
- Some examples

In Scope for Discussion

- FDA Risk Class: all FDA Risk Classes (I, II and III) IVDs
- CLIA complexity: Point-of-care testing for CLIA non-waived settings (i.e. CLIA moderate and high complexity settings)
- Point-of-care testing utilizing any human specimen type (i.e. blood, body fluid, or tissue)
- Point-of-care testing that is performed under the direction of a laboratory director
- Point-of-care testing that requires a prescription

Out of Scope

- Point-of-care testing that is CLIA-waived by application or regulation
- Point-of-care testing that is addressed in assay specific guidances (i.e. Blood Glucose Monitoring Test Systems for Prescription Point-of-Care Use)
- Point-of-care testing that is direct-to-consumer (DTC), over-the-counter (OTC), or for prescription home use

Poll the Audience

My company is planning on developing POC in vitro diagnostics in the next 2 years.

a) Yes

b) No

Definition of POC Testing

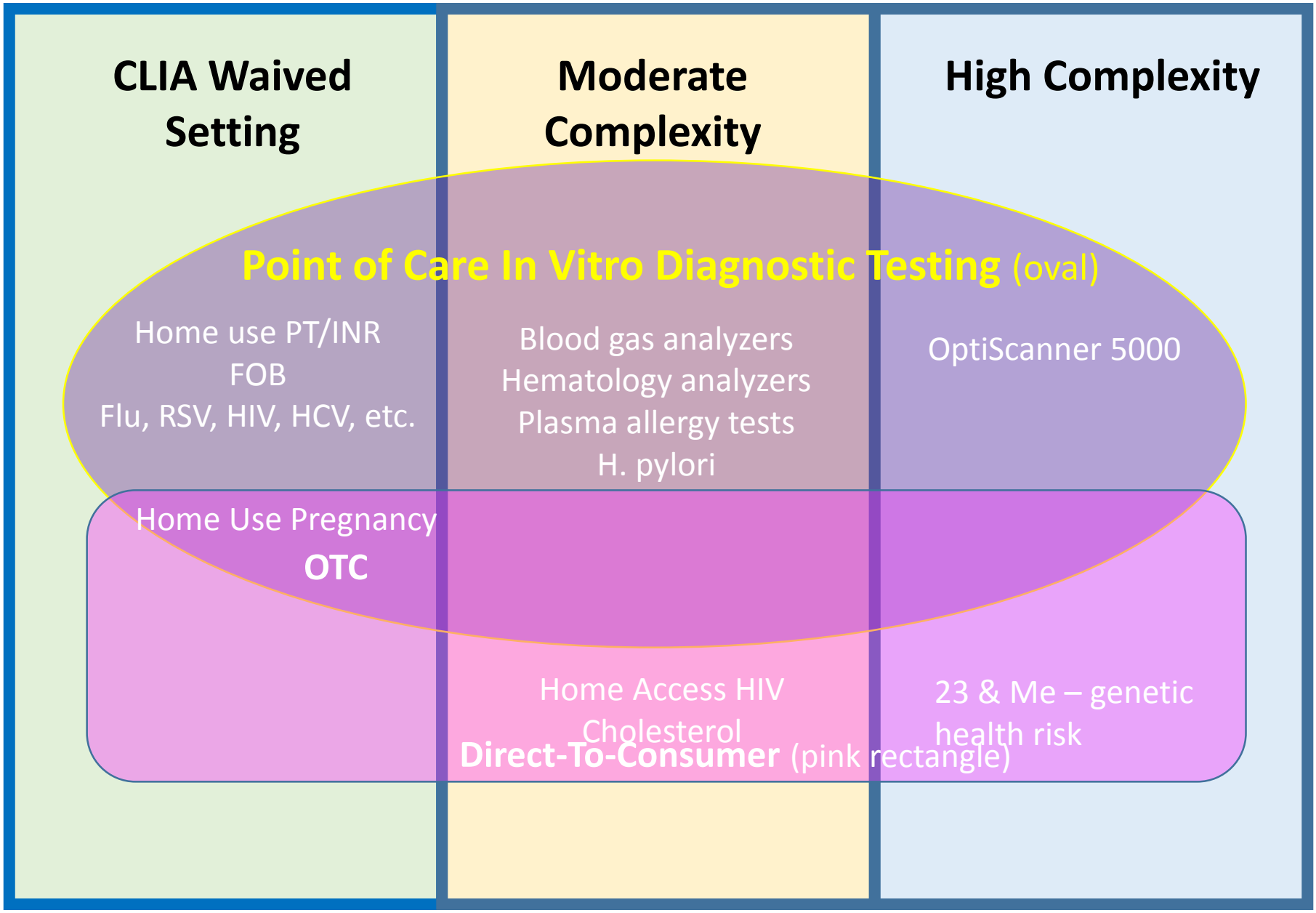
Point-of-care in vitro diagnostic testing:

- Refers to testing that is performed near a patient
- Is decentralized testing, outside of centralized laboratory testing facilities
- Is not intended to refer to sample collection procedures only

FDA stand point on POC term

- FDA considers “point-of-care” testing (POCT) as diagnostic testing performed near the patient, i.e., **where all steps from sample collection to the availability of results are performed near the patient, and where transportation of the sample to another functional area (e.g., a central laboratory or other specialized area) is not required.**

US Clinical Laboratory Testing

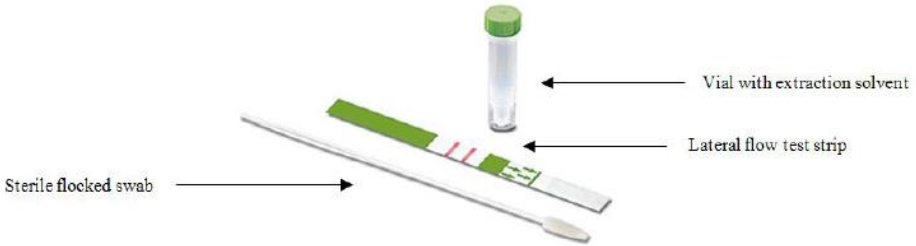


Dx Testing Locations

	POC (Type 1)	POC (Type 2)	POC (Type 3)	CENTRAL LAB
Healthcare Setting	Doctor's Office	Small Lab (group of MDs)	Medical Institution	
			ER, OR, Bed-side	Hospital Lab
Relative to Patient	(Near Patient)	(Near Patient)	(Near Patient)	(Away from Patient)
Type of Testing (CLIA Complexity)	**Waived**	**Non-waived** (Moderate Complexity)	**Non-waived** (Usually Moderate Complexity)	**Non-waived** High and Moderate Complexity
Oversight	Lab Director	Lab Director	Lab Director and POC Coordinator	
CLIA Certificate	CoW	Certificate of Compliance	Certificate of Compliance	
Operators (Testing Staff)	Nurses, Doctors, PAs, Office Staff	Professional Laboratory Staff	Trained Nurses Professional Laboratory Staff	Professional Laboratory Staff

POC devices are diverse

Figure 1: PartoSure test kit



Audience Knowledge Test

General POC Claim Questions

Could an IVD have FDA cleared laboratory and POC claims?

a) Yes

b) No

Audience Knowledge Test

General POC Claim Questions

Does a 510(k) POC submission require a predicate with a POC claim?

a) Yes

b) No

POC claims

- POC claims are given for assays or test systems
- FDA does not provide clearance for an instrument alone, without an associated assay.
  - To claim POC use of an instrument, performance of that instrument should be evaluated with an assay at POC sites
- FDA will conduct a labeling review for a new device to determine whether POC claims can be appropriately applied to the device labeling

Example Intended Use With POC

The cobas HbA1c Test is an in vitro diagnostic test designed to quantitatively determine glycated hemoglobin (HbA1c) in capillary finger-stick or venous whole blood, collected in EDTA (K2 or K3) or lithium heparin tubes, on the cobas b 101 instrument. This test is intended for professional use in a clinical laboratory setting or **point-of-care (PoC)** locations. This test is not for screening or diagnosis of diabetes or neonatal use. Measurement of hemoglobin A1c is used to monitor long term blood glucose control in patients previously diagnosed with diabetes.

Analyte

Matrices

Indication for Use

Ref: https://www.accessdata.fda.gov/cdrh_docs/reviews/K163633.pdf

Studies to support POC claims

Complete list varies depending on:

- **Claims** in the intended use
- Type of assay: qualitative, semi-quantitative, quantitative
- Components of the test system: unitized device, cartridges, instrument, collection devices, etc.
- Assay principle or chemistries
- Others

Studies to support POC claims

Typically included (for Quant)

- Precision
- Linearity
- Limit of detection
- Interfering substances
- Method comparison
- Matrix comparison
- Reference range
- Traceability

Depending on the device…

- Clinical Studies
- Electrical safety testing
- EMC testing
- Software documentation
- Disinfection studies

[instruments]

- Altitude studies [if sensitive to oxygen levels or pressure]
- Hematocrit effect
- Cross reactivity and Hook effect [immunoassays]
- Biocompatibility
- Etc...

Studies to support POC claims

- **The method comparison or clinical study (as applicable) and reproducibility study should be conducted at POC settings with POC operators**

- We recommend at least **3 sites** with at least **2 operators at each site** participate
- For a general POC claim, sponsors should select sites that are diverse and representative (e.g., emergency room, outpatient clinic, etc.)
- Selected POC sites should provide healthcare to the patients from the intended use population

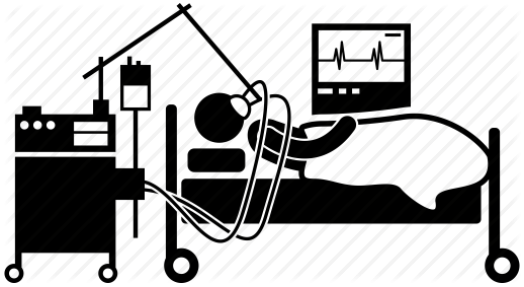
Studies to support POC claims

- FDA strongly recommends you perform studies at POC sites in the U.S. POC sites outside of the U.S. may be acceptable in some circumstances
  - Demographic differences between U.S. and foreign population do not affect test results
  - POC site operations and POC operators at foreign sites reflect the typical POC site operations and POC operators in the U.S.
  - We would recommend that you come in with a list of potential study sites to obtain our feedback before initiating any study outside of the U.S.

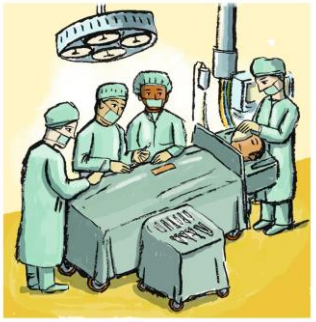
POC Testing Sites

- POC Sites (active clinical sites)

Examples:



Bedside testing in hospital wards



Surgical Wards

Urgent care clinics

Physician office labs

POC Operators

- Testing performed by healthcare personnel (laboratory and non-laboratory)
- Personnel are subject to CLIA regulations with regard to personnel qualifications, training and Laboratory Director oversight
- Examples:
  - Nurses
  - Medical assistants
  - Doctors
  - Medical technologists

Operator/Site Requirements

- For POC devices that are used for multiple patients what are the disinfection requirements?
  - Handheld vs. tabletop
  - How do perform repeatability/reproducibility for fingerstick sample collection devices?

Sample Matrix Requirements, an example

- Difficulties encountered with fingerstick whole blood sample
  - Limited sample stability makes interference testing difficult/impossible
  - Limited sample stability does not allow for contrived sample development
- Remedy?
  - Where possible consider adding a stable sample matrix to your IU, for example plasma
  - Surrogate samples will enable some analytical studies (interference, reagent stability, etc.) that are not possible with fingerstick samples
  - Surrogate samples will enable ability to contrive samples

Examples of FDA Cleared POC IVDs

- Abbott i-STAT Alinity system with Hematocrit test (k163342) and Glucose test (k163271)
- Roche Cobas 101 system with HbA1c test (k163633)
- Instrument Laboratory GEM Premier 5000 with electrolytes (k160225), blood gas (k160412), glucose, lactate, tBili (k160402), hematocrit, tHb (k160415)
- Sysmex XW-100 Automated Hematology Analyzer (k143577)

Summary

- Definition of Point-of-Care testing is critical to discussing testing requirements
- A 510(k) clearance with a POC claim in the Intended Use represents permission to market the device to all CLIA moderate or high complexity settings where the testing is performed near patient by prescription
- Clearance based on data obtained at POC sites does not mean you are able to distribute your device to CLIA waived sites

Help is available!

- FDA/OIR decisions are publicly available
  - Class II - Decision Summaries of 510(k) clearances

    https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm
  - Class III - Summary of Safety and Effectiveness Data

    https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pma.cfm

- If you have specific questions about your POC IVD development and study designs:
  - Pre-submission process

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