Field Tests for Drug Quality Assurance

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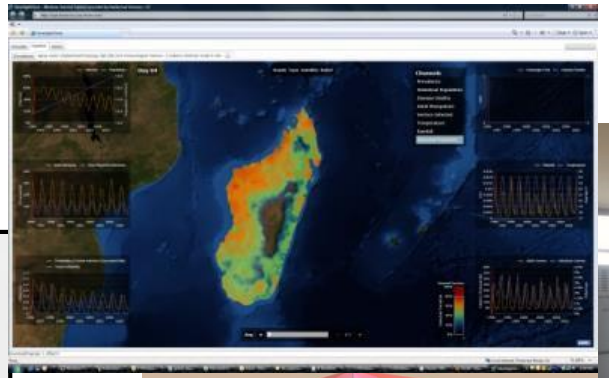

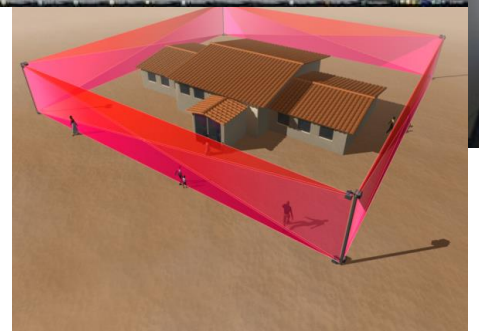

Developing World Technologies

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Global Good / IV Lab priorities

- **Focus around significant diagnostic gaps (and projected gaps) in major (high-burden) diseases - e.g.:**
  - Human health
    - Infectious diseases
    - Maternal /child health
    - Vaccine transport
    - Clinic /health systems support
  - Agriculture /animal health
- **Synchronize with the Gates Foundation's main objectives**
- **Focus IV Lab expertise in areas that are poorly addressed elsewhere**
- **Develop external partnerships (developers, and field) to achieve the above**

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Drug QC Tasks

Product Recognition

Is this genuine packaging?

Counterfeit Identification

Is this pill what the packaging says it is?

Active Pharmaceutical Ingredient Detection and Quantification

Is there API in this pill and, if so, how much?

Determining Composition (Verification)

What is this pill made of?

Our goal is to encourage drug quality control adoption by enabling it to be cheaper and easier to use.

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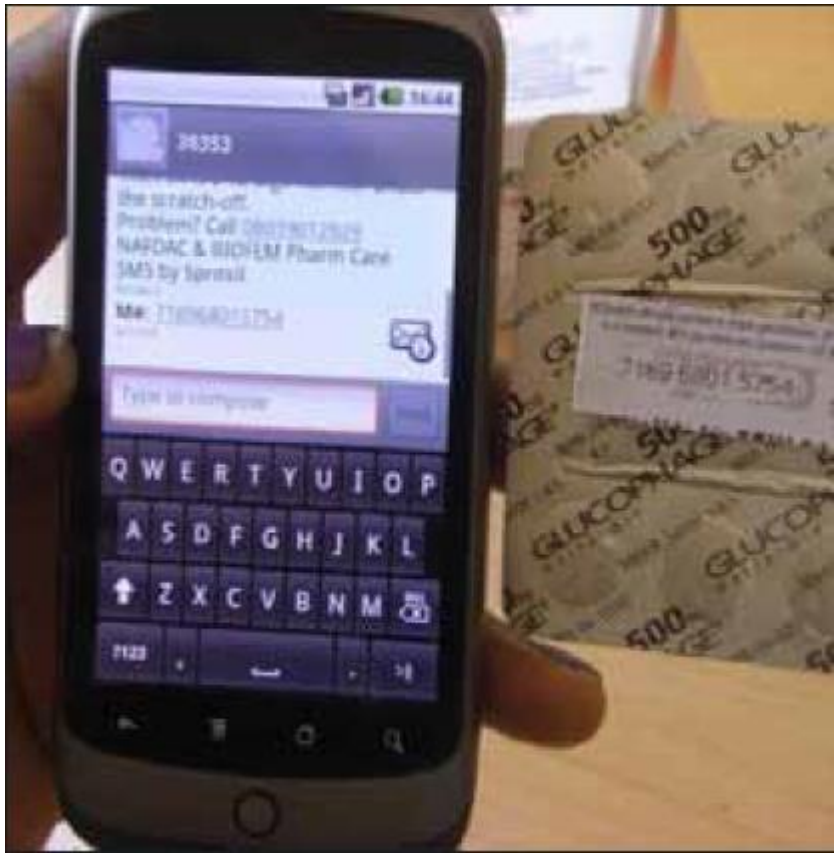
Package Recognition

- Various solutions have been developed for packaging validation.
- Use cell phones to verify labeling is genuine.
- Sproxil has done extensive development of their system in Africa.



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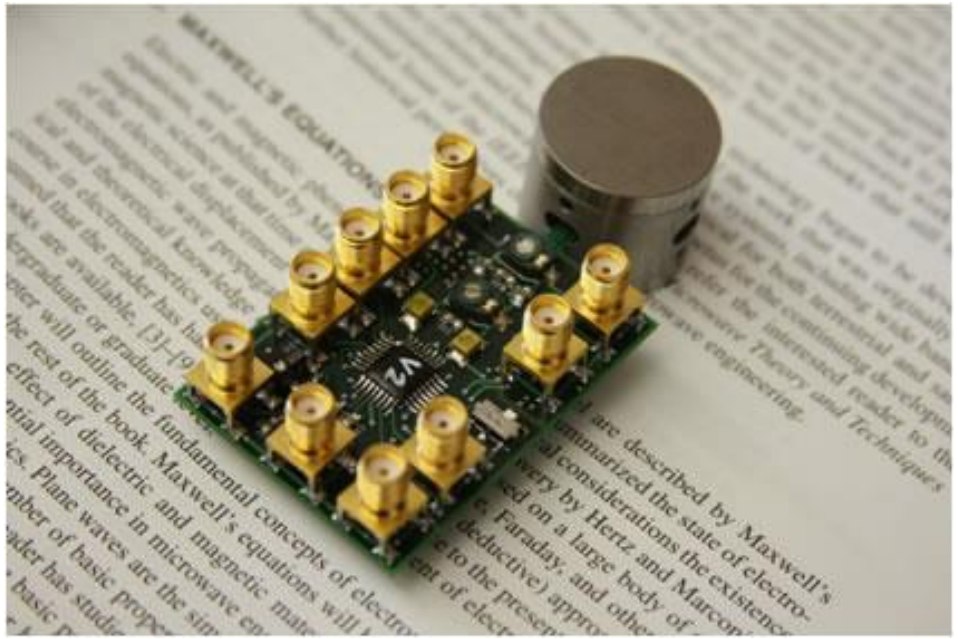
Verification

Handheld NMR (Harvard)



Portable Mass Spectrometer (BaySpec)

- Verification tests can determine the chemical composition of a drug.
- These tests require rigorous sample prep and a chemist to interpret the results.
- Advances in miniaturization and integration will not likely make these test field deployable.

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Technology Solutions for API detection

Table 2. Technologies for confirmation testing.

Technology	Purpose	Sample preparation needed	Performance	Laboratory supplies	Speed	Need electricity	Level of training Required	Facility Requirements	Device Price[a]	Suitab for us LMIC score[a]
Sample Preparation Techniques										
Liquid Chromatography	Identification and quantification of APIs	Yes	Gold Standard	Solvents	Slow	Yes	Highly trained chemist	Research laboratory	High	0
Gas Chromatography	Identification and quantification of APIs	Yes	Gold Standard	Solvents	Slow	Yes	Chemist	Research Laboratory	High	0
Plasma Pencil Atmospheric Mass Spectrometry (PPAMS) [40]	Identification and quantification of APIs	Yes	Unknown	Solvents	Fast	Yes	Highly trained laboratory technician	Research Laboratory	Medium	4
Flow Injection Gradient Ratio Standard Addition MS (FI-GRSA-MS) [41]	Identification and quantification of APIs	Yes	Moderate: Validated against HPLC methods but not as sensitive	Solvents	Fast	Yes	Chemist	Research Laboratory	High	1
Ionization Techniques										
Desorption Electrospray Ionization (DESI) [42]	Identification and quantification of APIs	No	Moderate: Not as sensitive as other MS techniques	None	Fast	Yes	Highly trained laboratory technician	Research Laboratory	Medium	4
Direct Analysis in Real Time (DART) [43]	Identification and quantification of APIs	No	Moderate: Not as sensitive as other MS techniques	None	Fast	Yes	Highly trained chemist	Research Laboratory	Medium	3
Atmospheric Pressure Solids Analysis Probe (ASAP) [44]	Identification and quantification of APIs	No	Moderate: Comparable to DART and DESI	None	Fast	Yes	Chemist	Research Laboratory	Low	3
Surface Acoustic Wave Nebulizer (SAWN)	Identification and quantification of APIs	Yes	Moderate: More Sensitive than DART or DESI	Solvents	Fast	Yes	Chemist	Research Laboratory	High	1
Direct Analysis in Real Time with SAWN	Identification and quantification of APIs	Yes	Moderate: More sensitive than DART or DESI alone	Solvents	Fast	Yes	Chemist	Research Laboratory	High	1

21 technologies surveyed for compatibility with developing world use

Scored on an out-of-ten scale, with ten being the most suitable for low-resource settings.

S. Kovacs et al *PLoSone* (2009)

Separation Techniques

Method	Score	Notes
Gas Chromatography	2	Laboratory-grade chromatography requires extensive laboratory resources and a highly trained technician.
Anion Exchange Chromatography	2	
High-performance liquid chromatography	2	
Electrokinetic Capillary Chromatography	3	
Capillary Electrophoresis	2	Slow, hard to use
Thin Layer Chromatography	5	Easy to use and cheap, includes Mini-Lab
Paper Chromatography	6	Easy to use and cheap
PharmaCheck	6	Easy to use and cheap

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Spectroscopy Techniques

Method	Score	Notes
Near Infrared Spectroscopy	7	Flexible and high performing
FTIR Spectroscopy	8	
Raman Spectroscopy	7	
Fluorescence Spectroscopy	3	Slow and requires solvents
NMR Spectroscopy	0	Very Expensive, hard to use
NQR Spectroscopy	4	Slow, hard to use

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Other Techniques

Method	Score	Notes
Refractometry	5	Reagent required, poor sensitivity
Calorimetry	4	Reagents required, included in Mini-Lab
X-Ray Diffraction	1	Very expensive, hard to use

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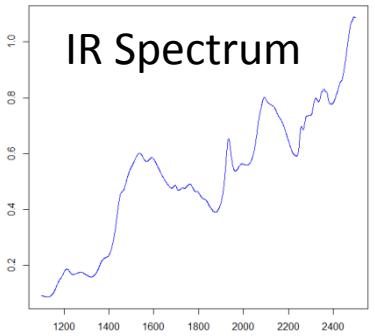
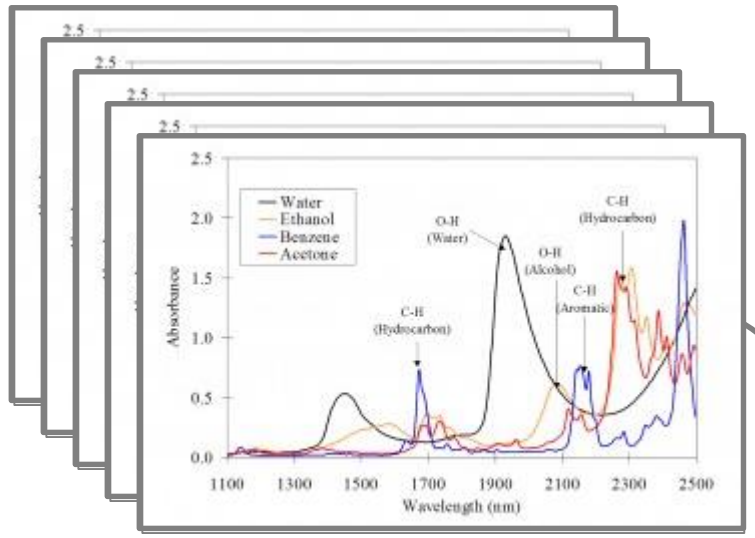
Infrared Spectroscopy

Conventional method requires grinding the sample, newer backscatter systems are non-destructive



Cloud-Based Library



Result

Acquired spectra are compared with a library. For optimal performance this should be done by cloud resources.

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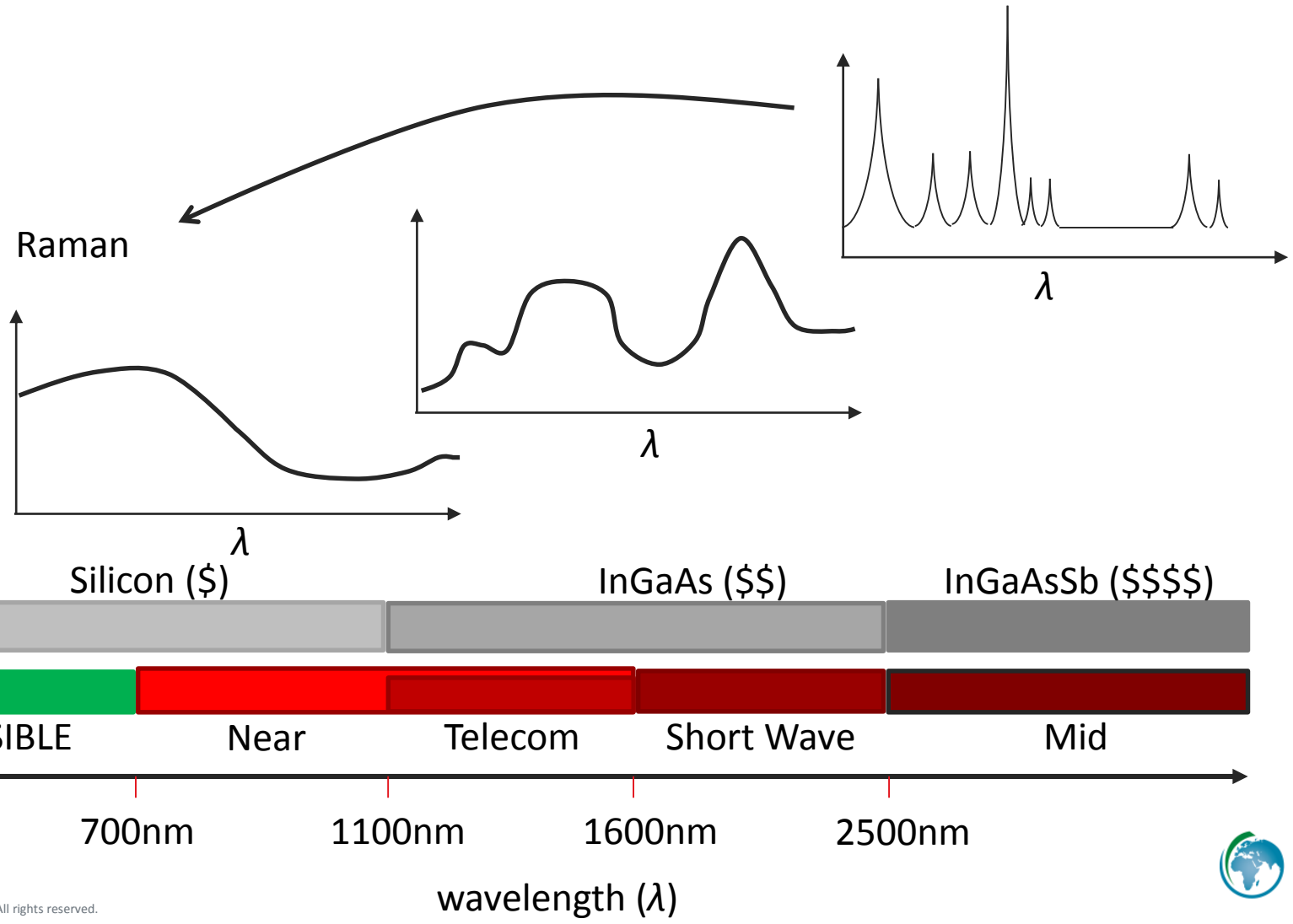
Types of Infrared Spectroscopy

- Raman allows Mid-IR features to be observed in the visible range, but requires expensive optics
- FTIR is a method of collecting a spectrum that can be used at a variety of wavelengths



IR spectroscopy cost and performance is dependent on the wavelength range

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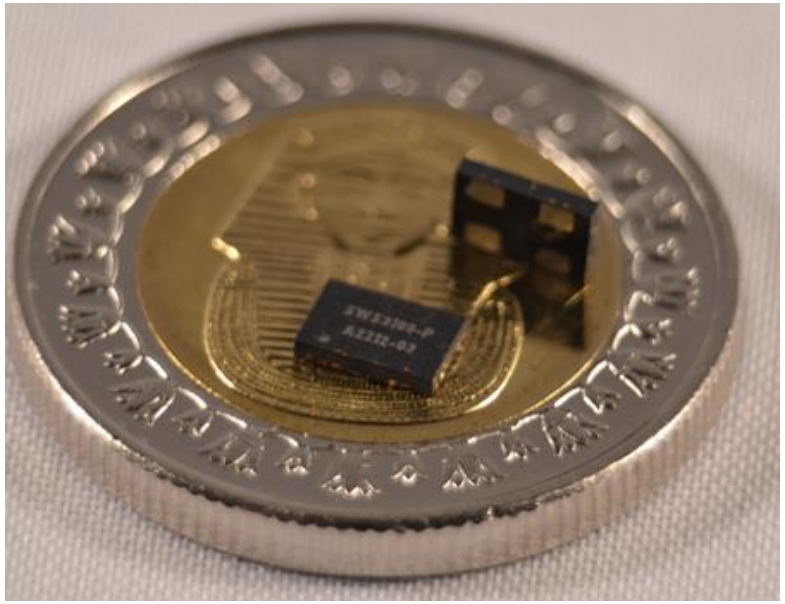
Next- Generation Spectrometers

SCiO – Consumer Physics
Near IR
Projected cost $200



NeoSpectra – Si-Ware
Telecom FTIR
Projected cost <$500

Microspectrometer - Hamamatsu
Optical and Near IR
Projected cost ???

Compact backscatter NIR systems have been shown to perform well with counterfeit identification, API quantification capability has not been verified.

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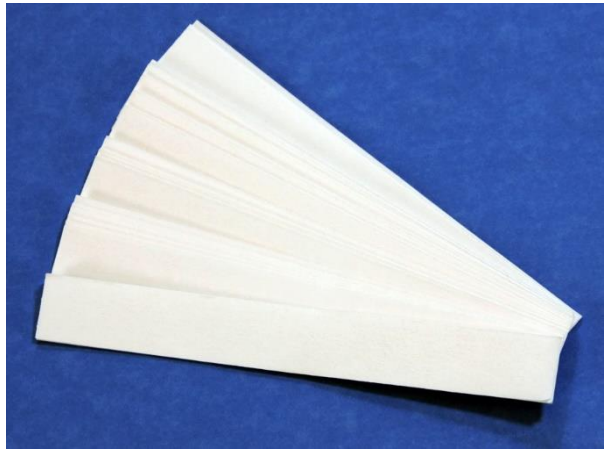
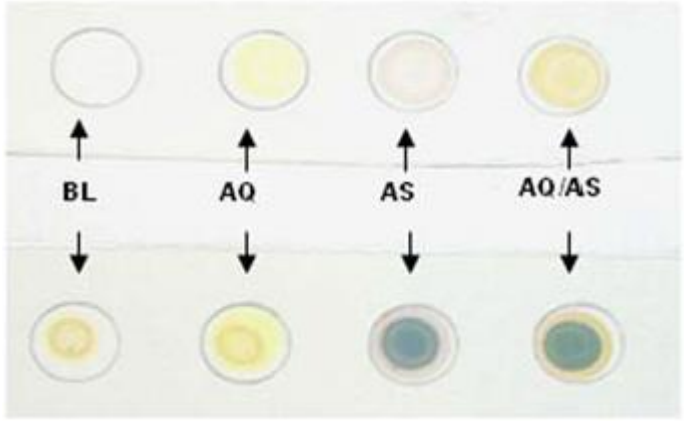
Chromatography Techniques

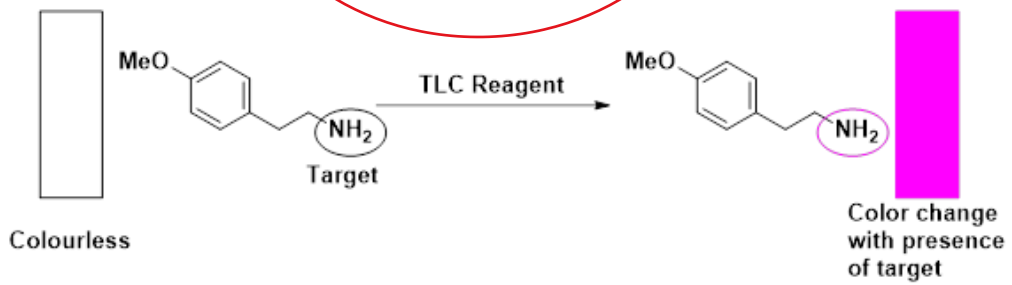
Pills are ground and sometimes dissolved



Color change read by eye



Reagents can be added, or be dry on the paper



Ioset et al, *PLoSone* (2009)

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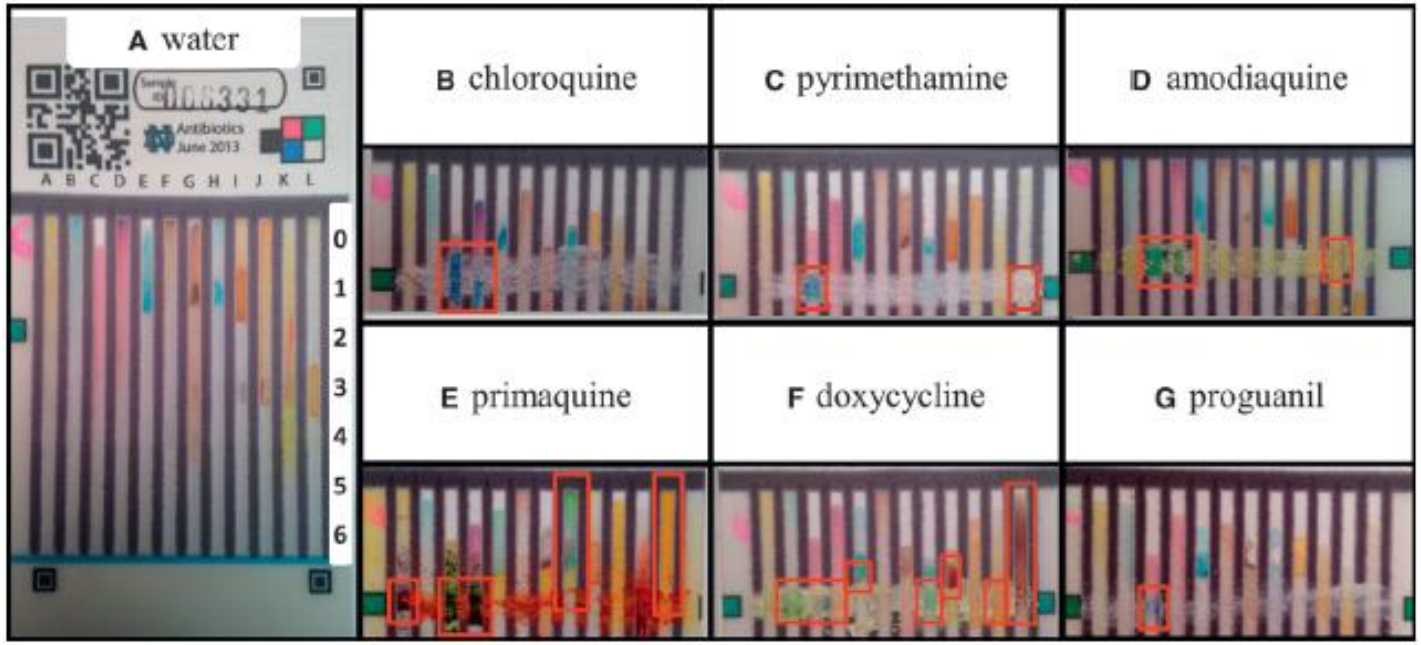
Multiplexing

- Multiplexing assays provides added utility to chromatography tests.
  - Multicomponent drugs
  - Multi-drug assay
- New chemistry needs to be designed for each new API



Weaver et al, *AJTHM* (2015)

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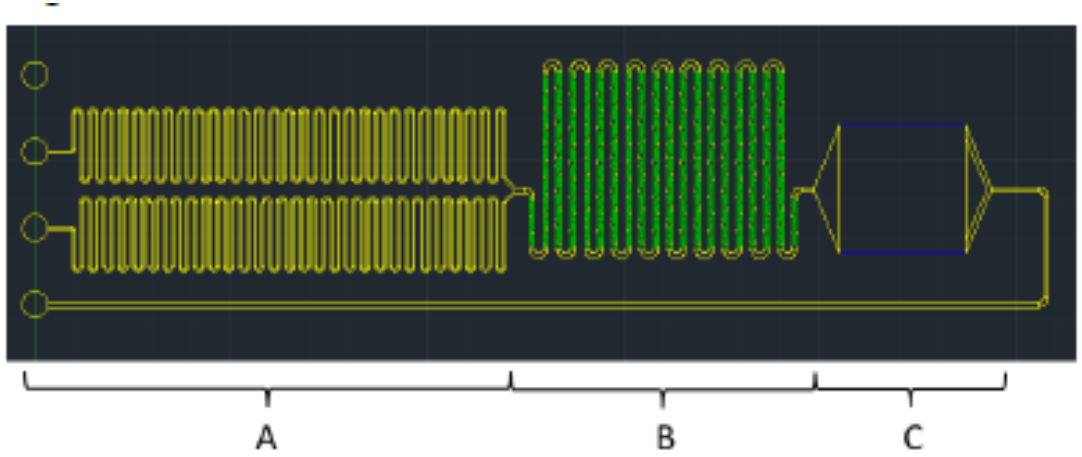
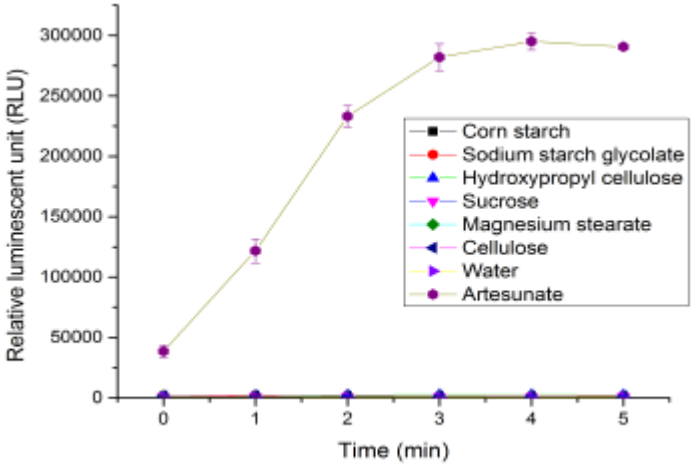
PharmaCheck

- Uses photoluminescence and microfluidics in place of paper and color change.
- Quantitative, can detecting substandard drugs.





Ho Et al, *AJHTM* (2015)

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Comparisons

	Estimated Cost per test ($)	Estimated Capital Cost ($)	Sample prep	Destructive?	API Quantitation	Infrastructure requirements
NIR	$	$	Remove from package	No	Excellent	Battery, data
Raman	$	$$$	None	No	Good	Battery, data
Mid IR	$$	$$$$	Grind	Yes	Fair	Intermittent power, data, water
Paper Chromatography	$$$	0	Grind	Yes	Poor	water
Pharmacheck	$$	$$	Dissolve	Yes	Good	Battery, water

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Summary

- Next-generation IR spectrometers could greatly improve access to drug QA.
- Paper chromatography cards are advantageous for certain applications with low volumes.

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- END

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QA Tasks

- There are different levels of QA
  1. Product Recognition
  2. Identifying counterfeits
  3. Detecting presence of active pharmaceutical ingredients (APIs)
  4. Determining composition (verification)

- There are three general classes of solution
  1. Package / tablet recognition
  2. Spectroscopy
  3. Chemical/Chromatography

- Our goal is to encourage drug quality control adoption by enabling it to be cheaper and easier to use.

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Quick GG/IVL intro

- Goals: get low on the chain
- Mention USP minilab

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Add antibody based cards