BU College of Engineering

PharmaChk

Testing the quality of medicines in the field

Boston University

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February 1st, 2018

Engineering for Social Impact

- Active engagement from local stakeholders
- Multidisciplinary approach
- Working in the field
- Focus beyond the technology
  - Cultural barriers to adoption
  - Policy aspects
  - Field testing and feedback

Counterfeit and Substandard Medicines: A Global Challenge

- Poor quality medicines make up **10 – 30%** of drug sales worldwide
  - Causes over 100,000 preventable deaths annually
- Poor quality medicines account for US$ 75 billion of US$ 962 billion global pharmaceutical market
- Poor quality medicines contribute to drug-resistant infection and disease
  - Artemisinin resistant malaria on Thailand-Cambodia border

PharmaChk: The Mission

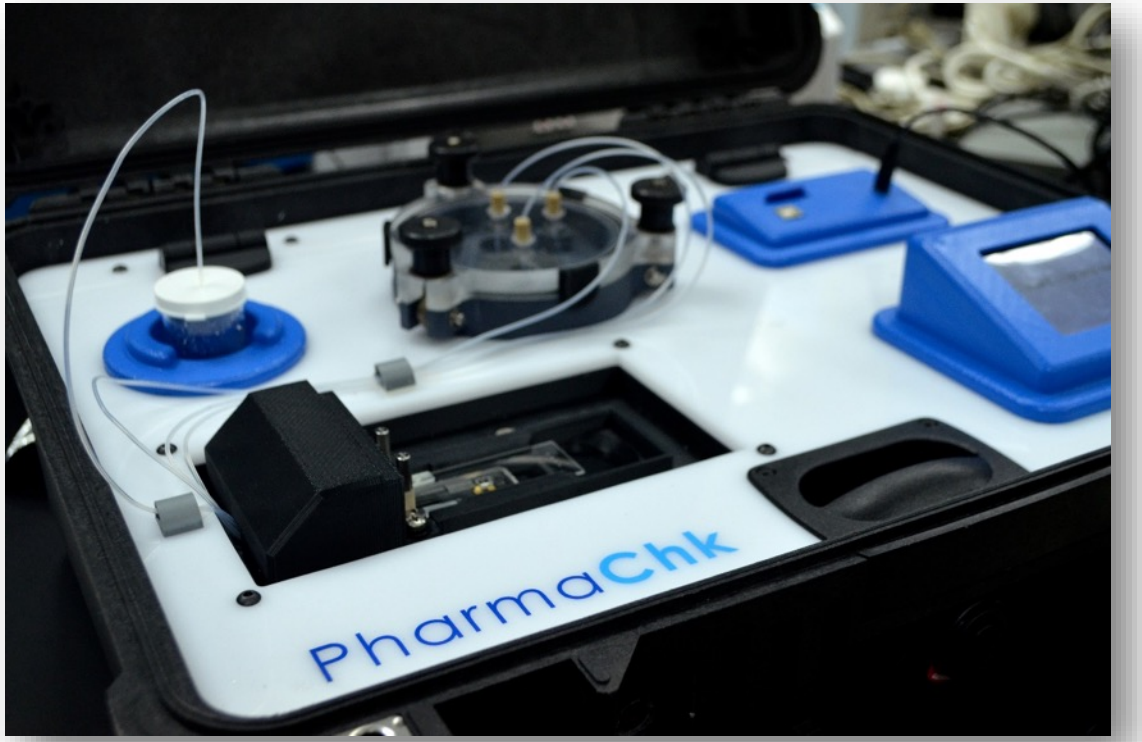
Improve access to good quality medicines and raise the quality of life around the world

- **Needs assessment** – understand and address the current gaps and bottlenecks in field-based testing
- **Technology innovation** – develop a user-friendly, accurate, and portable tool to address key challenges
- **Policy development** – work with local health authorities to develop and implement continuous monitoring
- **Long term goal** – reduce adverse health outcomes and support economic development of people living in areas with limited pharmaceutical regulatory oversight

PharmaChk: The Device

Accurately and affordably test the quality of medicines in the field:

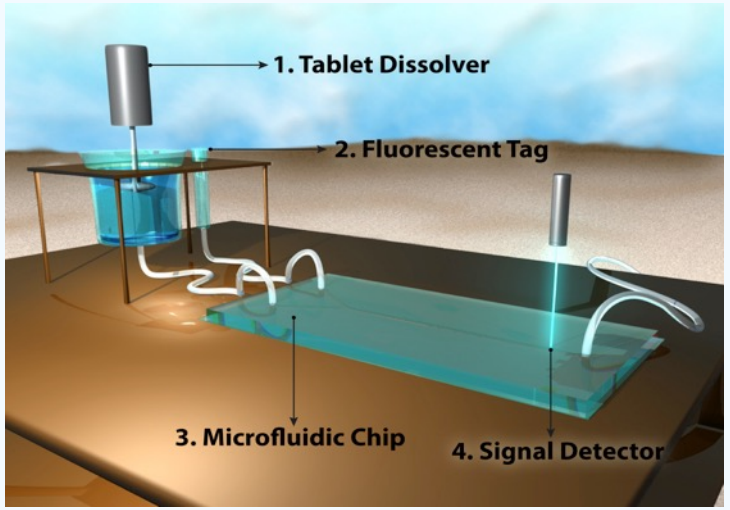
- **Quantification of active ingredient**
- **Analysis of API kinetic release**



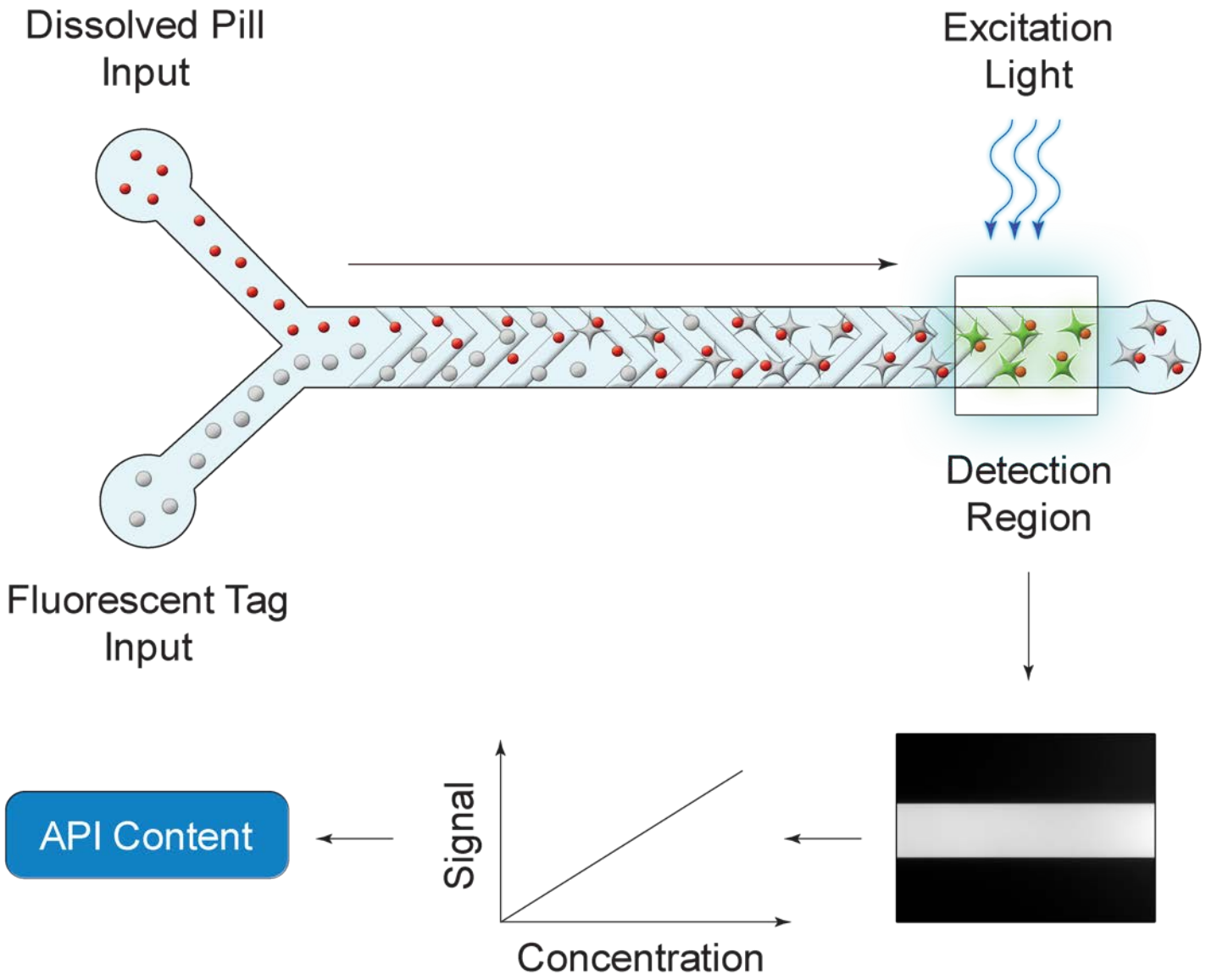
Key Challenges:

- Reducing/eliminating sample preparation
- Bringing quantitative results to field
- Rapid, portable testing for high-throughput

PharmaChk



- Portable platform
- Optical quantification
- Specific chemistry
- No sample preparation



PharmaChk: Prototype II

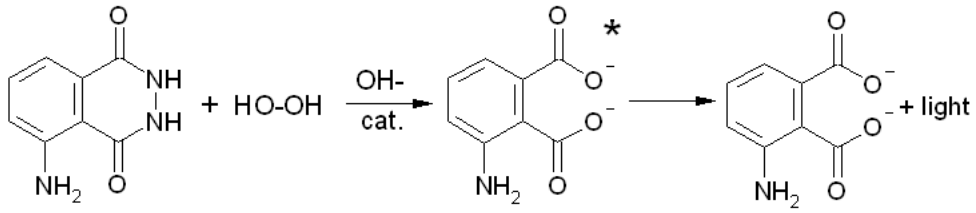
- **High precision pumping**
  Accurate and repeatable dilution and fluid delivery
- **Versatile CCD imaging**
  Flexible signal detection and multichannel imaging
- **Tunable ultrasonic disintegration**
  Automated disintegration and dissolution

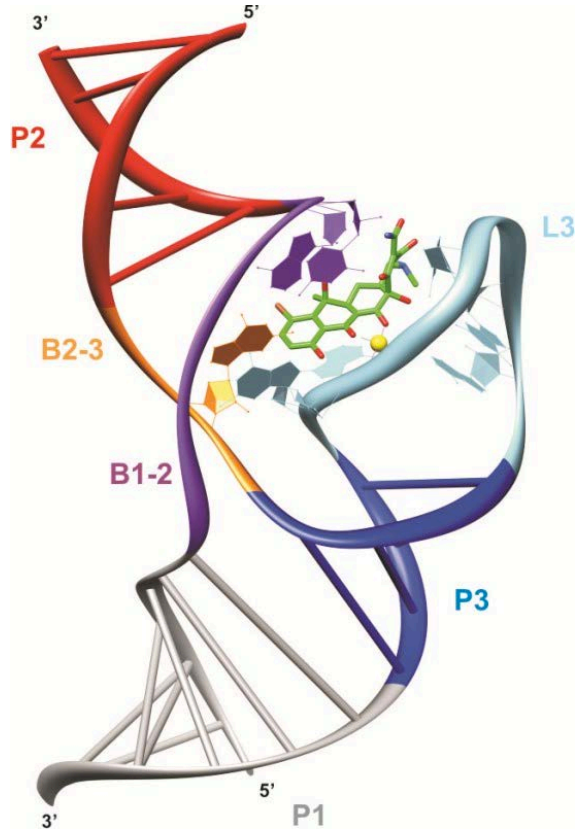
- Precision CNC plastic cartridges
- Improved signal detection
- Integrated waste containment
- Simplified tubing connection

More robust disposable

PharmaChk: Assay Development

- Fluorescent and luminescent assays are being developed to target highly specific chemistries for each API

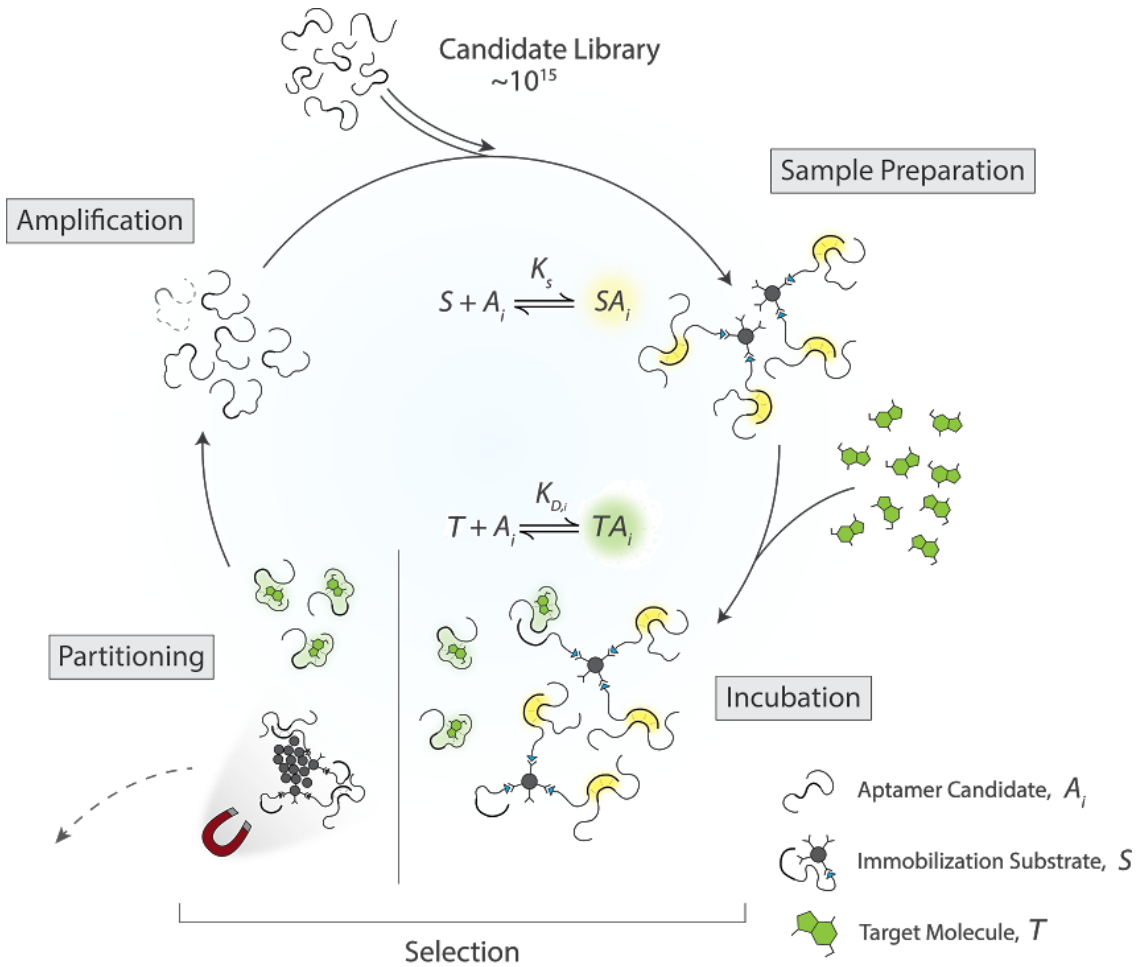




- Currently targeting antimalarial medication – able to test 5 front-line medications
- Developing aptamer chemistries for improved specificity and stability

Stoltenburg et al., *J. Anal Methods Chem*. 2012
Spiga et al., *ACS Comb. Sci.* 2015
Paniel et al., *Talanta* 2017

Capture-SELEX



Process

- Large initial pool of random DNA sequences
- Cyclic enrichment of high affinity binders
  - Incubation with target molecule
  - Separation of bound and unbound DNA

Advantages

- Target does not need to be immobilized
- Short cycle times (2-3 days)

Stoltenburg et al., *J. Anal Methods Chem*. 2012
Spiga et al., *ACS Comb. Sci.* 2015
Paniel et al., *Talanta* 2017

Stochastic Modeling Efforts

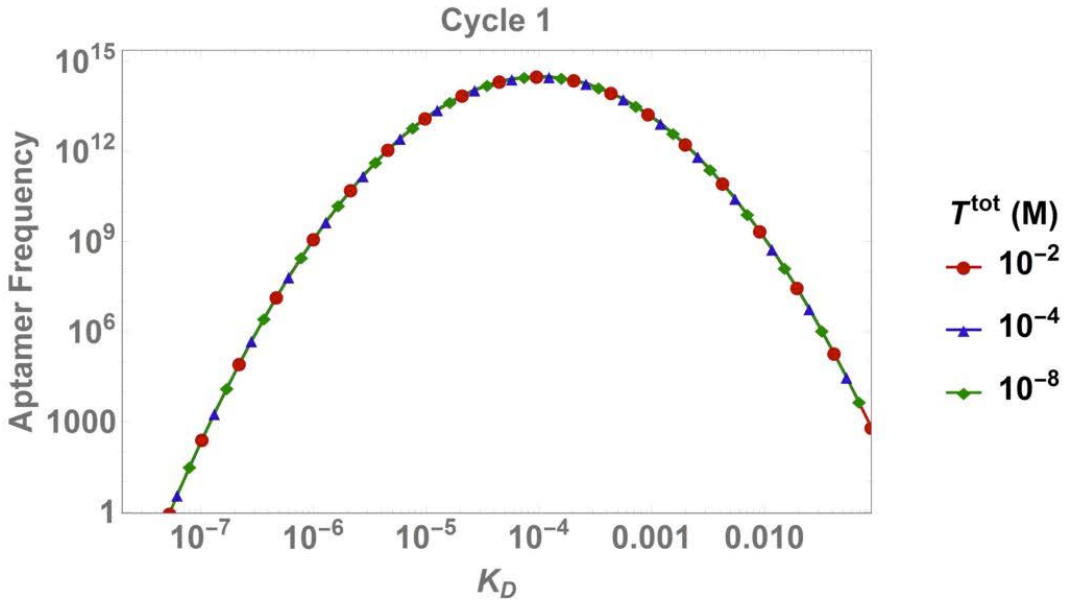
$$[SA_i] = \frac{1}{K_S}(A_i^I - [SA_i] - [TA_i])S^{free},$$

$$[TA_i] = \frac{1}{K_{D,i}}(A_i^I - [SA_i] - [TA_i])T^{free},$$

$$S^{tot} = \sum_{i=1}^{M^B} [SA_i] + S^{free},$$

$$T^{tot} = \sum_{i=1}^{M^B} [TA_i] + T^{free},$$

$$i = 1, \ldots, M^B.$$



- Existing models and protocol designs do not account for **random events**
- Protocol parameters can be very **sensitive**

- Many parameters exhibit **bimodal** behavior
- Modeling is important for identifying key protocol parameters

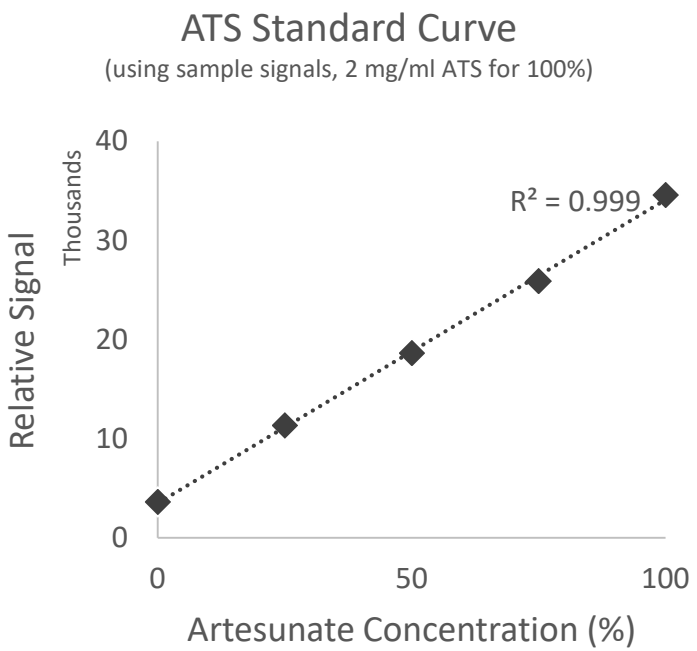
Chemistry-based

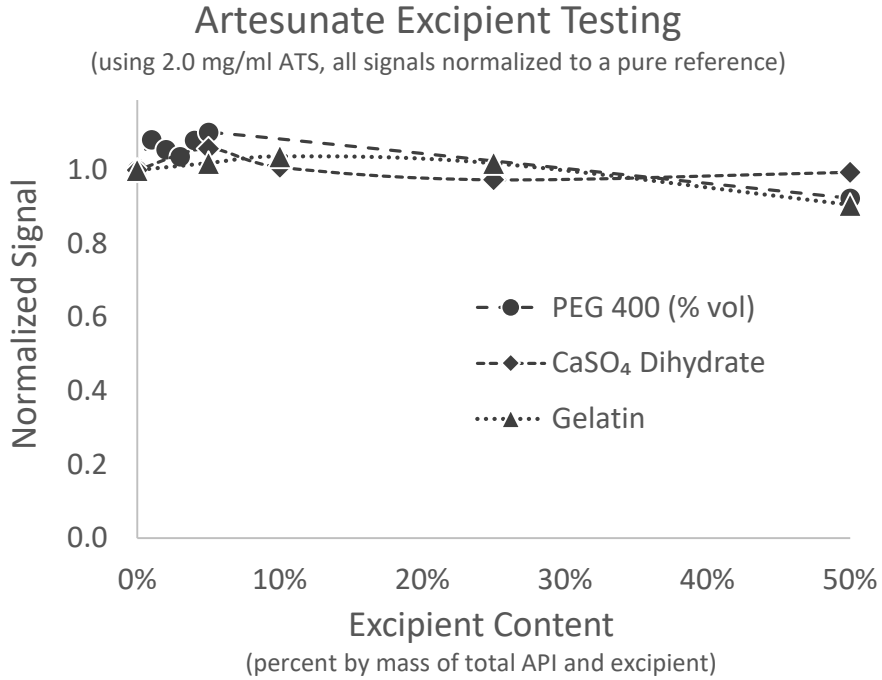
- Artesunate
- Amodiaquine
- Artemether
- Lumefantrine
- Dihydroartemisinin

Aptamer-based

- Tetracycline
- Under development

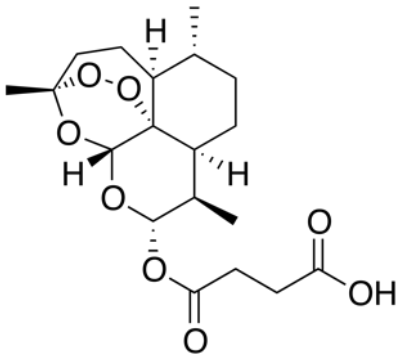
Current Assays





- Linear signals and minimal-to-no impact from common excipients
- Additional excipient testing ongoing

PharmaChk: Field Results



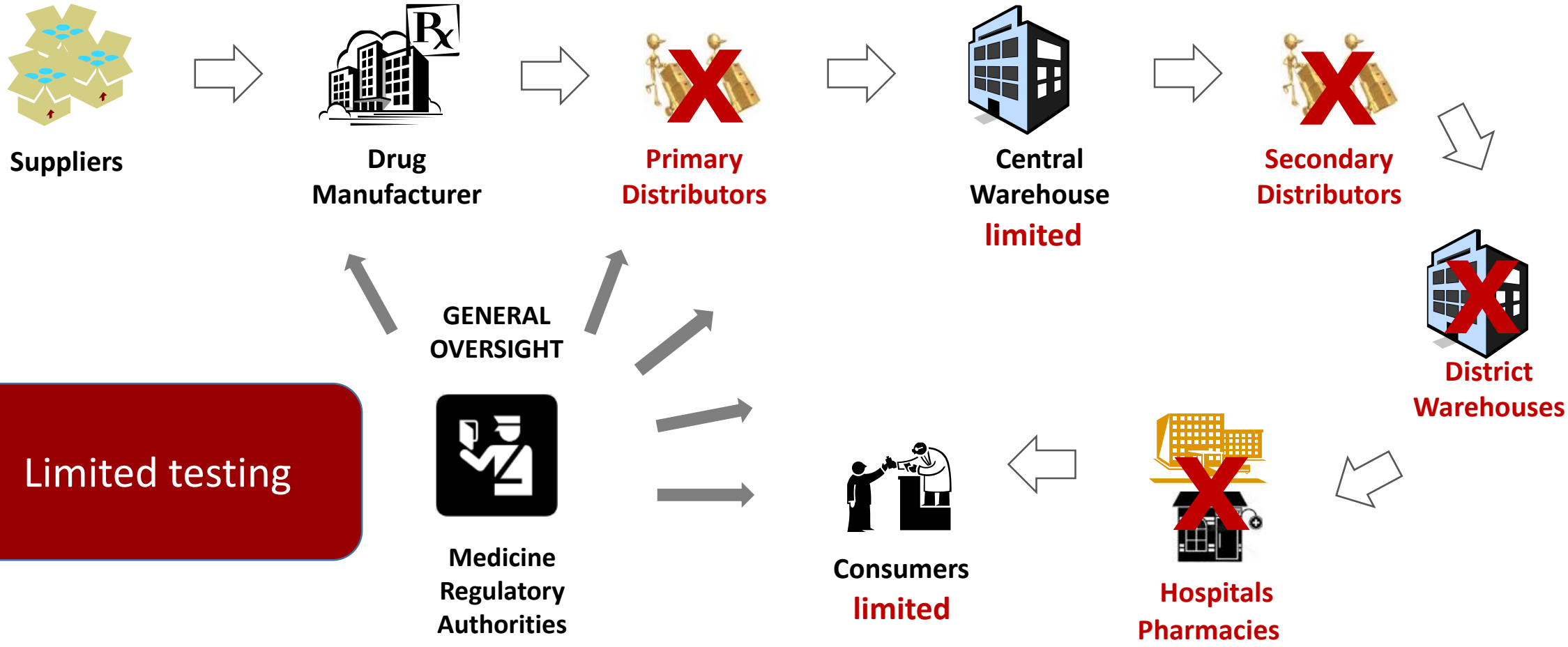
Artesunate (AS)

	Lever	Camosunate	Glunate
PharmaChk	**90.7%**	**97.8%**	**99.0%**
MiniLab®	**Pass**	**Pass**	**Unable**
HPLC	88.0%	94.9%	100.0%
Error	**3.1%**	**3.1%**	**1.0%**

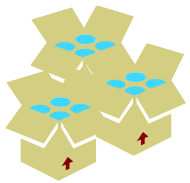
PharmaChk: Beyond the Lab

- Working extensively with USP and Ghanaian FDA to understand local logistical and policy challenges
- Involving local stakeholders in development to improve adoption

Current supply chain



Supply chain with PharmaChk



Suppliers

Drug Manufacturer

Primary Distributors

Central Warehouse

Secondary Distributors

District Warehouses

Hospitals Pharmacies

Consumers

Medicine Regulatory Authorities

GENERAL OVERSIGHT

Expansive Testing

PharmaChk: The Impact

Access to quality medicines, for all people, in all places, at all times.

- Improve morbidity and mortality caused by ineffective treatment
- Suppress development of drug resistance pathogens
- Support local capacity building and economic development