FRUGAL SCIENCE
DESIGNING DIAGNOSTICS IN LOW RESOURCE ENVIRONMENTS

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22 SEPTEMBER 2020

Setting the Scene: HIV

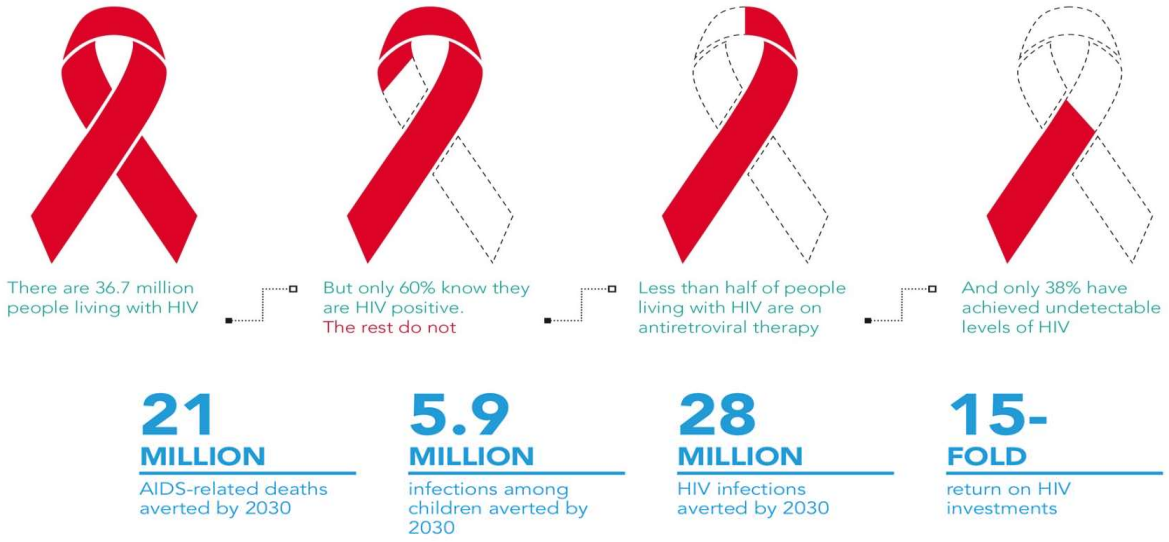
United Nations 90–90–90 global HIV targets – by 2030

- 90% of people living with HIV know their HIV status
- 90% of people who know their status are receiving treatment
- 90% of people on HIV treatment have a suppressed viral load

First target: diagnosis!

Third target: continuous measurement!

Cost and delivery to end user major hurdles



WHO Guidelines on HIV testing services, July 2015

Setting the Scene: Water

Main risk to communities utilising water supplies lies in bacterial diseases (cholera, typhoid, hepatitus A, etc) and other contaminants

Cheap tests are available (membrane filtration, multiple tube). More expensive tests also available (Colilert). Not rapid.

There are no rapid tests for bacterial contamination in water.

Do not know safety of water until it is tested. If it cannot be tested or testing takes too long, illness and disease outbreak.

Better diagnostics are still required!

Setting the Scene: Health and Environmental Facts

- Reducing environmental risks could have prevented more than a quarter of the 5.9 million deaths of children under 5 years.
- Key areas include safe water, arsenic/lead/mercury poisoning, poisons, contaminated food

- Malaria kills one child every two minutes

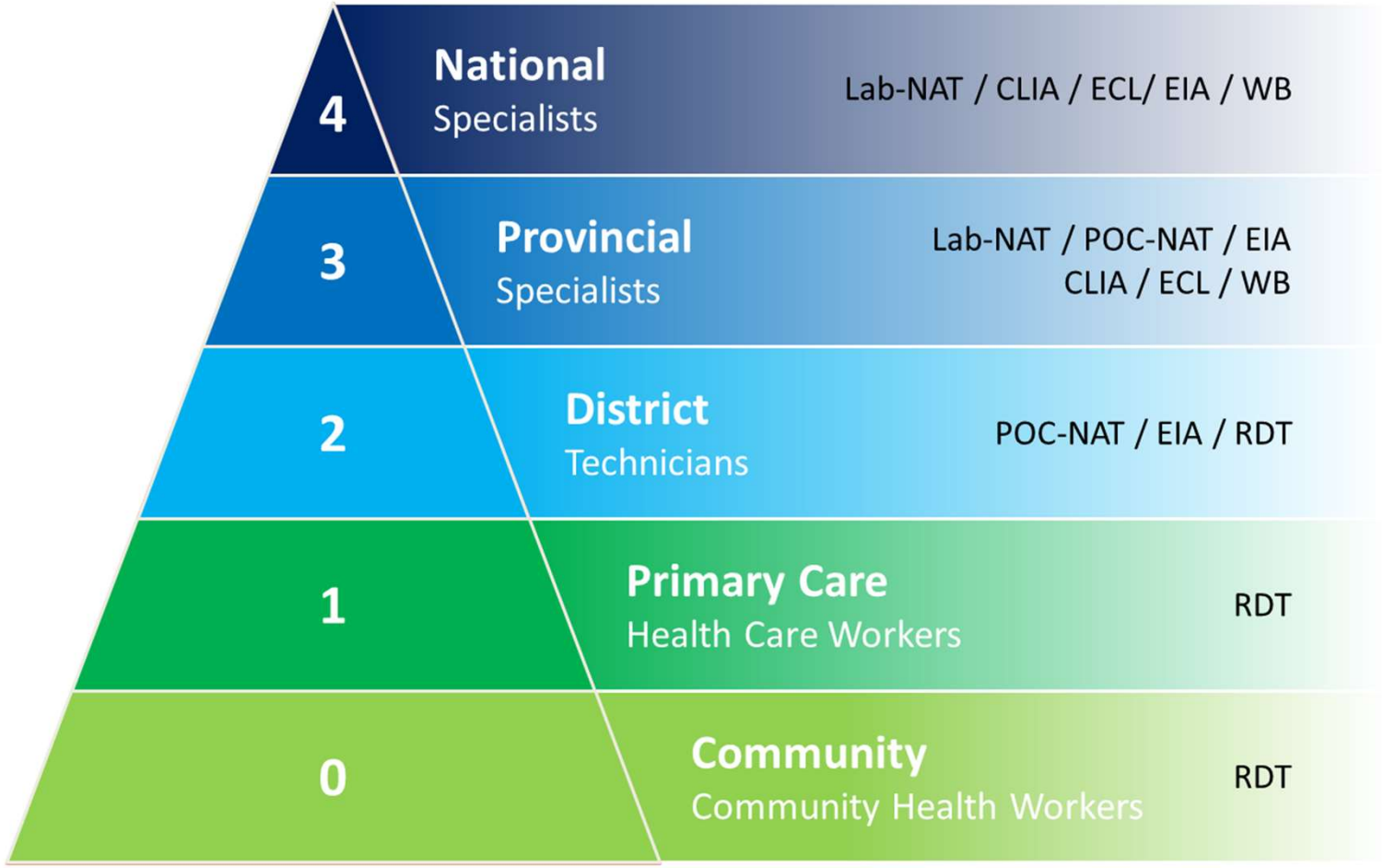
- Contaminated water kills one child every minute

- Ghana, Vietnam and the Dominican Republic: despite TB diagnosis and treatment being provided for free, the average total patient costs equivalent to one year of individual income, due largely to hospital costs and additional food items during treatment.

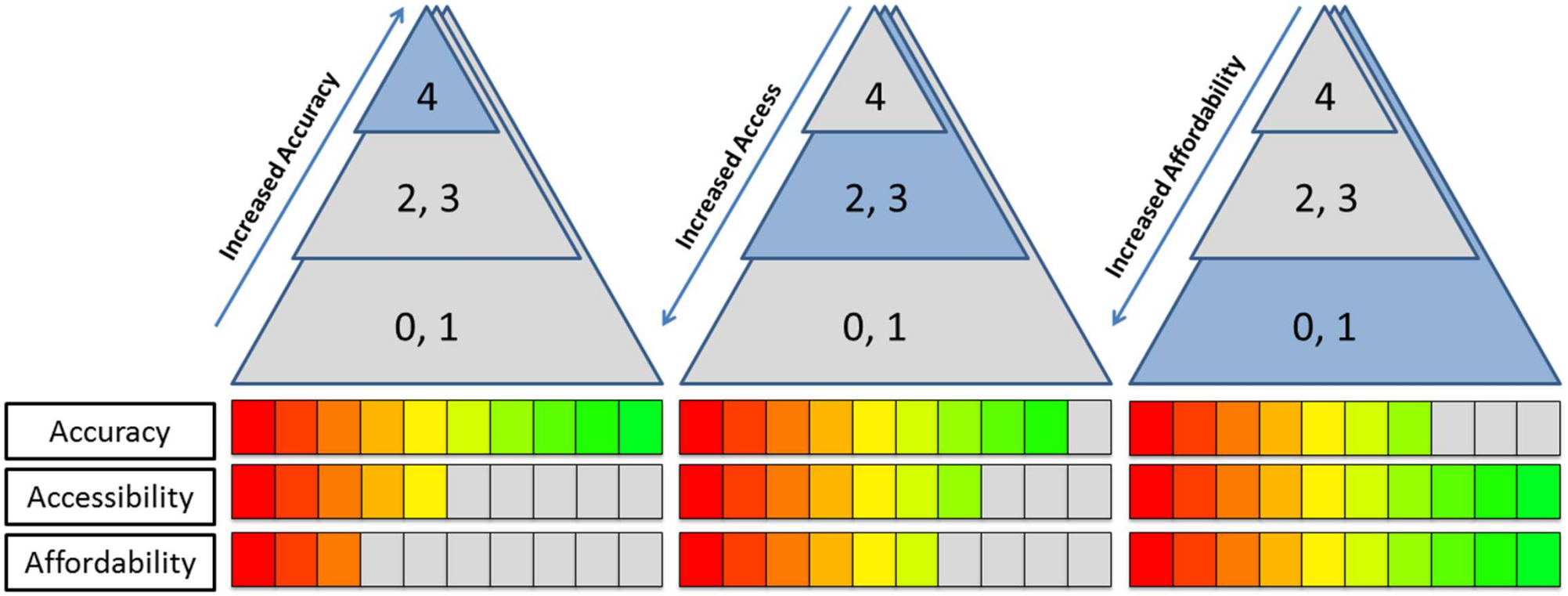
- South Africa: Drug-resistant TB comprises 2.2 percent of case burden, it consumed around 32 percent of the total estimated 2011 national budget of US $218 million.

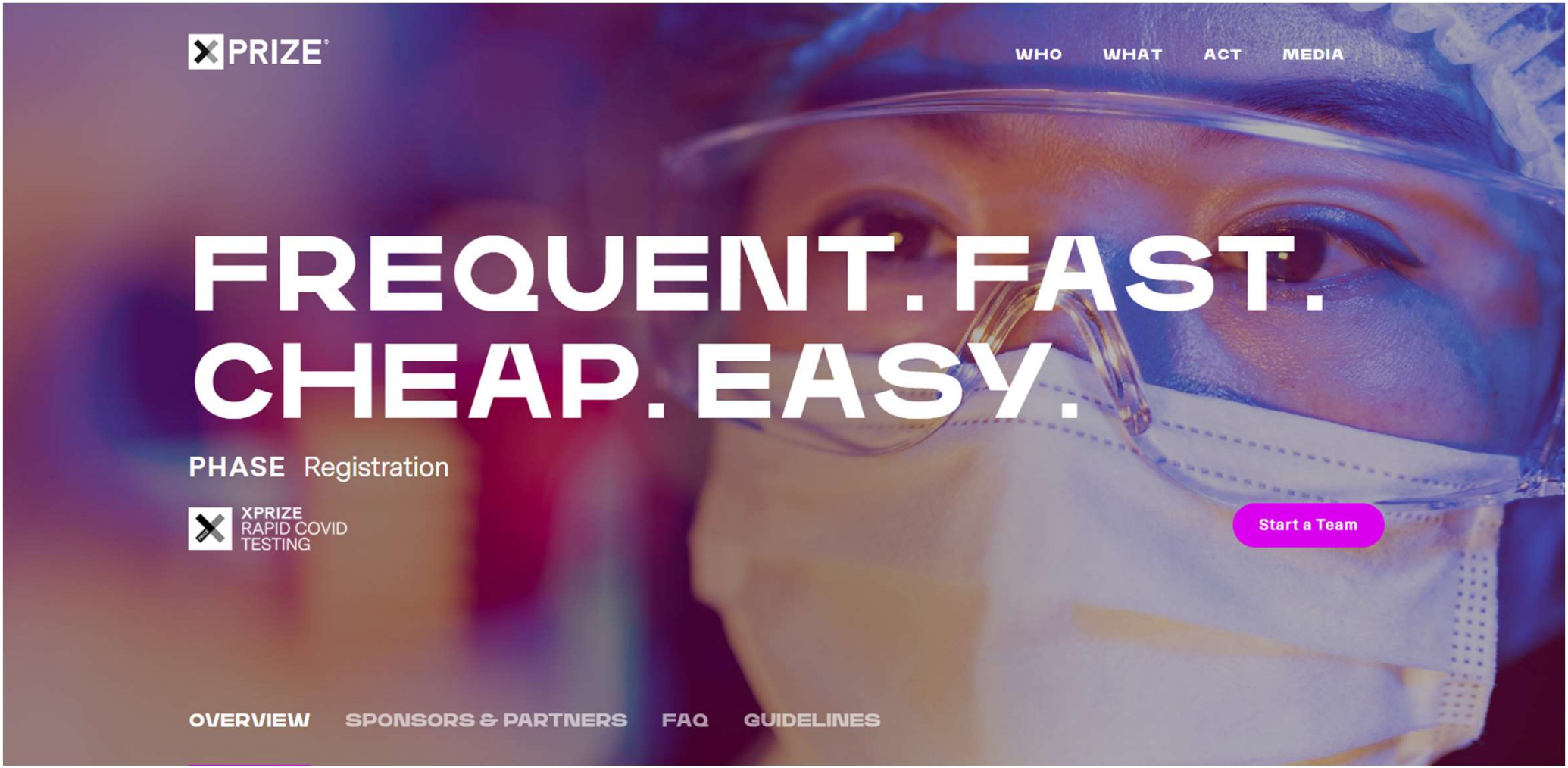
(March 2017, WHO: Second edition of Inheriting a sustainable world: The atlas on children's health and the environment) and AERAS.ORG

Healthcare Tiers (very similar for animal health/environment)



3A's of diagnostics





https://www.xprize.org/prizes/covidtesting

COVID-19
DIAGNOSTICS & TESTING

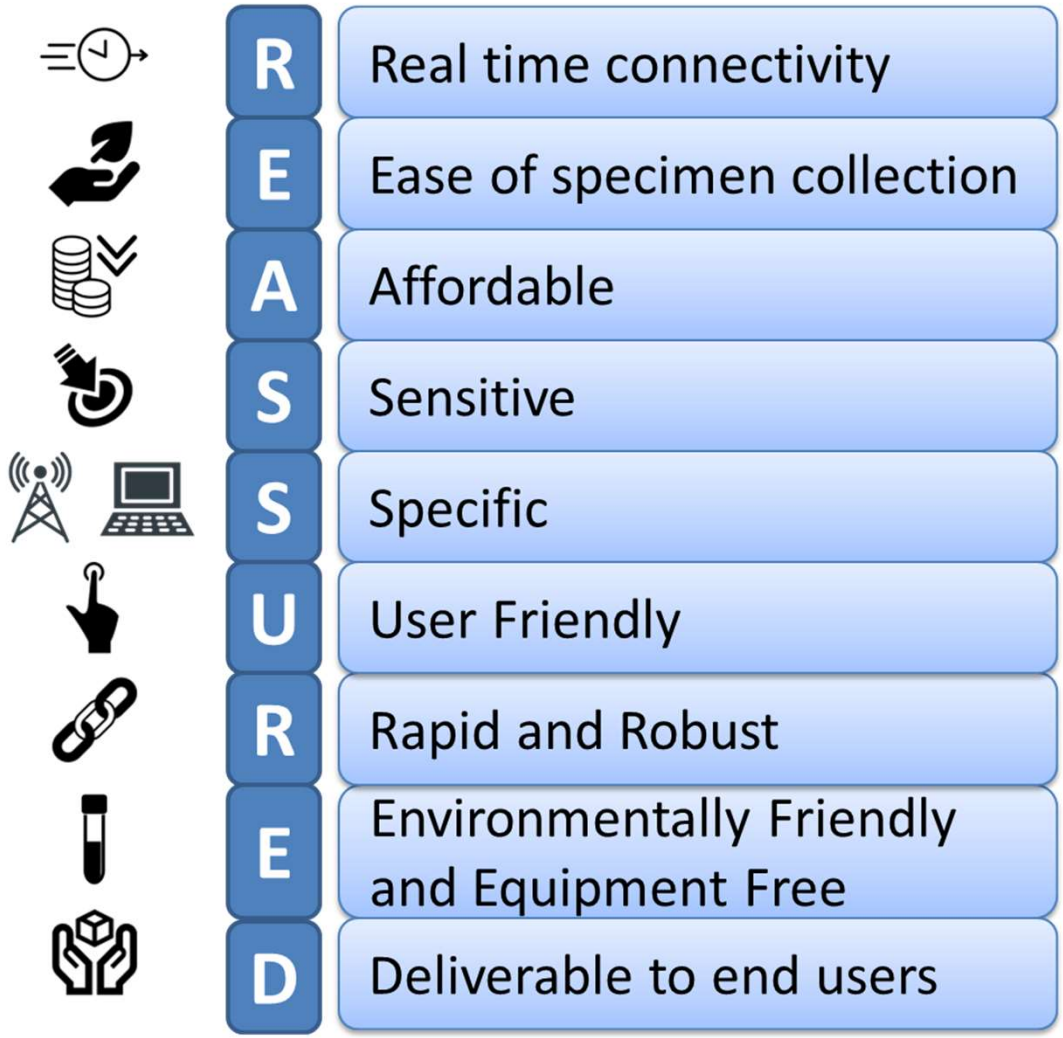
FIND and The Global Fund to Fight AIDS, Tuberculosis and Malaria are co-conveners of the Access to COVID-19 Tools (ACT) Accelerator Diagnostics Pillar. The ACT-Accelerator is a ground-breaking global collaboration to accelerate the development, production, and equitable access to COVID-19 tests, treatments, and vaccines. It was set up in response to a call from G20 leaders in March and launched by the WHO, the European Commission, France and the Bill & Melinda Gates Foundation in April 2020.

This diagnostics resource centre provides information, updates and progress on tests and testing, in support of the agenda set out in the ACT-Accelerator Diagnostics Pillar investment case.

ACTaccelerator
ACCESS TO COVID-19 TOOLS

TECHNICAL ENQUIRIES →

MEDIA ENQUIRIES →



Land, K.J., Boeras, D.I., Chen, X.S., Ramsay, A.R. and Peeling, R.W., 2019. REASSURED diagnostics to inform disease control strategies, strengthen health systems and improve patient outcomes. *Nature microbiology*

Thinking about REASSURED criteria

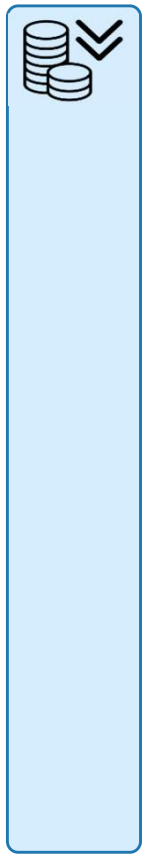
Of course, tests must be low cost, but what is low cost?

What is affordable?

Easy definition – lower than current costs

< $1, < $10

Thinking about REASSURED criteria

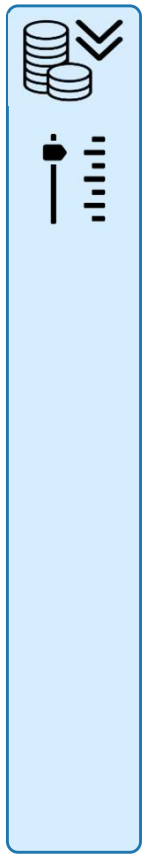


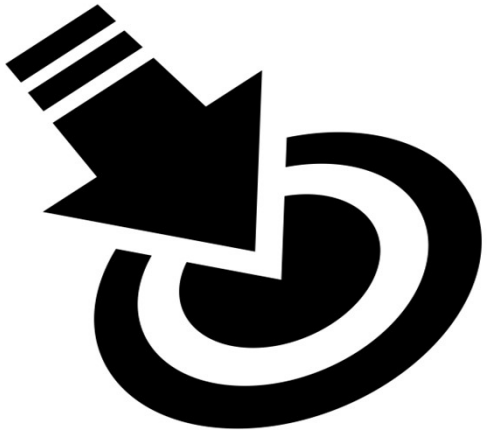
Include: people with disease
Exclude: people without disease

Sensitive:

- Low false negatives
- Screening
- Rule-out

Thinking about REASSURED criteria

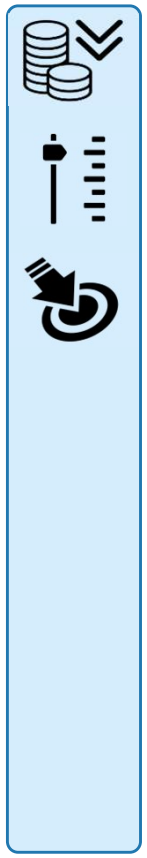




Specific:

- Low false positives
- Rule-in

Thinking about REASSURED criteria



Number of user steps to result

Who can do the steps? Skills

What sample is used?

Sample preparation required?

Thinking about REASSURED criteria

Compare to current tests

TB example

15 min, 2 hrs, same day?

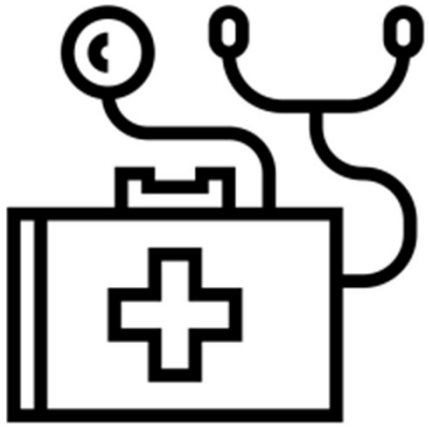
Entire ecosystem counts – time to treatment?

Thinking about REASSURED criteria

Tests must survive:

- supply chain (manufacture to patient)
- storage (temperature, humidity, transport, etc)
- usage

Thinking about REASSURED criteria



Minimal requirements for:

- Electricity
- Clean environment
- Maintenance

Additionally, equipment is expensive

Thinking about REASSURED criteria

Consider environment where test is used

Available and accessible when needed

Good Enough?

Access (%)	Sensitivity (%)					
	100	90	80	70	60	50
100	100	90	80	70	60	50
90	90	81	72	63	54	45
80	80	72	64	56	48	40
70	70	63	56	49	42	35
60	60	54	48	42	36	30
50	50	45	40	35	30	25
40	40	36	32	28	24	20
30	30	27	24	21	18	15
20	20	18	16	14	12	10
10	10	9	8	7	6	5

Further analysis – Frugal project?

Setting the Scene: Combining Technologies

Cartridge-based microfluidics with readout systems

World Health Organisation
ASSURED criteria
Affordable, **S**ensitive, **S**pecific, **U**ser-friendly, **R**apid and robust, **E**quipment free, **D**eliverable to end-users

Lateral flow devices

Printed Microfluidic Channels

Printed Electrodes/Electronics

Sample Introduction

Detection

Printed Communication

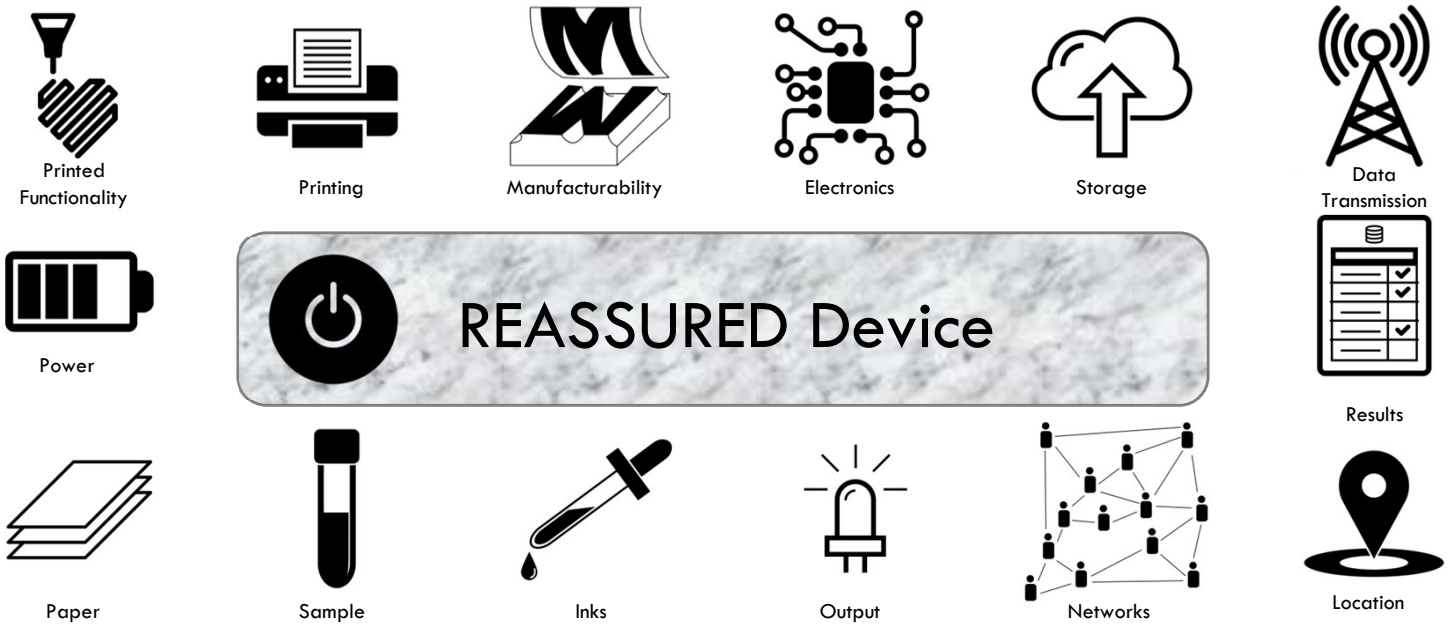
Molecular and synthetic biology

IoT, Industry 4.0

REASSURED
Real time connectivity, **E**ase of specimen collection, **A**ffordable, **S**ensitive, **S**pecific, **U**ser-friendly, **R**apid and **R**obust, **E**quipment free or simple and **E**nvironmentally friendly, **D**eliverable to end-users

Land, K.J., Boeras, D.I., Chen, X.S., Ramsay, A.R. and Peeling, R.W., 2019. REASSURED diagnostics to inform disease control strategies, strengthen health systems and improve patient outcomes. *Nature microbiology*

Technologies



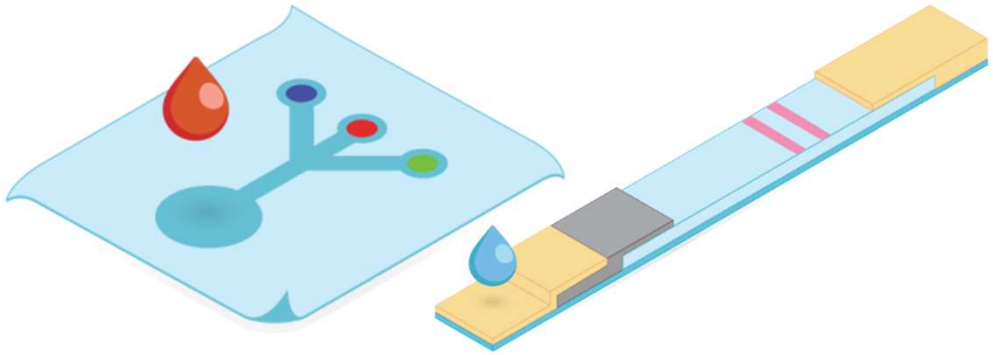
REASSURED

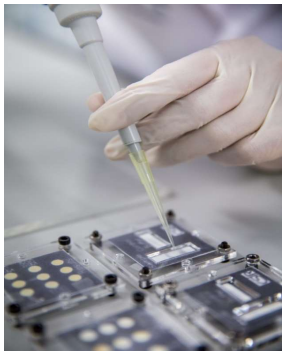
Real Time, **E**nvironmentally Friendly, **A**ffordable, **S**ensitive and **S**pecific, **U**ser-friendly, **R**apid and **R**obust, **E**quipment Free, **D**eliverable to end-users

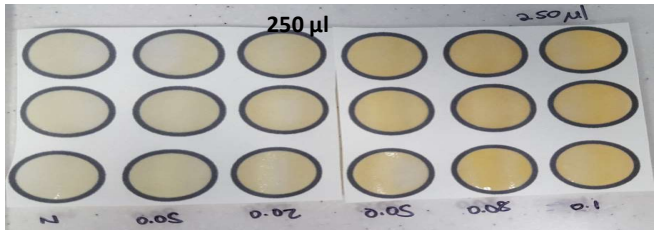
The Noun Project: Bohdan Burmich, Arafat Uddin, Sarah Marquez, Jhun Capaya, Michael Wohlwend, DewDrops, AA, Dant, Icon Fair, Vectors Market, Alvarobueno, Alex Muraviov, Creative Stall, Santiago Arias, Marie van den Broek, Hunotika, Gregor Cresnar, Bonegolem, Michele Zamparo, Andrew Hainen, Ralf Schmitzer, Arthur Schlain

Land, K.J. ed, Paper-based Diagnostics: Current Status and Future Applications, Springer Cham, 2019

Paper Based Diagnostics





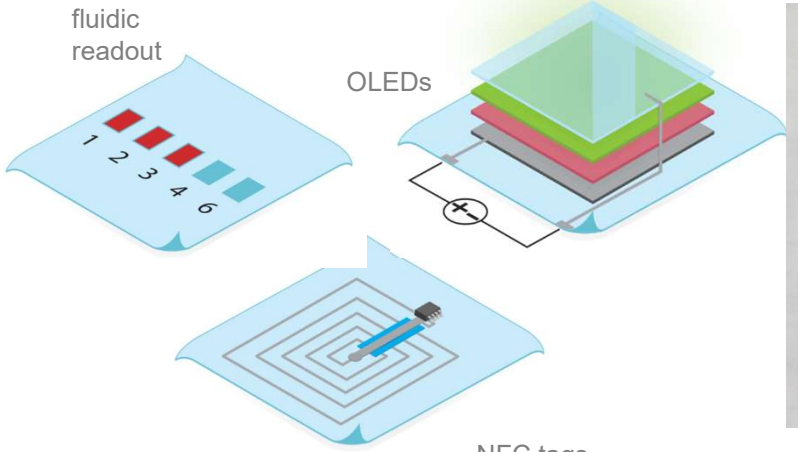


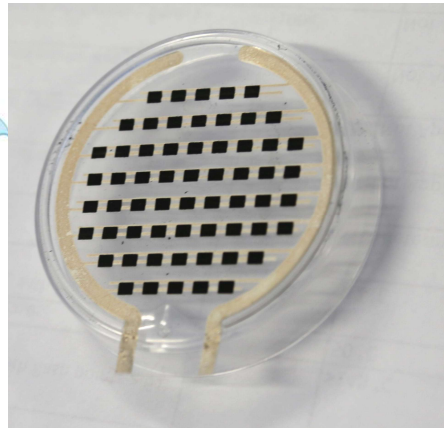
Strengths	Opportunities
Low cost	Conforms to WHO ASSURED criteria
Usage not reliant on laboratory facilities	Closely linked to other emerging technologies (e.g. printed electronics)
Single step sample preparation	Decentralised testing
Equipment free	Manufacturing on a distributed basis
Used by unskilled people	Easy distribution to remote sites
Paper is easily available	Paper can be used for prototyping
Instrument free fluidic transport	Underutilised as a testing platform
Bio compatible	Excellent tool for education
Bio degradable	Possibility of more than simple Yes/No answers
High surface to volume ratio	Multiplexing of tests
Disposable	

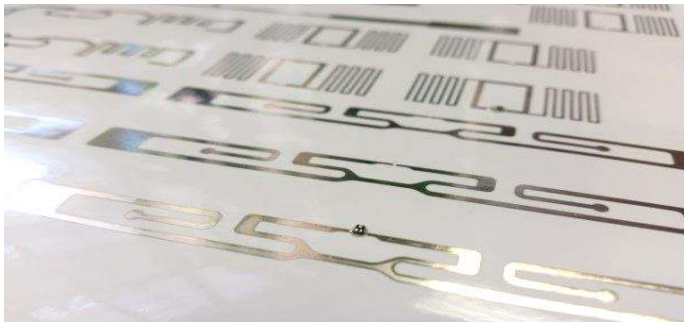
Weaknesses	Threats
Sample retention	Regulatory approvals
Not always ideal in wealthy first world environments	More expensive, more sensitive and specific equipment (competitor products).
Technical hurdles to be overcome	Market (health services and end user) acceptance
Quantitative results not always possible	Technical hurdles take longer than expected
Difficult to build business model	
Flow control	
Compatible barrier materials	

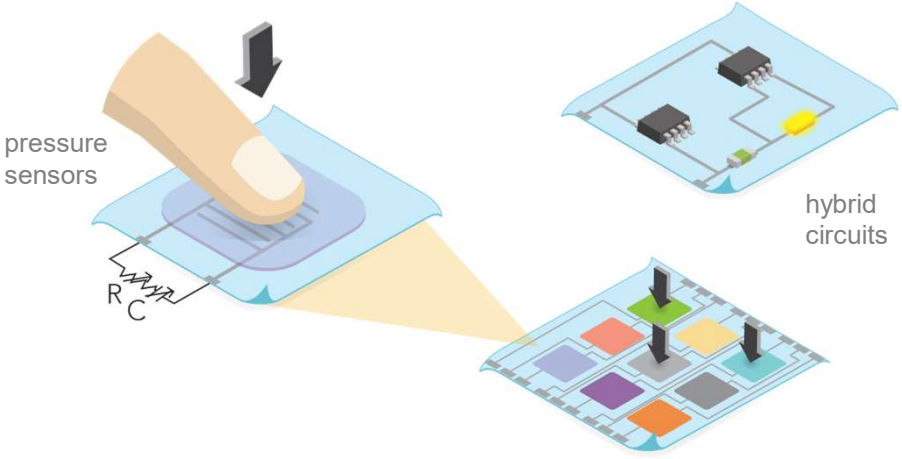
Smith, S. et al. (2018). The potential of paper-based diagnostics to meet the ASSURED criteria. *RSC Advances, 8, 34012.*

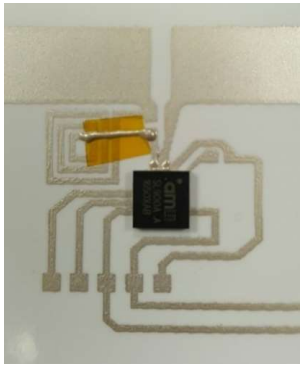
Printed Functionality

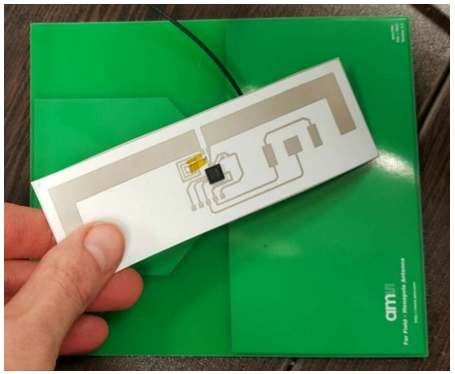






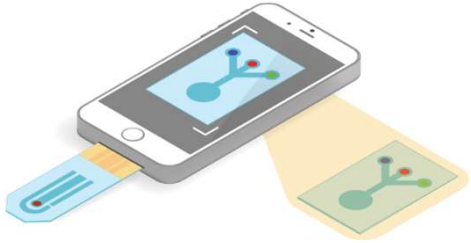


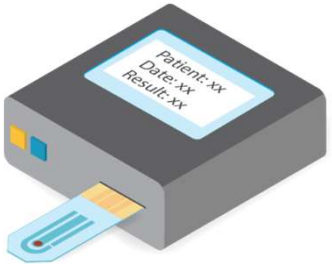


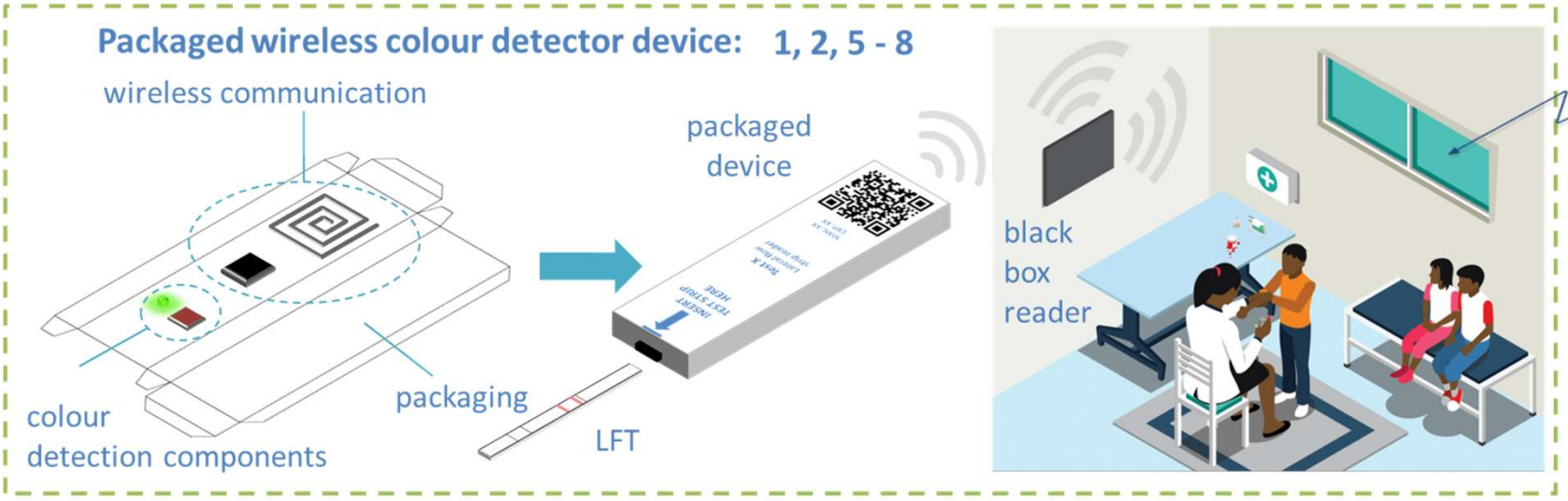


Smith, S. et al. (2019). Printed functionalities on paper substrates towards fulfilment of the ASSURED criteria. In: Land K. (ed) Paper-based Diagnostics, Springer, Cham.

Diagnostics Readers and Communication

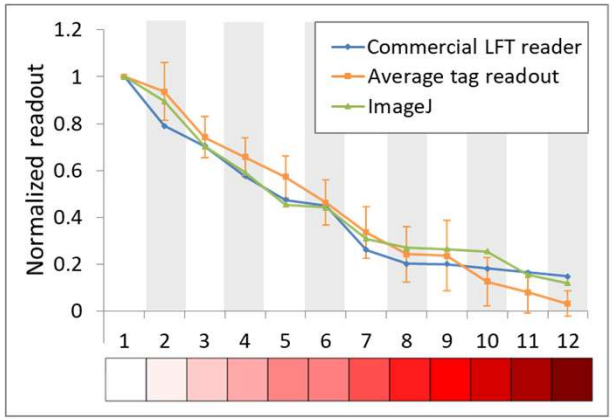






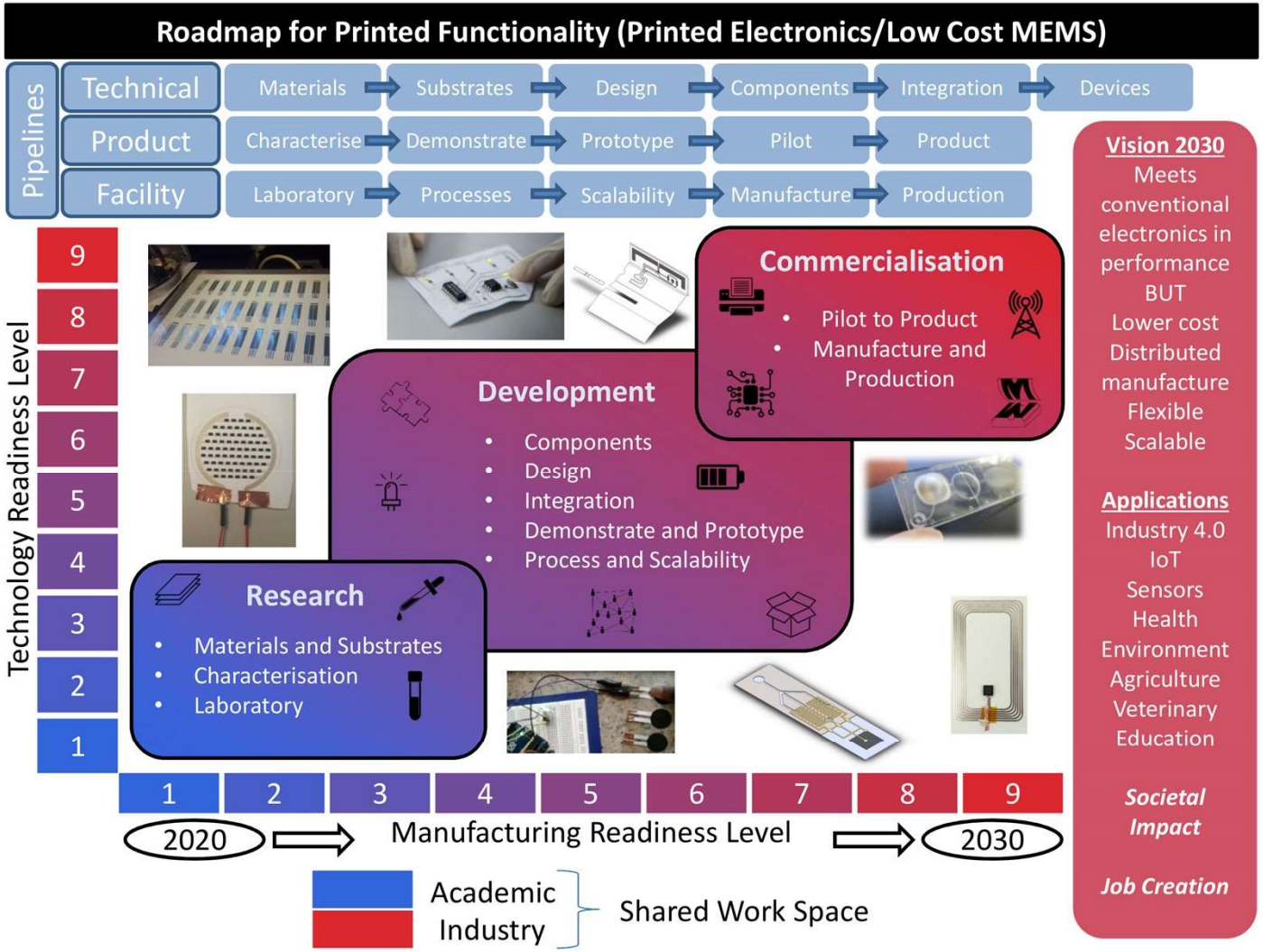
Smith, S., Oberholzer, A., Korvink, J., Mager, D. and Land, K., 2019. Wireless colorimetric readout to enable resource-limited point-of-care. *Lab Chip*

Diagnostics Readers and Communication - Result



Scalability

Smith, S., Oberholzer, A., Land, K., Korvink, J.G. and Mager, D. (2018), "Functional screen printed RFID tags on flexible substrate s, facilitating low-cost and integrated point-of-care diagnostics", IOP Flexible and Printed Electronics


Roadmap for Printed Functionality (Printed Electronics/Low Cost MEMS)
Pipelines
Technical
Materials
Substrates
Design
Components
Integration
Devices
Product
Characterise
Demonstrate
Prototype
Pilot
Product
Facility
Laboratory
Processes
Scalability
Manufacture
Production
Technology Readiness Level
9
8
7
6
5
4
3
2
1
Commercialisation
Pilot to Product
Manufacture and Production
Development
Components
Design
Integration
Demonstrate and Prototype
Process and Scalability
Research
Materials and Substrates
Characterisation
Laboratory
1
2
3
4
5
6
7
8
9
2020
Manufacturing Readiness Level
2030
Academic
Industry
Shared Work Space
Vision 2030
Meets conventional electronics in performance
BUT
Lower cost
Distributed manufacture
Flexible
Scalable
Applications
Industry 4.0
IoT
Sensors
Health
Environment
Agriculture
Veterinary
Education
Societal Impact
Job Creation

Thank You

We choose to go to the moon. We choose to go to the moon in this decade and do the other things, not because they are easy, but because they are hard…