
Potential role of ivermectin and ivermectin-like compounds for malaria elimination

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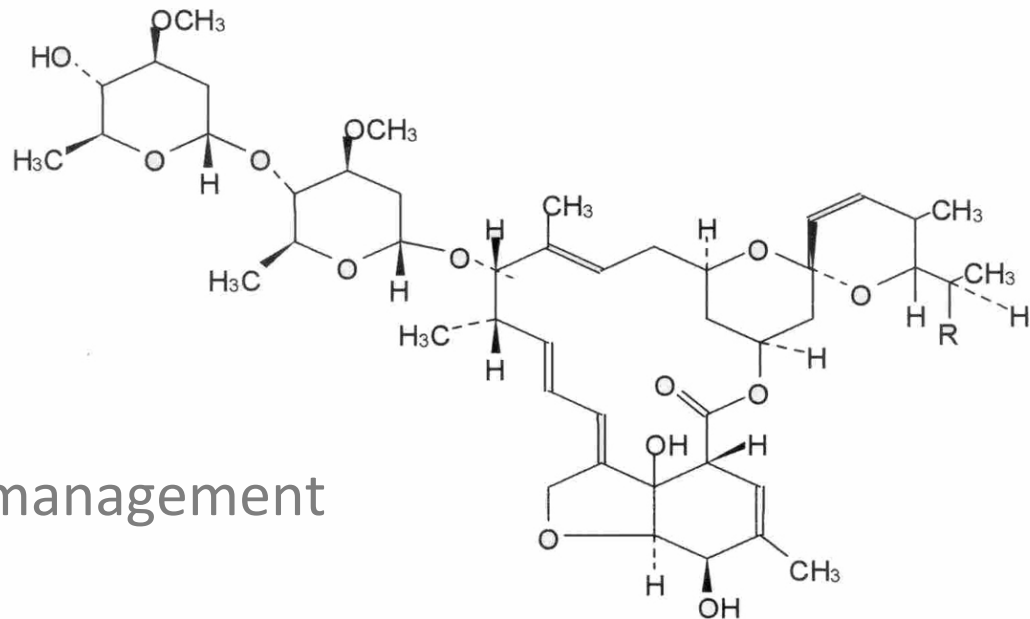
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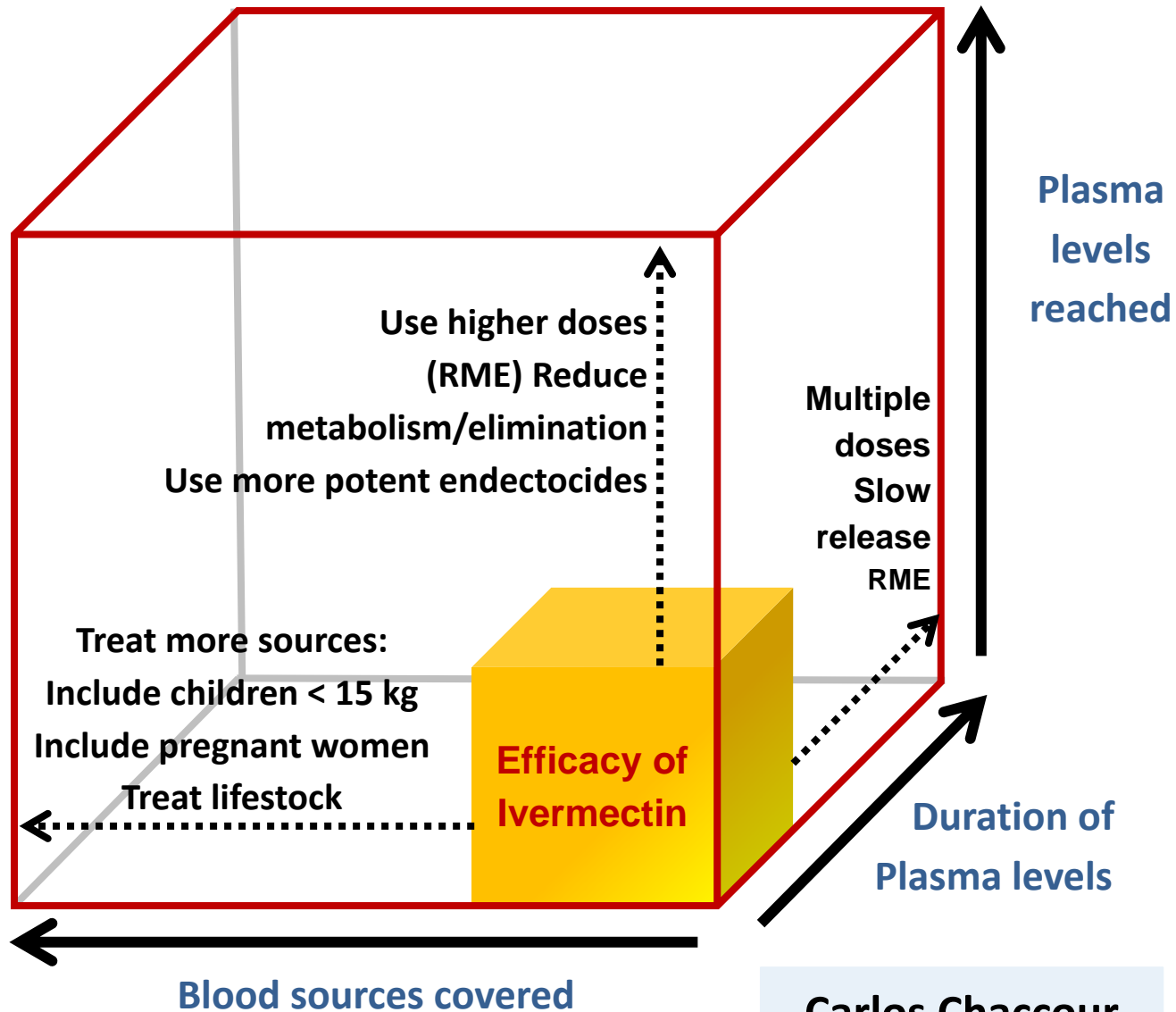


The potential role of ivermectin for malaria elimination

- Endectocide
- **First concept : MDA**
 - ✓ Assuming good VC
 - ✓ Assuming good case management
- Complementary tool

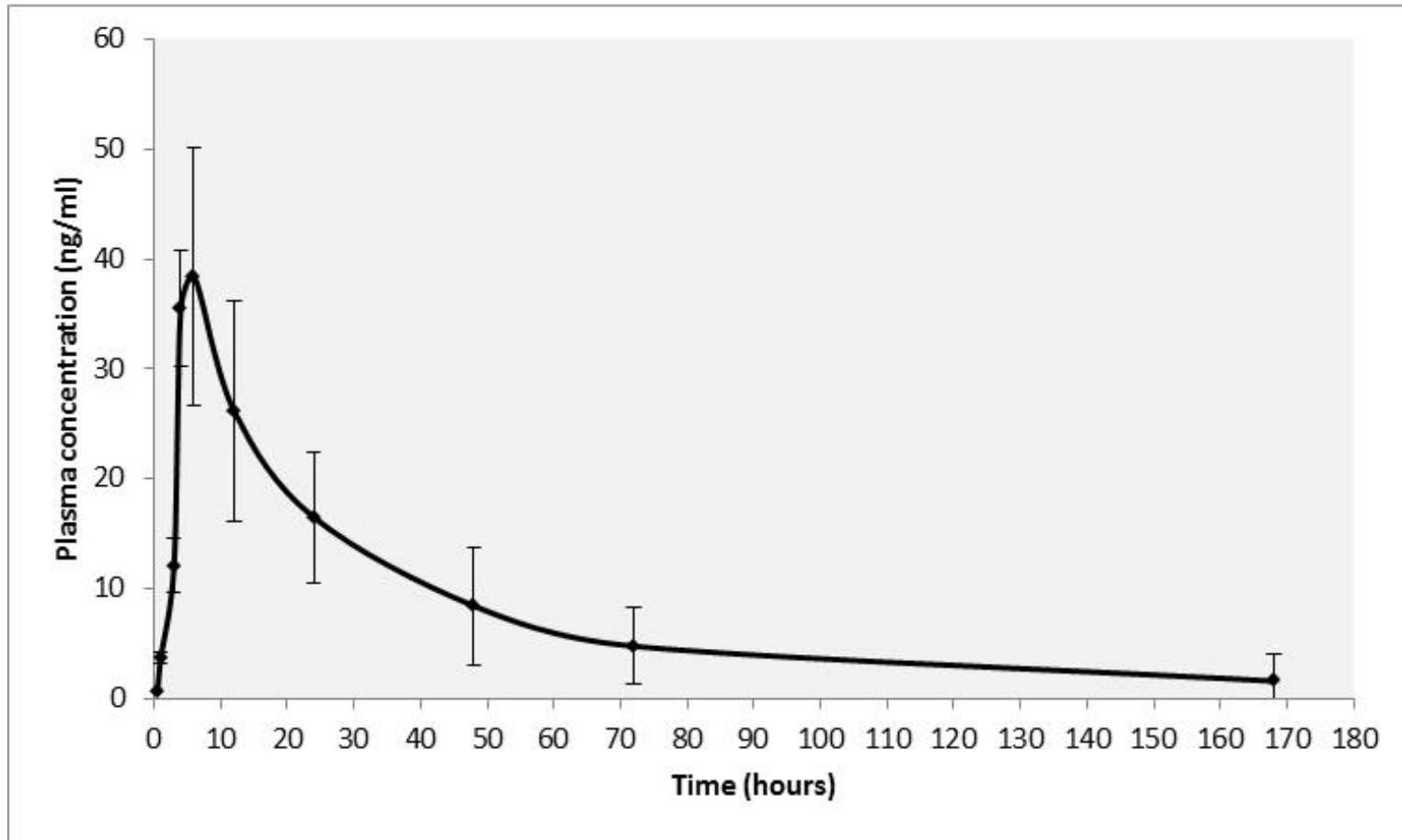


How does it work?

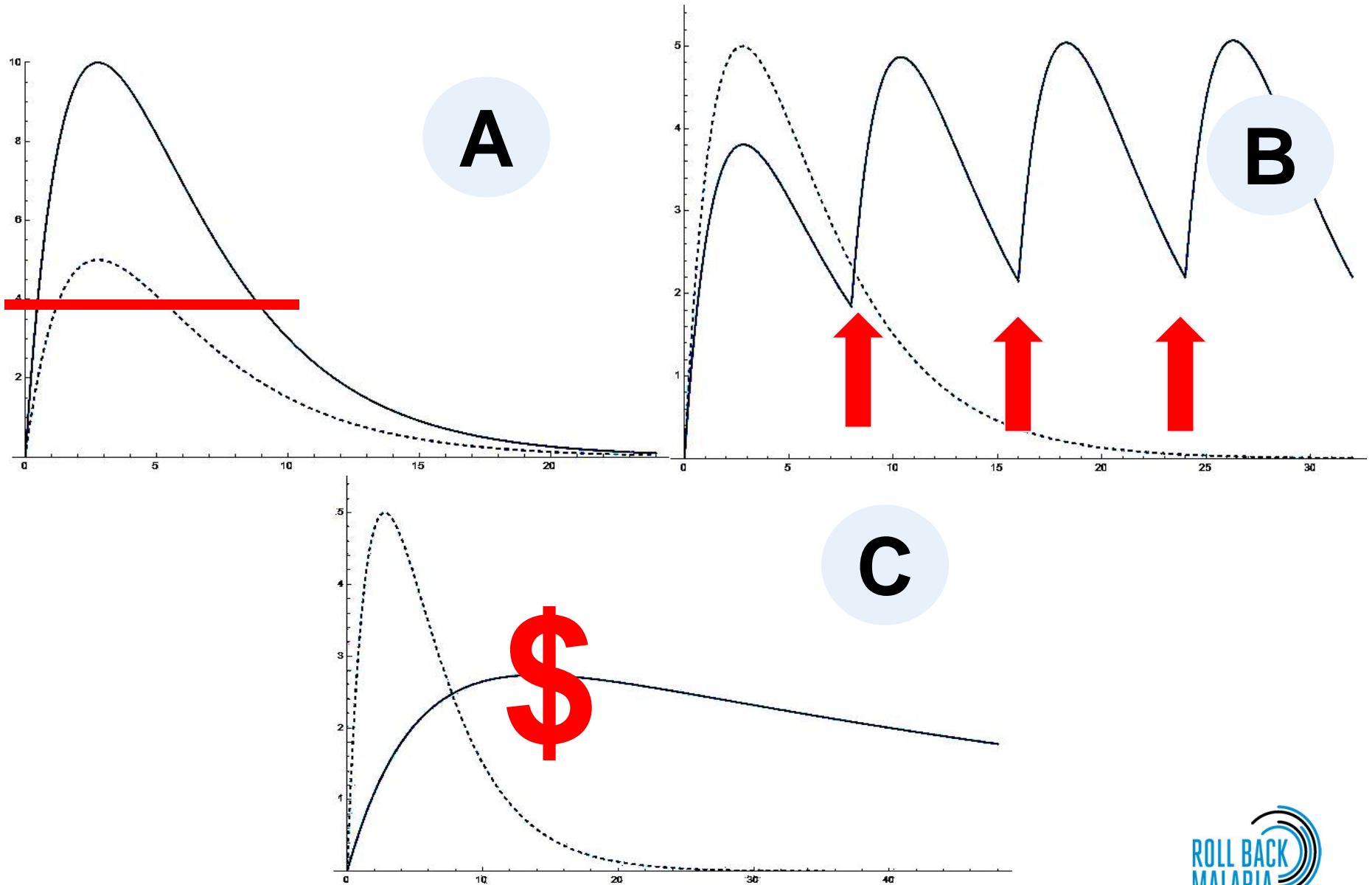


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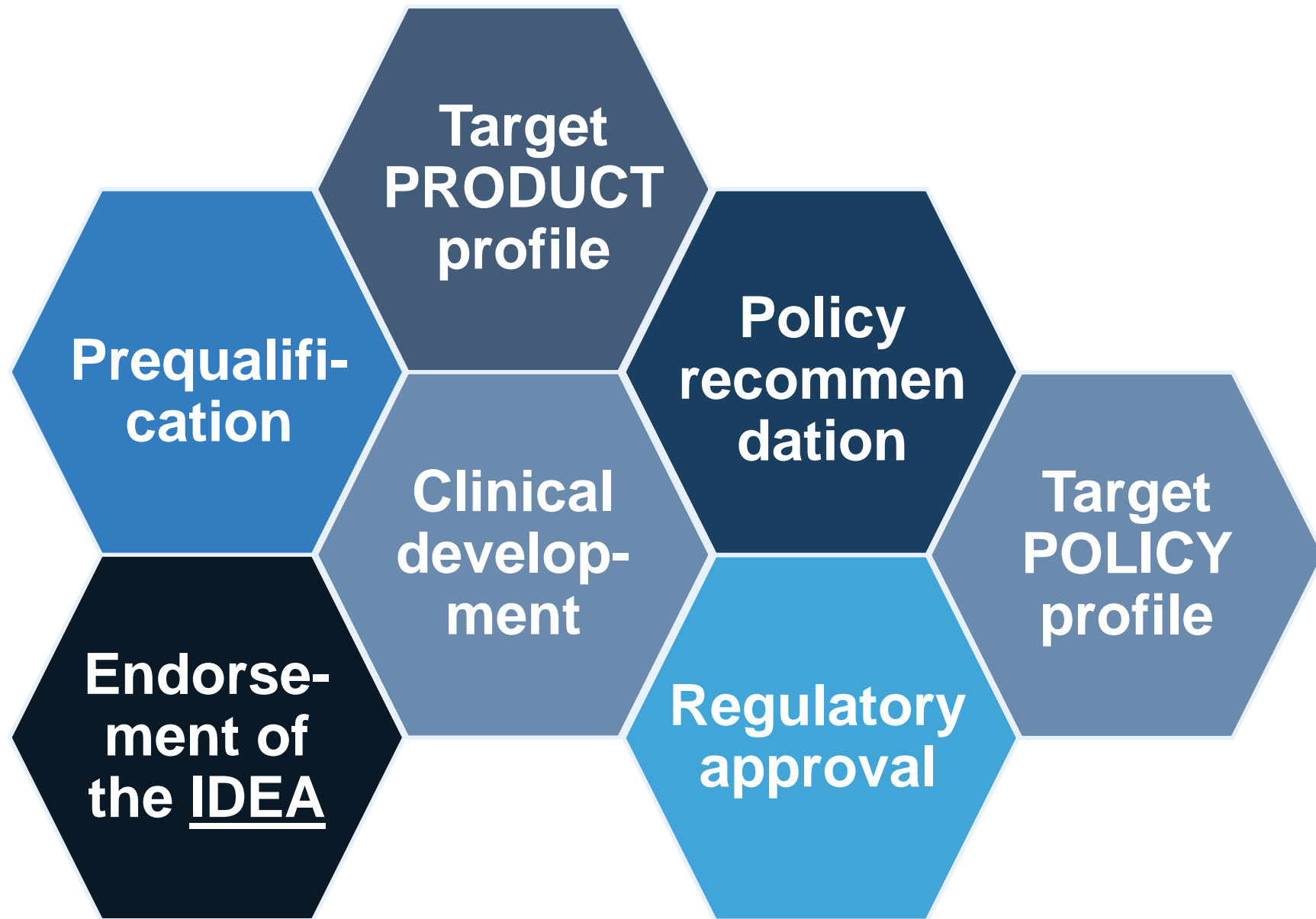
How could we use it?



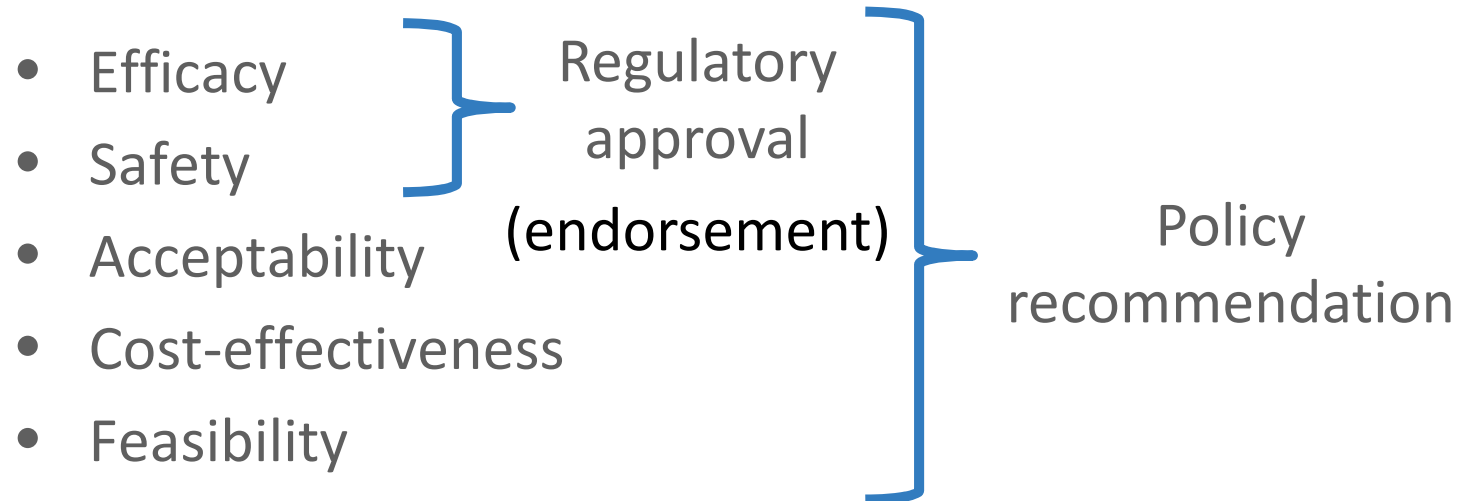
“Highlight the key linkages with policy”

- New use for malaria **would need to be** endorsed/approved
- **Gaps in the databased** identified and addressed
- New use for malaria **would need to be** recommended to NMCPs
- Need a framework to **ensure enough API is available** without affecting NTD programs
- It is **affordable** (funding source: GFATM, UNITAID, NMCPs...)





What evidence is needed?



What evidence is needed: **efficacy**

- Mosquito-killing effect
 - ✓ Insectary
 - ✓ Field
- Other effects (fertility, flying...)
- Modelling (Slater et al – JID 2014)
- Reduces malaria incidence
 - ✓ **RIMDAMAL** (Foy et al – Burkina Preliminary data **ASTMH**)
 - ✓ 150 mcg/kg every three weeks (x 6) during rainy season
 - ✓ 575 cases averted per 1000 children treated (NNT < 2)

What evidence is needed: **Safety**

- Dose & formulation
 - ✓ 150-200 mcg/kg once
 - ✓ Repeated dose
 - ✓ High dose
 - ✓ Slow release formulation
- **ACTIVE** (Burkina – Ouedraogo et al) Artemether-Lumefantrine
- **IVERMAL** (Kenia – Ter-Kuile) DHA-Piperaquine
- **NCT02568098** (Thailand - Jittamala) PQ + DHA-Piperaquine
- **The (potential) role of WHO-Prequalification**

What evidence is needed?

- Key question: **total dose and spacing?**

Data will inform whether current formulation is enough to meet the required effect

- Key question: **current vs new formulation?**

Formulation discussions need a clear definition of the desired entomological/epidemiological targets

What evidence is needed?

- **What regulatory agency?**
FDA seems receptive...
- What pathway?
 - ✓ Repurposing: 505(b)(2)

What evidence is needed: **Acceptability**

- By the population
 - ✓ “only” transmission blocking
 - ✓ Community vs individual impact
- By other programmes (NTDs)
 - ✓ Concerns regarding resistance & procurement
 - ✓ Synergies

What evidence is needed: **Cost-effectiveness**

- Current costs
 - ✓ Mectizan donation program: 1.50/ 3-mg-tablet
 - ✓ Veterinary market: 18Eu/800 mg (1 ltr)
- The role of competition
 - ✓ What is an acceptable price for vector control?
 - ✓ What is the expected annual volume?
- Procurement through GFATM
 - ✓ Pre-qualification

What evidence is needed: **Feasibility**

- Production
 - ✓ Current: 150 tons/year
 - ✓ Less than 1.5% is for human use
- Programmatic suitability
- Do we need a new formulation?

Who would need to assess the evidence?

Different perspectives

- ERG
- VCAG
- MPAC
- NTD program
- WHO-PQ

What is the way forward? (1)

- Generate evidence using current formulation
 - ✓ Different eco-epidemiological scenarios
 - ✓ **Does it really add value to the current paradigm?**
- Start conversations for endorsement of **the concept**
GMP/VCAG/MPAC
- Start conversations for regulatory approval (new indication)
Using the current formulation to generate data

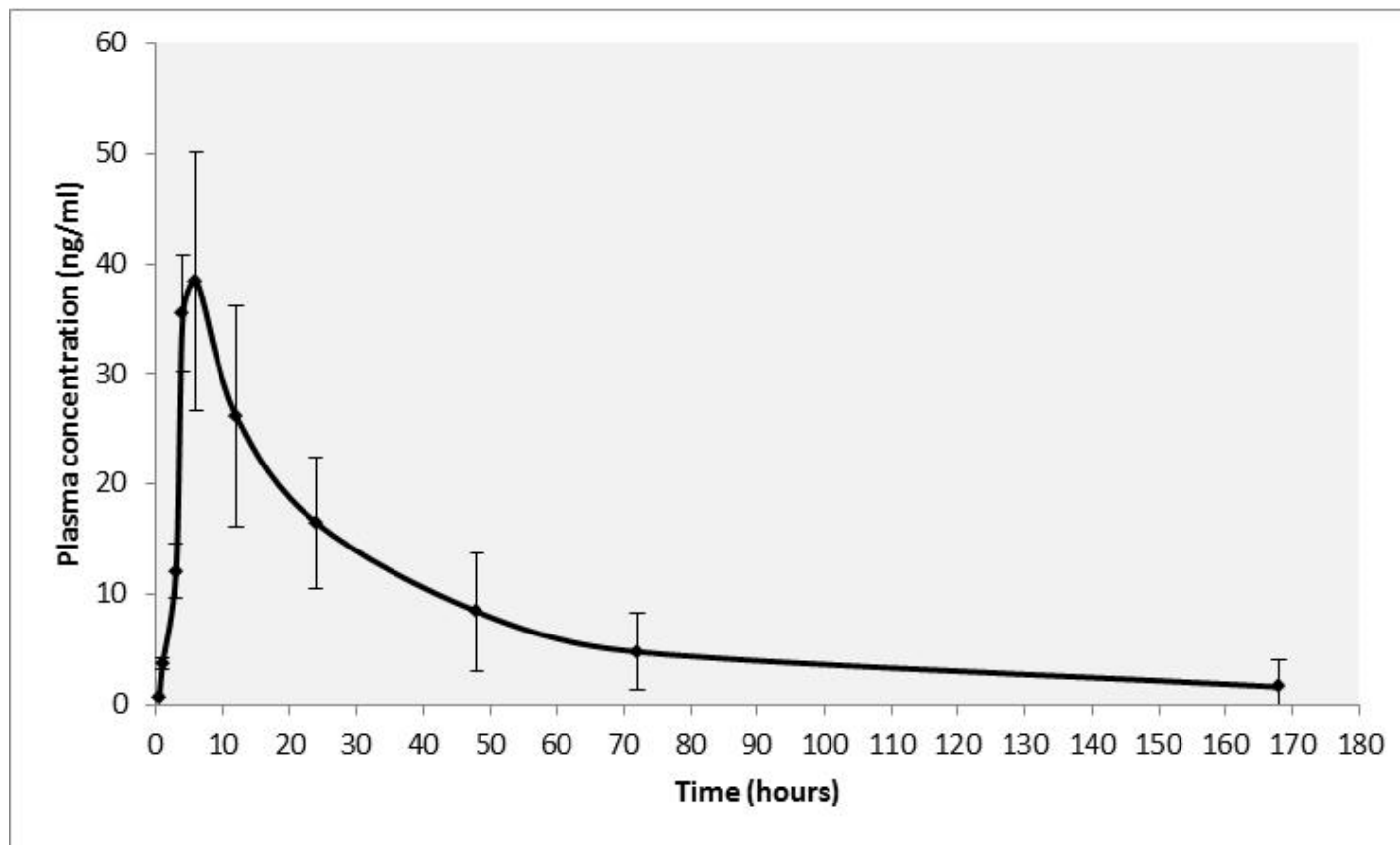
What is the way forward? (2)

- Define what MPAC and NTDs would need in order to give a recommendation
- Start pre-qualification process (>1 dossier)
 - ✓ Healthy competition (reduce prices)
 - ✓ Assure scalability



How does it work?

Second concept: how it works (PK)



How does it work?

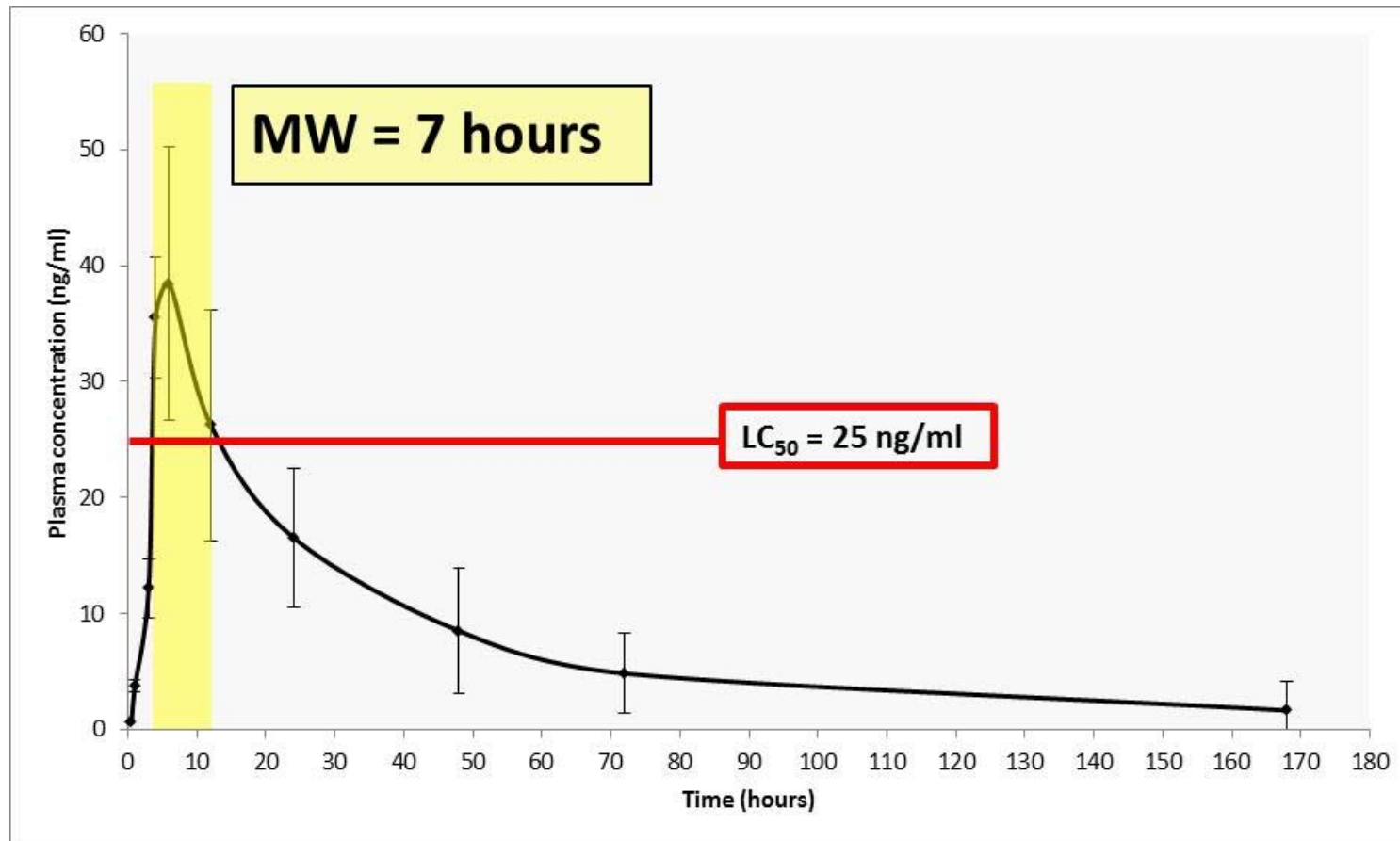
LC50

The plasma concentration needed to kill 50% of the biting *mosquitoes* in a given time

A measure of efficacy similar to the MIC₅₀ and MIC₉₀ used in microbiology

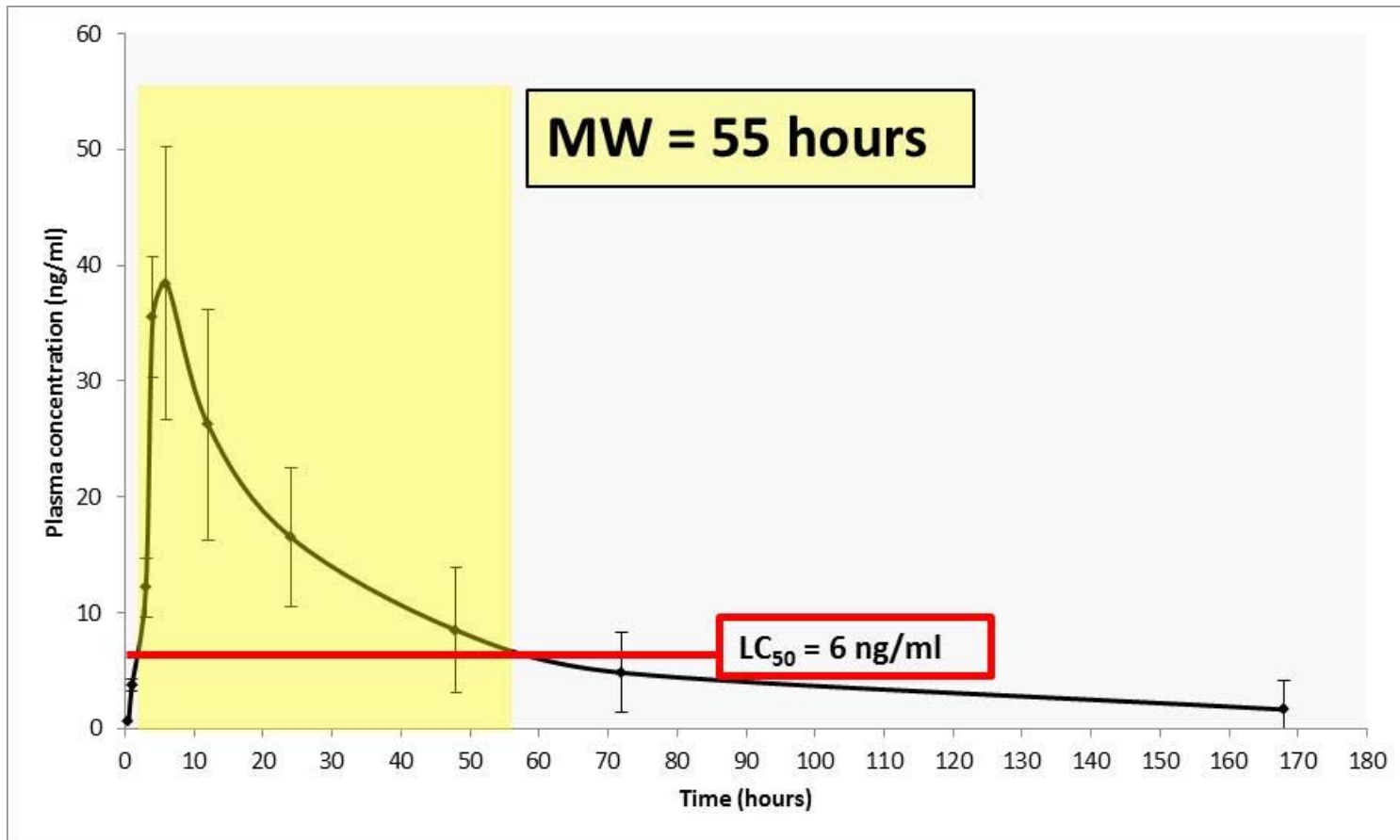


How does it work?



Kobylinski 2010

How does it work?



Quedraogo 2013

How does it work?

