Making the Case for Method Validation

20th April 2021

Why validate methods?

Consistent, reliable data are needed to properly evaluate and monitor vector control tools

- Different entomological effects need to be measured
- Existing methods focused on pyrethroid-type effects
- No validated methods to indicate the performance of dual-AI ITNs
- Cannot do QA without reliable data
- New methods underpin innovation

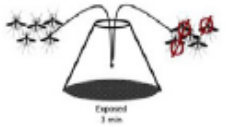
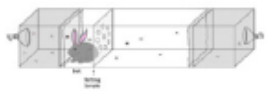
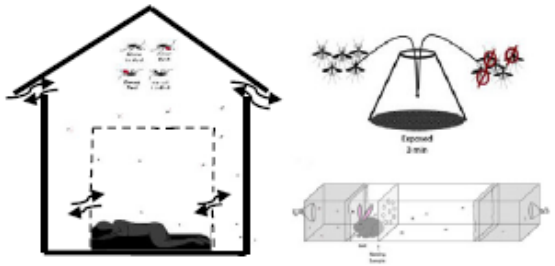
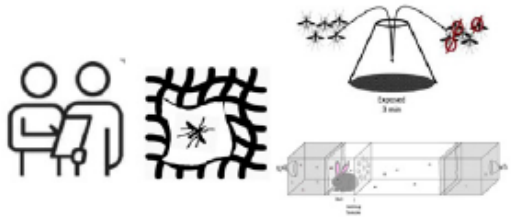
Characterization of materials are often inconsistent

- Need clarity on what is being tested
  - How are test products defined (specs, lot/batch etc.)?
  - How are test insects defined, particularly with regards to resistance status?
  - What is mud?

Validated methods are needed to indicate the performance of a product, but need to be specific to the product and it properties

Without validated methods, evaluation of new tools is not possible and will result in delays to access

The product should drive choice of method, not vice versa

	Laboratory evaluation, phase 1 *Confirmation of bioefficacy up to 20 washes in laboratory tests*	Semi-field evaluation, phase 2 *Confirmation of bioefficacy up to 20 washes against wild mosquitoes*	Community evaluation, phase 3 *Confirmation of bioefficacy and fabric integrity under user conditions for up to 3 years*
Test methods	• Cone tests expose mosquitoes directly to netting for 3 minutes and measure the proportion of mosquitoes that are knocked down and killed  • Tunnel tests are conducted overnight for 12-15 hours and allow mosquitoes to pass through a piece of netting with 9 small holes and feed on a small mammal and measure the proportion of mosquitoes blood fed and the proportion dead 	• Experimental hut tests allow wild mosquito populations to enter huts and interact with humans sleeping beneath bednets overnight for 12 hours and measure the proportion of mosquitoes blood fed and the proportion dead • Confirmatory laboratory bioassays (cone and tunnel) and test of chemical content are also performed 	• Community tests monitor the proportion of bednets that are no longer in use through observation • Of those remaining, the fabric integrity (damage) is assessed each year • Laboratory bioassays (cone and tunnel) are performed each year • Confirmatory laboratory tests of residual chemical content are performed each year • The test measures bednet duration of efficacy 
	Insecticide content by gas chromatography with flame ionisation detection (GC-FID) high performance liquid chromatography with UV diode array. Detection (HPLC-DAD) or product-specific test validated in collaboration with the Collaborative International Pesticides Analytical Council (CIPAC)		
Outcomes	• Loss of AI per wash (insecticide retention index) • Time to regenerate after washing • Bioefficacy against a standard strain up to 20 washes • Chemical content up to 20 "laboratory" washes 	• Bioefficacy against wild mosquitoes unwashed and after 20 "field" washes • Confirmatory bioefficacy against a standard strain up to 20 "field washes" • Chemical content up to 20 "field washes" 	• Bioefficacy against a standard strain up to 3 years of use • Fabric integrity up to 3 years of use • Chemical content up to 3 years of use • Proportion of nets still in use in a serviceable condition • Median years of effective life in test setting 

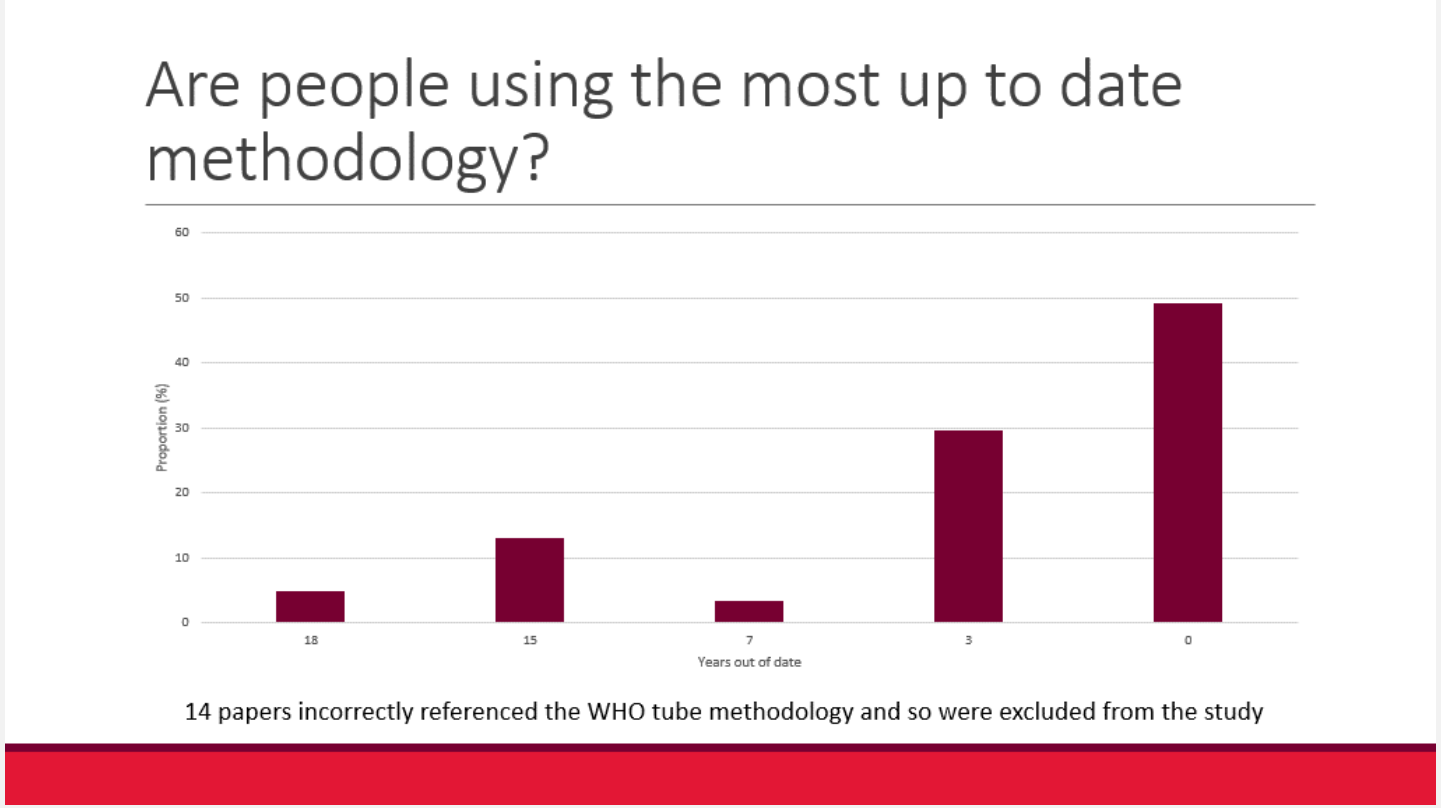
Karl S, Katusele M, Freeman TW, Moore SJ. Quality Control of Long-Lasting Insecticidal Nets: Are We Neglecting It? Trends Parasitol. 2021 Mar 25:S1471-4922(21)00056-8. doi: 10.1016/j.pt.2021.03.004. Epub ahead of print. PMID: 33773912.

Even well known methods are applied inconsistently

Literature review of WHO Tube tests

by Giorgio Praulins, LITE (unpublished data)

- Review of 61 papers
- 4 guideline references identified (1998, 2006, 2013, 2016)
- Numerous inconsistencies in methodology and reporting identified



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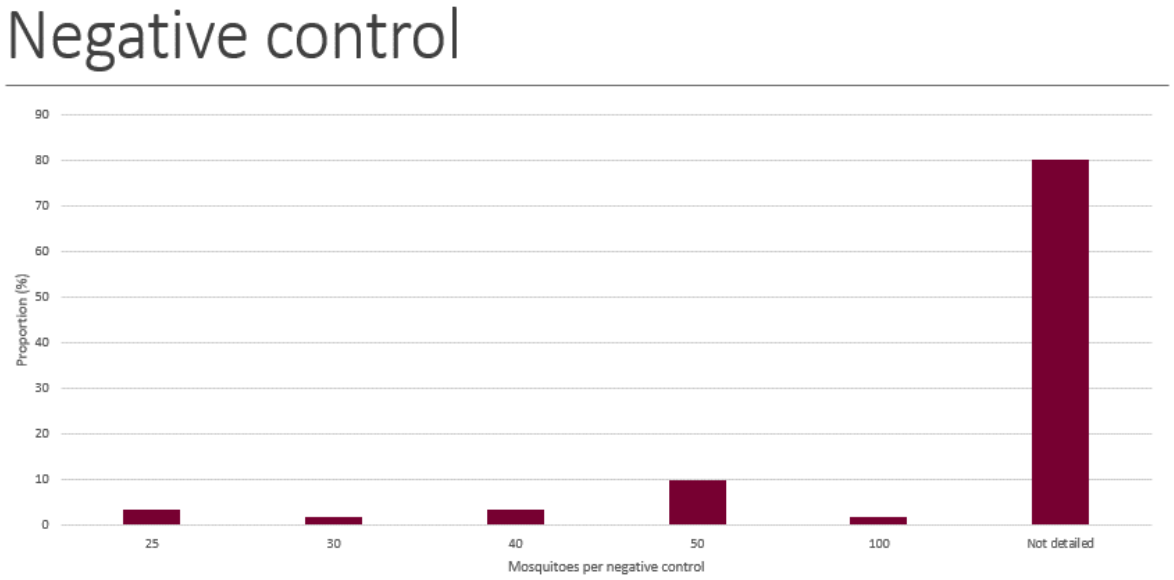

2013 WHO guidelines onwards say to expose 50 mosquitoes in 2 lots of 25 to control papers.

What does validation look like?

Four Stage Method Validation

Preliminary Development

- Define desired outcomes, design and refine methodologies

Feasibility Experiments

- Quantify inherent error in the method

Internal Validation

- Evaluate the ability of the method to accurately characterise VC product(s)

External Validation

- Affirmation of results by two external laboratories

Next steps

Identify issues for current products

- Agree methods for dual AI-ITNs and validate them asap
- Work to characterise inputs/materials
- Can we accurately capture necessary data points?
- Landscape methodological issues and prioritise

Engage with next gen products under development

- Are developers working to validate methods?
- What assistance may be needed?
- How can we identify resources to address these issues?

Identify underlying methodological issues, tighten up or update with new advances

- Can we apply new technology to answer old

Thank you