FIND

Because diagnosis matters

Lessons Learned: Bringing diagnostics to market in low and middle income countries

Workshop on New & Innovative Approaches to Laboratory Diagnosis of Zika, Dengue & Other Arboviruses

PDC, Fondation Merieux, Annecy, May 2-4, 2017 ¦ *Dr Cassandra Kelly, Head of AMR & Outbreaks, FIND*

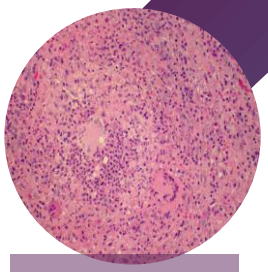
Diagnostic Solutions – more than a test

Catalyse Development

Guide Use and Policy

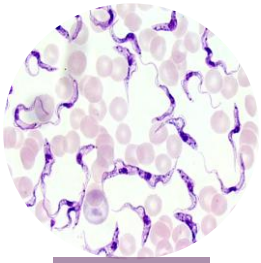
Accelerating Access

Shape the Agenda

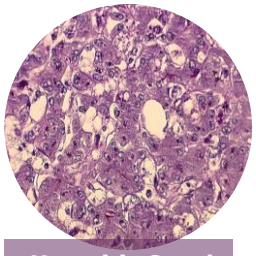


Tuberculosis

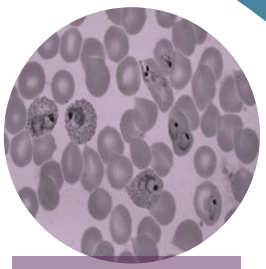
AMR / Outbreak



NTDs



Hepatitis C and HIV



Malaria

E-Diagnostics

SCIENCE PRODUCTS SOLUTIONS PATIENTS

When bringing products to the LMICs…

Early partnerships are critical to ensure the "right product at the right time" and drive coordinated development, introduction and scale

1. Partnerships and Market Opacity

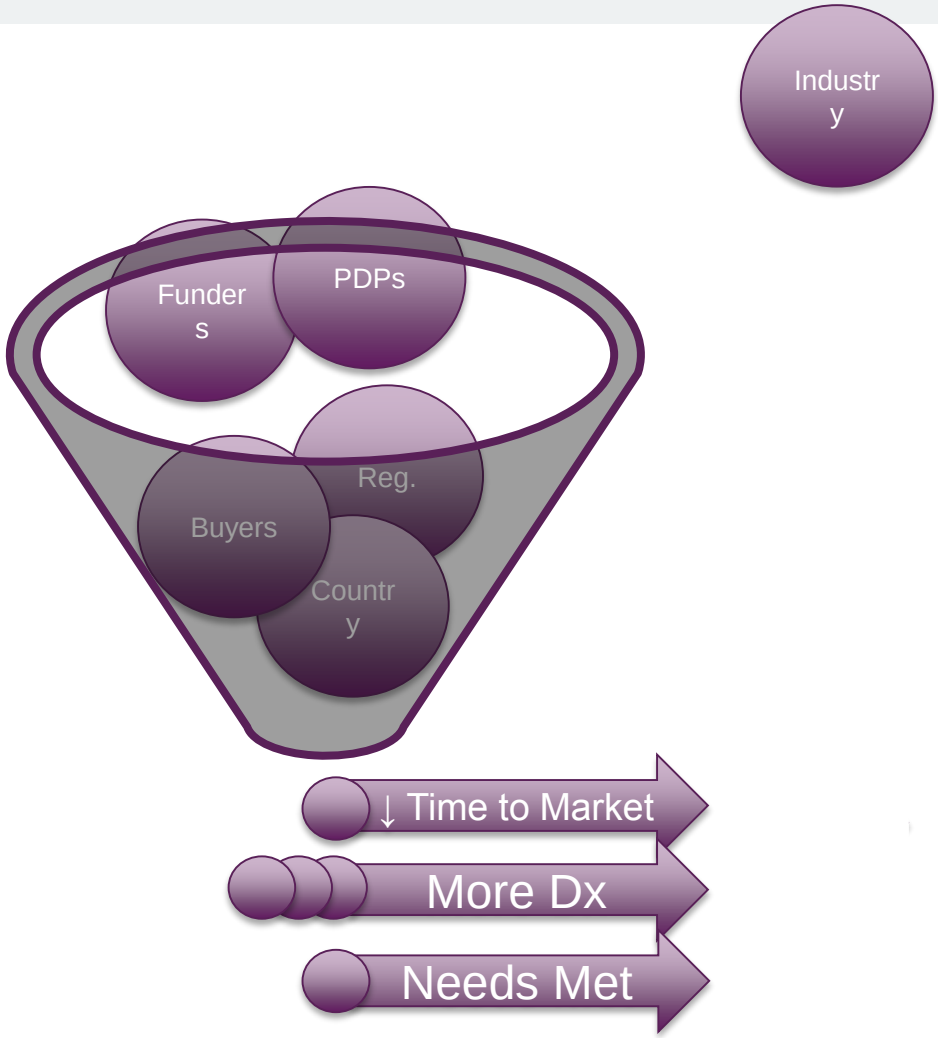
2. "Normal" environment vs Outbreak environment

3. Tactical challenges:
   - Imperfect reference standards
   - Access to clinical samples during multiple stages of development
   - Diagnostic assessment in an evolving outbreak

4. Solutions:
   - Moving from Response to Preparedness in Diagnostic development
   - Diagnostic Preparedness Consortium to ensure a proactive global public health response

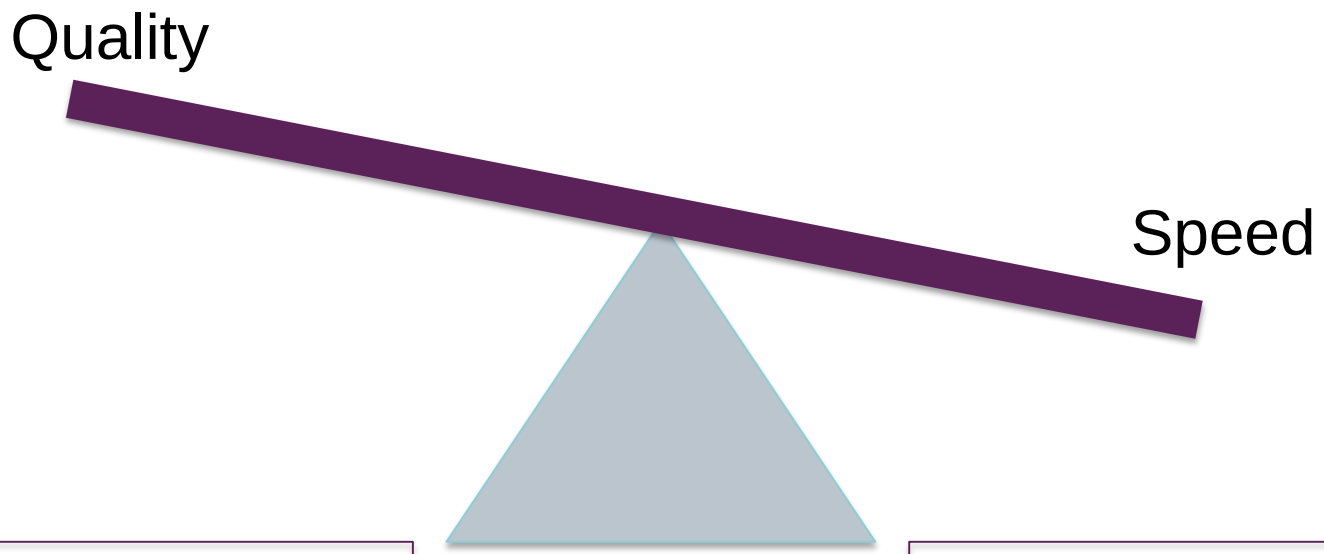
Early Partnerships are Key

- **Market opacity** is a critical barrier to success for **all stakeholders**
- **Early partnerships** are key for development, validation, introduction and scale
- Balancing speed with quality is essential to ensure the **right products** are available at the **right time** in the **right markets**
- **Outbreak** situations **intensify** these challenges



Early partnerships can clear market opacity, reduce investment risk and improve ROI for all stakeholders

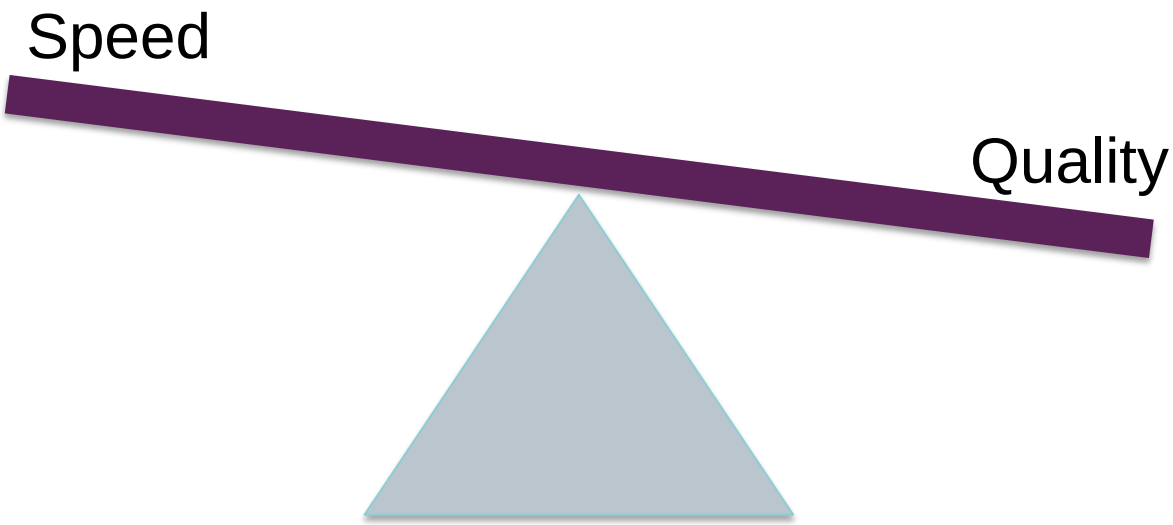
Quality over Speed in a “Normal” Environment



- Specificity & Sensitivity
- Identify pathogen + modes of transmission
- Track epidemiology
- Support patient care and contact tracing

- Assay development 1-5 y
- Access to samples
- Long validation phase
- Long regulatory review (conventional)

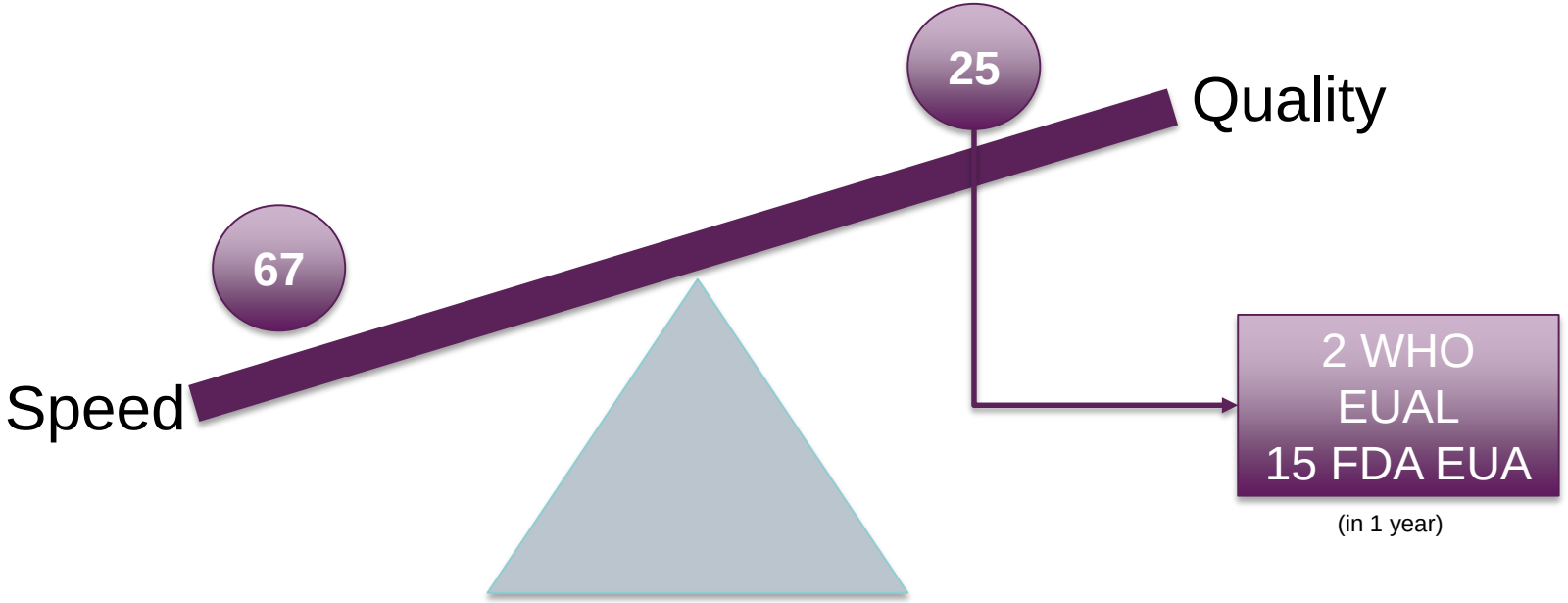
Added complexity in active outbreaks



- Needed at start of outbreak
- Rapid scale up & delivery
- Rapid regulatory & policy guidance
- In-country acceptance

- New companies
- Unproven performance
- Imperfect gold standards
- No clinical data
- Access to samples
- Episodic market

Zika Product Dynamics



altona DIAGNOSTICS

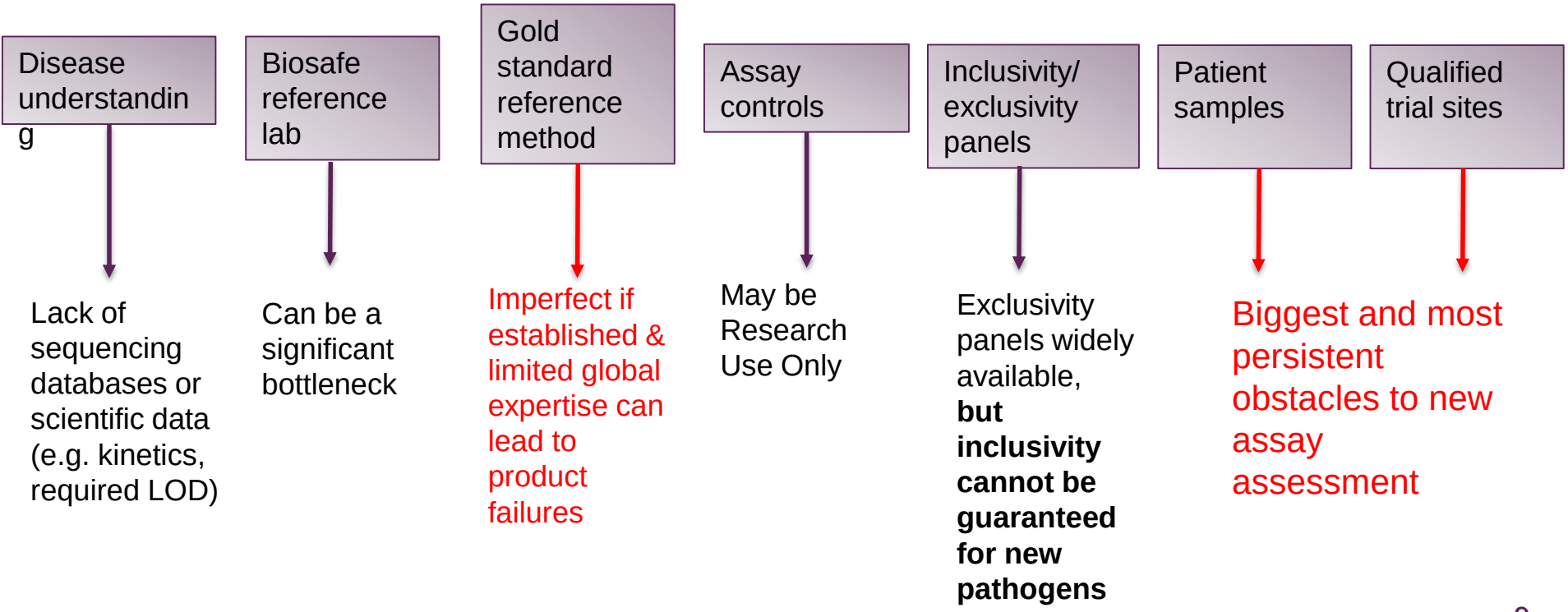
Only 3 FDA EUA are immunoassay based → No RDTs approved

Differences in outbreak geographies changes product needs & adds complexity

Partnerships are key to evaluate technologies, ensure appropriate market placement and drive impactful funding allocations

Tactical challenges to product development

Outbreak product development pathway is compressed but need for quality remains



Evolving reference method during outbreaks

Performance of Reference Test (CDC MAC

Table 4: Data for Sera Submitted to CDC Ft. Collins for Testing 2015-present

		PRNT Results			
		Zika	flavivirus	dengue	negative
Zika MAC-ELISA	positive	156	263	60	137
	equivocal	10	30	29	156
	negative	0	8	33	131

Positive % Agreement: 156/166 = 93.98% (95%CI: 89.27 – 96.7%)

The Washington Post

D.C. Politics

DC lab botched Zika tests involving pregnant women

Table 5: Data for Sera from Pregnant Women Submitted to CDC Ft. Collins for Testing 2015-present

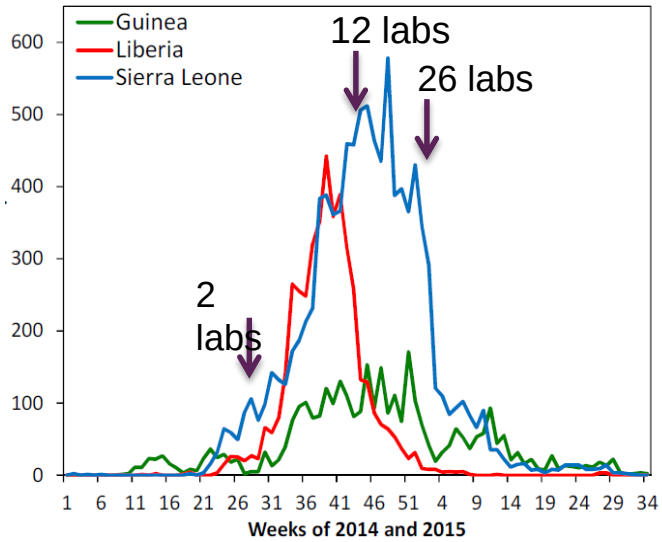
		PRNT Results			
		Zika	flavivirus	dengue	negative
Zika MAC-ELISA	positive	14	104	19	85
	equivocal	1	17	15	100
	negative	0	2	10	60

Positive % Agreement: 14/15 = 93.33% (95%CI: 70.18 - 98.81%)

Zika MAC ELISA Instructions for Use; Centers for Disease Control, USA.

Reference test performance challenges lead to unclear performance baselines for new tests

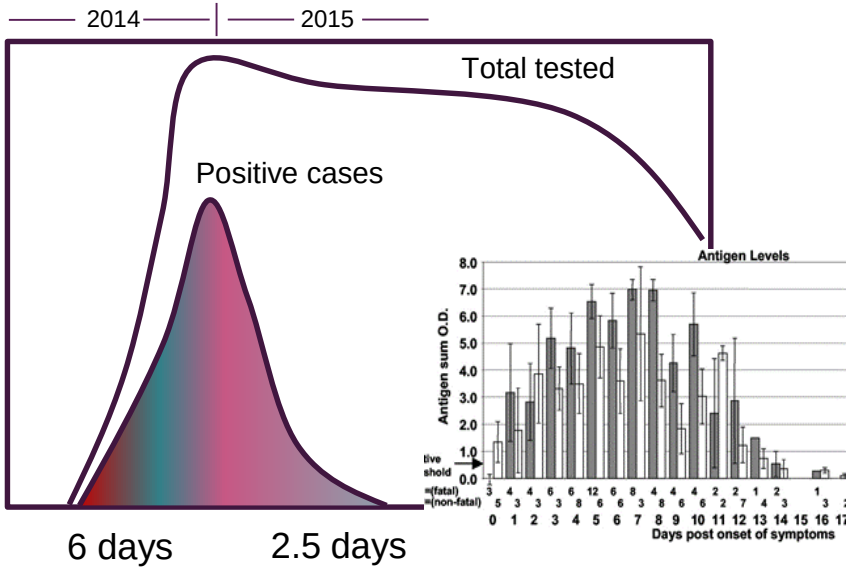
Rapid evolution of an outbreak leads to bias



Start of outbreak:
Few labs, with limited capacity to do new product testin

Peak of outbreak:
More labs with capacity, access to samples increases

Tail of outbreak:
High capacity, decreased access to samples

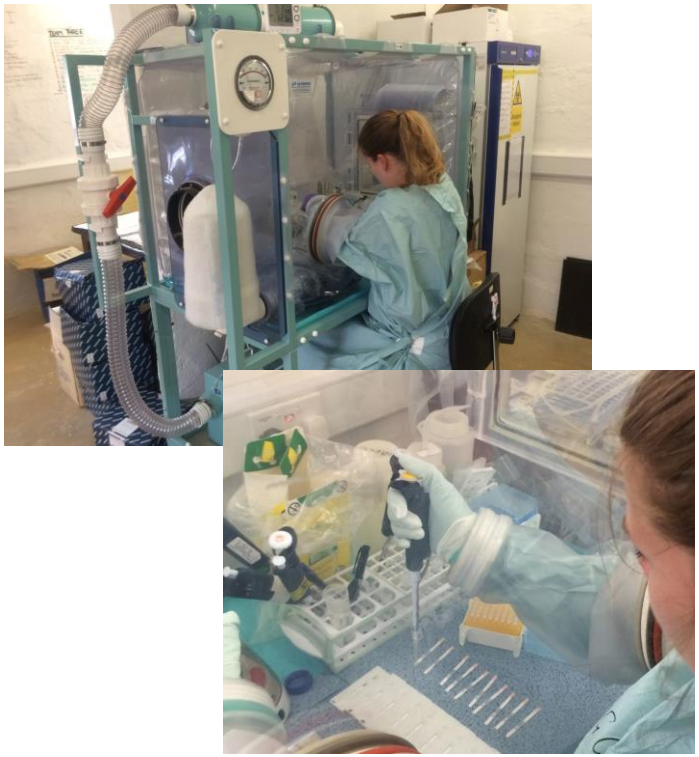


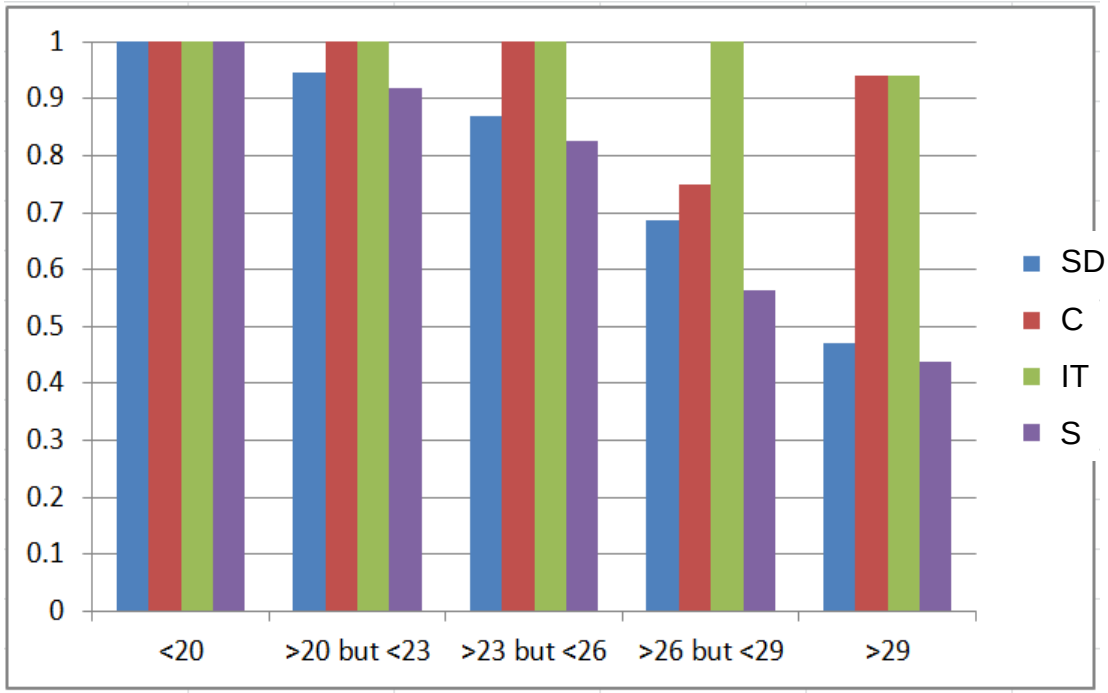
At start of outbreak:
High # positive cases with advanced disease and high viral loads

At tail of outbreak:
Lower # positive cases and identified earlier so lower viral loads

Product evaluation at start ≠ at tail

Comparative testing of RDTs in Port Loko





Log10 copies/ml RNA **>8.2** **7.2-8.2** **6.2-7.2** **5.4-6.2** **<5.4**

SD Biosensor: GP, NP, VP40

Corgenix: VP40

In**T**ek: NP

Senova: VP40

Sample selection identifies critical performance differences

Ethical collection and ownership of samples

Early outbreak collections tend to be ad-hoc:

- Ownership not defined
- May be under a blanket agreement covering emergency lab operations
- Individual informed consent often not feasible

Poor prioritization of needs:

- High number of sample requests for various groups including industry
- Significant IP and ethical concerns in the scramble for samples
- Sample use not driven by public health concerns

Lack of resources and expertise:

- Labs too overtaxed to curate samples and data
- Labs wary of sharing proprietary resources
- No coordinated response to facilitate sample banking and prioritization

Reactive not Proactive Dx Development

Challenges intensified during an Outbreak

- Clinical & public health needs and TPP specifications have not been established
- Regulatory pathways are not well established
- Reference assays & reference standard reagents do not exist
- Clinical specimens become an arena for combat rather than collaboration

Outbreaks are episodic markets

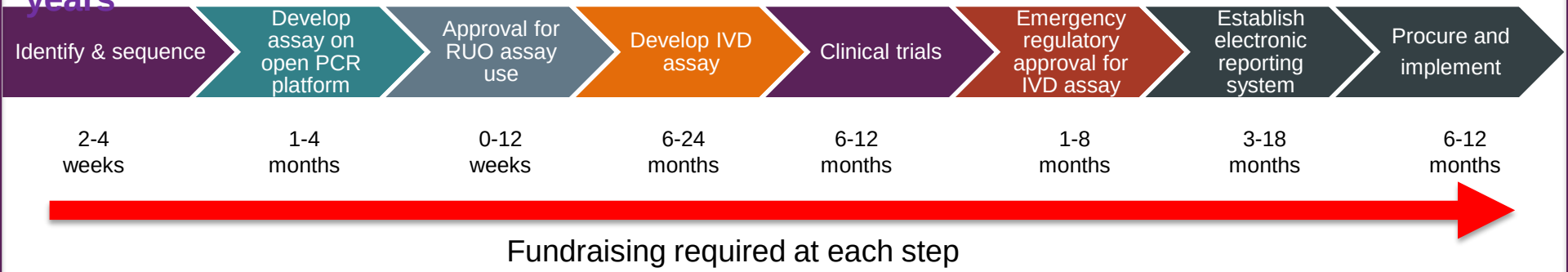
- Companies have almost no ability to make realistic risk/reward assessments
- Emergency needs not identical to long-term clinical, public health and research needs
- Unsustainable for a business to stay in an outbreak space with no market stability

Scarce diagnostic performance data

- Company data limited given lack of sample access and sometimes closely held
- Emergency Use Authorizations necessarily allow for limited product validation studies in clinical and spiked samples
- Objective, comparative assessments of clinical and operational performance are needed for strong national policies

Proactive Dx development to accelerate preparedness

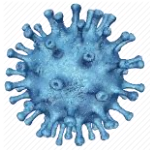
Current REACTIVE diagnostics response process: 2 to 6 years



PROACTIVE diagnostics response process

- Pre-outbreak R&D contracts
- Pre-outbreak sample agreements
- Diagnostic response plan
- Parallel rather than sequential R&D steps
- Efficient regulatory processes

Shortened time to deployment



Clinical diagnostic

2 weeks

RUO assay 2 months

Clinical diagnostic 4 months

Proactive: A Diagnostics Preparedness Consortium

- ✓ Multi-disease approach
- ✓ Highly cost-effective compared to a one-by-one response
- ✓ Known and unknown pathogens
- ✓ Ensure pre-qualified, pre-registered, and stockpiled for rapid deployment
- ✓ Providing solutions and diagnostic strategies, rather than tests
  - ✓ Connectivity for monitoring and surveillance post-outbreak
  - ✓ Utility during outbreak and post-outbreak


WITHOUT
DIAGNOSTICS,
MEDICINE IS
BLIND.

New diagnostic solutions bring game-changing possibilities and can spark real progress in the health of people in lower- and middle-income countries.

TO LEARN MORE, VISIT: www.finddx.org

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