

Diagnostic Tools for the Elimination of Visceral Leishmaniasis

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Accessible Quality-assured Diagnostics

Objective:

To facilitate the Development, Evaluation and Application of Diagnostics Appropriate for Developing Country Settings

The Ideal Diagnostic Tool

A = Affordable by those at risk of infection

S = Sensitive

S = Specific

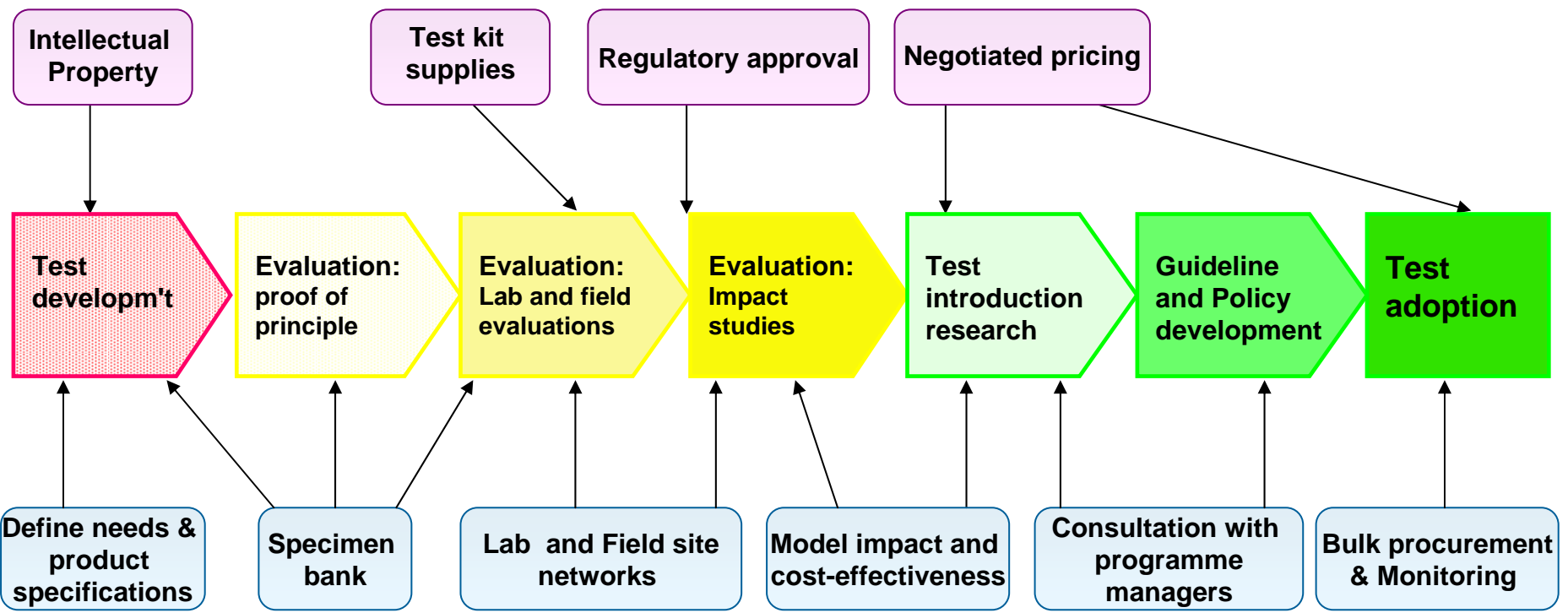
U = User-friendly (simple to perform, minimal training)

R = Rapid/robust (enables action at point of care)

E = Equipment-free

D = Deliverable to those who need it

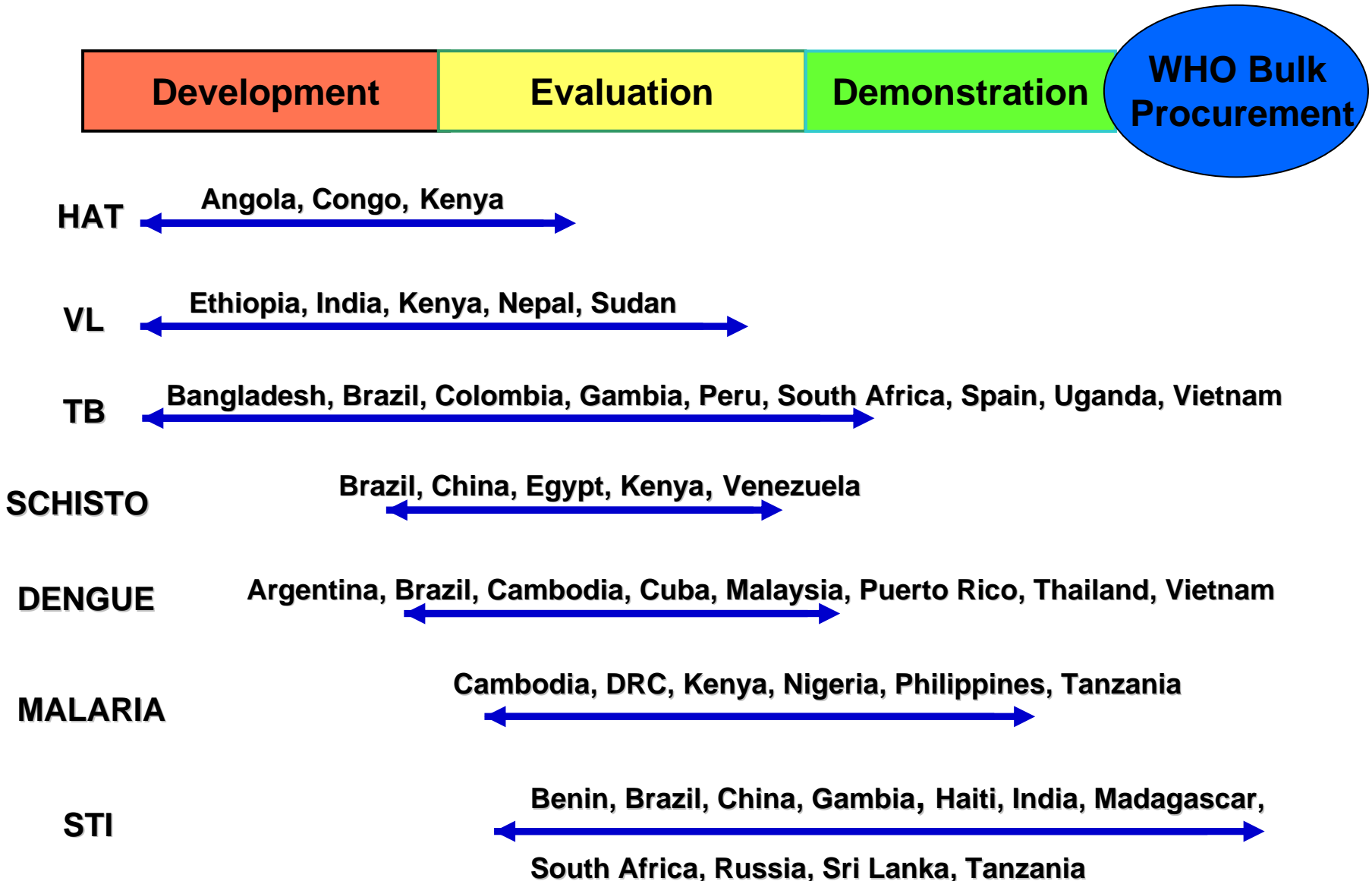
Test Developer



WHO/TDR DRD Strategy



WHO/TDR Diagnostic R&D Sites in 34 countries



Proposed Priorities for VL Diagnostics R&D

Purpose	Target Population	Diagnostic Type
1. Case detection	Symptomatic patients – to guide treatment	Point of care
2. Test of cure	Treated patients	Point of care
3. Relapse	Symptomatic patients - after prior treatment	Point of care
4. Surveillance	Community – monitor prevalence/incidence	Laboratory
5. Drug resistance	Treated patients - drug susceptibility	Reference lab

Field Trials of Rapid VL Diagnostic Tests

Multi-centre field trials:

- Ethiopia, Kenya & Sudan, India & Nepal

Tests evaluated (specimen used):

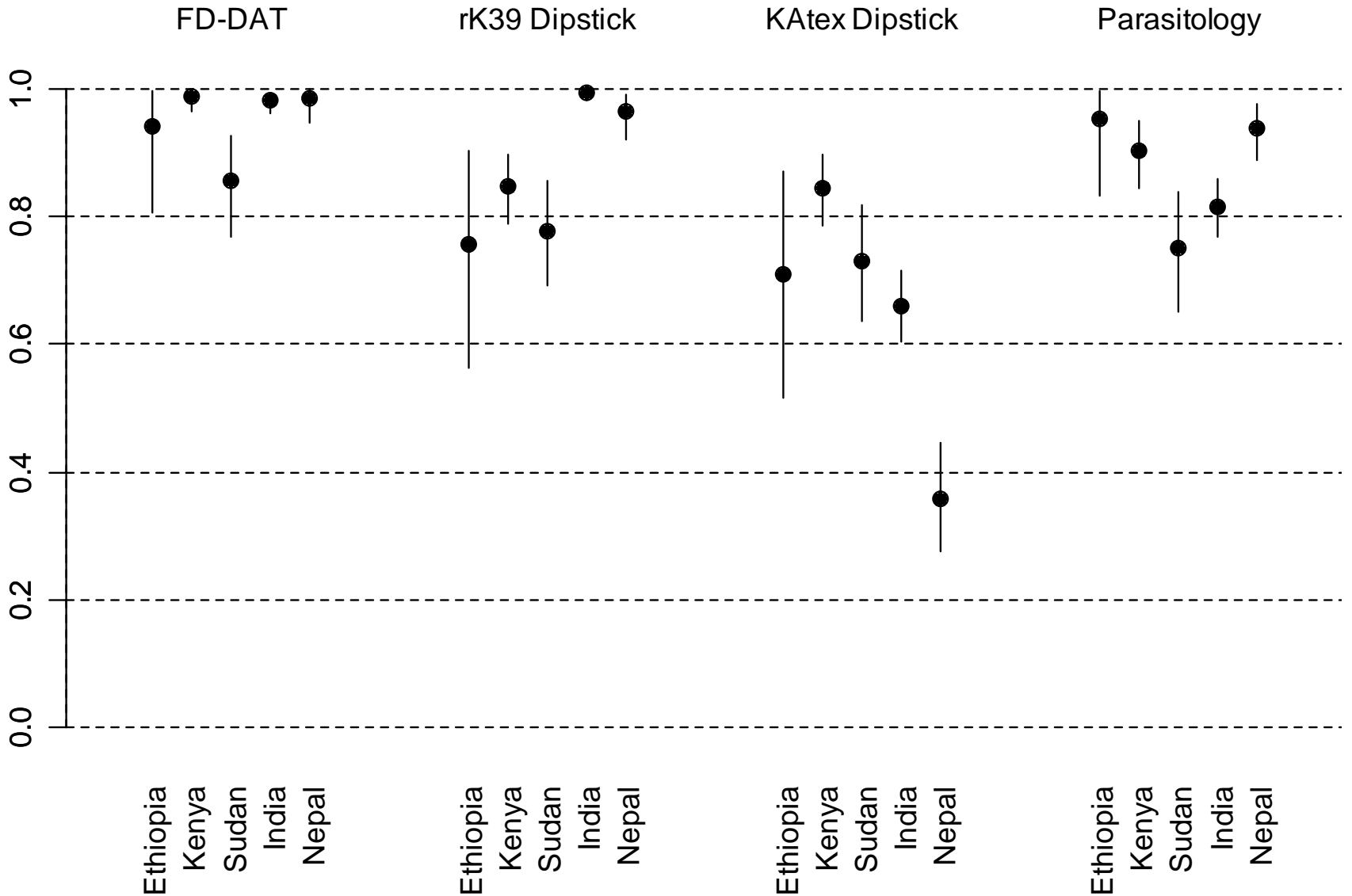
- Antibody detection tests:
 - rK 39 dipstick test (sera)
 - Direct Agglutination Test, freeze-dried, DAT-FD (sera)
- Antigen detection tests:
 - latex agglutination test, Katex (urine)

Other evaluations:

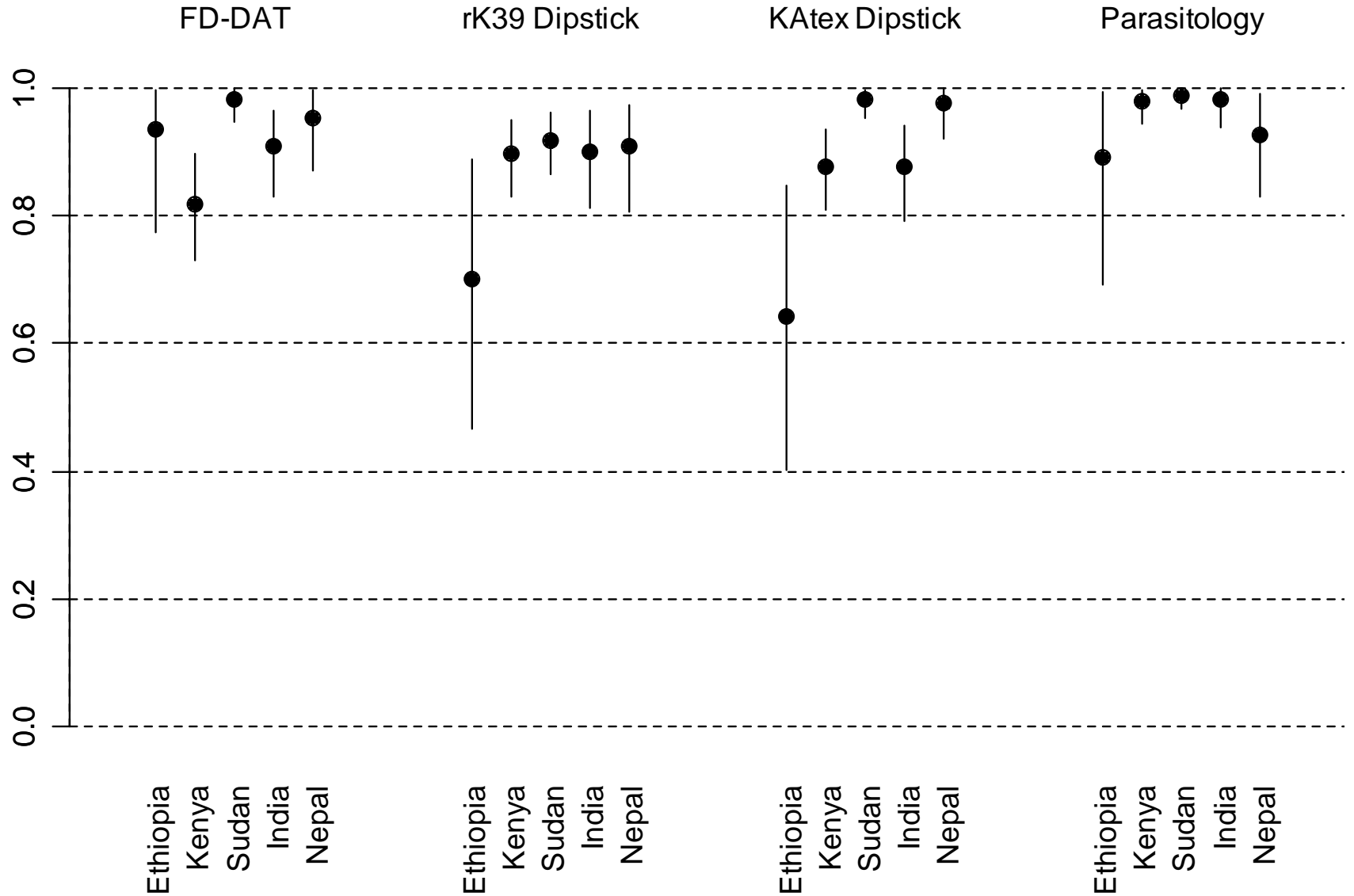
- Antibody detection: rK26 dipstick (serum)
- Antigen detection: Rapid Sialic Acid Chromatography (SAC) test (whole Blood)



Sensitivities



Specificities



How Good Are Rapid VL Tests?

<u>Sites</u>	<u>Para.*</u>	<u>DAT-FD*</u>	<u>rK39*</u>	<u>Katex*</u>
1. India	82/98	98/91	99.6/90	66/88
2. Nepal	94/93	99/95	97/91	36/98
3. Sudan	75/99	86/98	78/92	73/98
4. Kenya	90/98	99/82	85/90	85/88
5. Ethiopia	95/89	94/94	75/70	71/64

* Estimated sensitivity/specificity by latent class analysis

Rapid VL Diagnostic Tests

Antibody detection tests:

cannot be used to distinguish between past and active infection (some areas >30% seropositive)

- **Freeze dried Direct Agglutination Test, DAT-FD**
 - Sensitivity >98% , specificity 94%
 - Reconstituted reagent needs refrigeration
 - Multiple pipetting steps
 - Several hours incubation
 - Uses serum – requires centrifugation
 - Cost = \$1.25-2.25/test
- **rK 39 dipstick test**
 - Sensitivity >98% only in South-Asia, specificity 94%
 - Simple to perform
 - Room temperature storage for 18 months
 - Uses serum – requires centrifugation
 - Cost = \$1.00/test

Rapid VL Diagnostic Tests

Antigen detection tests:

- **Latex agglutination test (Katex)**
 - Detects a VL carbohydrate antigen in urine
 - Has potential to be test of cure
 - Uses non-invasive specimen
 - Need to boil urine for 10 min.
 - Lack sensitivity (36-84%)
- **Rapid Sialic Acid Chromatography (SAC) test**
 - Detects an altered sialic acid residue on rbc's
 - Can use whole blood
 - Simple to perform
 - Performance = ? (under evaluation)
 - Cost = ?

How Good Are Rapid VL Tests?

Purpose	DAT-FD	rK39	Katex	SAC
1. Case detection	++	++++	+	+
2. Test of cure	-	-	++	++
3. Relapse	-	-	+	+
4. Surveillance	+++ (prevalence)	+++ (prevalence)	+	+
5. Drug resistance	-	-	-	-

++++ = suitable; + = needs improvement; - = not suitable

Accessible Quality-assured Diagnostics

Visceral Leishmaniasis

2007:

- **Recommendations for use of diagnostic tools to support control programmes and elimination initiatives – testing algorithms?**
- **5 diagnostics projects funded:**
 - **preliminary evaluation of the rapid SAC test (Sundar)**
 - **development and field trial of a rapid urine test (Chance)**
 - **development and evaluation of tandem repeat antigens to improve sensitivity of rK39 test for Africa (Goto)**
 - **evaluate performance of rapid tests in HIV+ and TB+ coinfections**
 - **development of a novel serologic test (El Safi)**
- **Setting standards for diagnostic evaluations (Nature supplement)**
- **Specimen bank/reference materials to facilitate diagnostic development, evaluations and QA/QC.**



Evaluating diagnostics: the VL guide



Illustration by Nature Publishing Group

Roadmap for the Use of Diagnostic Tools for VL Elimination

1. **Need advocacy and political commitment in the importance of diagnostics in case management and disease control**
2. **Need to establish a policy platform to translate research findings into policy and practice**
3. **Need to pilot how different tests can be used in control programmes, esp. in primary health care settings:**
 - Education of care givers
 - Organization of training and assurance of proficiency
 - Reference laboratories to develop system for ensuring test quality
 - Develop system for forecasting demand to avoid stock-outs of drugs and tests
 - Monitor treatment practice related to diagnostic results
4. **Need to select a test for VL surveillance to monitor transmission in communities – incidence and prevalence**