GLOBAL INSTITUTE FOR DISEASE ELIMINATION

STAKEHOLDER ROUNDTABLE

MOXIDECTIN USE FOR ONCHOCERCIASIS ELIMINATION

MEETING REPORT

14 NOVEMBER 2024

HILTON RIVERSIDE, NEW ORLEANS, LA, USA

ACRONYMS

ASTMH	American Society of Tropical Medicine and Hygiene
CDDs	Community Drug Distributors
EML	Essential Medicine List
GLIDE	Global Institute for Disease Elimination
MDA	Mass Drug Administration
NOECs	National Onchocerciasis Elimination Committees
RCT	Randomized Controlled Trial
WHO	World Health Organization

CONTEXT

The last mile of disease elimination is often the most anticipated as countries approach their elimination targets. However, this phase is also the most challenging, requiring significant financial investment and carefully tailored strategies to ensure the most effective technologies and tools reach the communities that need them most. At the 2023 Reaching the Last Mile Forum, global donors announced a milestone expansion of the Reaching the Last Mile Fund (RLM Fund) from $100 million to $500 million. This landmark investment aims to bolster global efforts to eliminate onchocerciasis and lymphatic filariasis (LF) in Africa and Yemen[1]. Despite this progress, critical questions persist: how, where, and to whom should these resources be allocated to achieve maximum impact?

Recognizing the urgency of these challenges, GLIDE hosted a stakeholder engagement roundtable on November 14, 2024, on the sidelines of the American Society of Tropical Medicine and Hygiene (ASTMH) Annual Meeting in New Orleans, Louisiana, USA. The focus was on moxidectin, a promising tool for accelerating the elimination of onchocerciasis.

The objectives of the roundtable included to:

- Explore and raise awareness of moxidectin's role as an additional tool for elimination;
- Examine the conditions necessary for its adoption, barriers to implementation, and potential solutions;
- Engage stakeholders in discussions on investment opportunities to support onchocerciasis elimination.

Participants and format of the roundtable:

The roundtable brought together 24 strategically selected participants, representing diverse sectors including NGOs, academia, funding agencies, implementation organizations, and national programs. This diversity ensured meaningful and strategic engagement. This roundtable provided a platform for in-depth discussions and actionable recommendations on leveraging moxidectin as a complementary tool to accelerate onchocerciasis elimination.

The 90-minute session began with a presentation by the co-hosts, setting the stage for an interactive discussion structured around guiding questions (see Appendix for the event agenda). These questions, collaboratively developed by GLIDE and the co-hosts, aimed to foster targeted and solution-oriented dialogue.

> *"There has only been one tool for 30 years, [...] we have to see how other tools can be involved"*

1 Pledge RLMF 2023

The guiding questions for this session were as follows:

[For all stakeholders]

- Where would moxidectin be helpful to accelerate achieving the elimination goals for your country or the countries you support?
- At what scale do you anticipate using it?
- What are the necessary elements to enabling moxidectin adoption?
- What are the potential barriers?
- What would be needed to address these?

[For country representatives]:

- How can moxidectin be effectively integrated into national strategic plans?
- How soon could that happen?

[For implementing partners]:

- How do you envisage supporting countries with the introduction of moxidectin?

Key insights from the roundtable discussion:

Where would moxidectin be helpful to accelerate elimination goals?

Participants identified specific contexts where moxidectin could have significant impact, the main scenarios were:

1. **High-transmission hotspots:** These are areas where persistent transmission continues despite high ivermectin coverage. In such contexts, annual mass drug administration (MDA) with ivermectin has proven insufficient. While biannual MDA with ivermectin could be considered, this approach would increase implementation costs. Modeled impact projections, from the NTD Modeling Consortium, suggest that annual moxidectin administration is broadly as effective as biannual ivermectin in reducing program duration, presenting a feasible and potentially cost-effective alternative for these focal hotspots[2,3,4]. Participants emphasized that moxidectin could play a critical role as a last-mile tool in such areas.
2. **Targeted populations:** Moxidectin could also be prioritized for ivermectin-naïve populations or marginalized groups, including refugees, mobile populations, and those in hard-to-reach areas. These populations often miss MDAs more frequently, serving as reservoirs of transmission. The longer-lasting effect of moxidectin reduces risk of transmission in a shorter period with annual MDA, making it operationally and logistically advantageous for these high-cost, hard-to-serve areas. An illustrative example provided was the Yanomami indigenous population in the Amazon rainforest on the border of Brazil and Venezuela, where onchocerciasis transmission persists due to geographic inaccessibility and the nomadic lifestyle of the community[5]. In this setting in particular, treatment frequency could be decreased from 4 times a year and have potential cost savings.
3. **Areas with reliable coverage data:** In addition, moxidectin could be particularly successful in areas where reliable coverage data is available, ensuring informed decision-making and programmatic success. Participants emphasized the importance of accurate and up-to-date data in planning interventions, citing examples where insufficient data has undermined the introduction

2 The potential impact of moxidectin on onchocerciasis elimination in Africa: an economic evaluation based on the Phase II clinical trial data
3 Can mass drug administration of moxidectin accelerate onchocerciasis elimination in Africa?
4 The potential impact of moxidectin on onchocerciasis elimination in Africa: an economic evaluation based on the Phase II clinical trial data
5 Onchocerciasis: The last Challenge - PAHO/WHO

of new tools. For instance, lessons from the LF program highlight the risks of deploying a new therapy such as the IDA (ivermectin, diethylcarbamazine, and albendazole, or IDA) triple therapy before achieving expected high coverage rates. These insights underscore the value of robust programmatic readiness in areas with high endemicity and reliable high coverage.

> *"Moxidectin can carve out a niche in focal hotspots rather than replacing ivermectin entirely."*

At what scale do you anticipate using it?

Participants proposed starting with pilot implementations to test feasibility, effectiveness, and community acceptance before scaling up. The consensus was that clearly defined criteria and use cases are necessary to establish a structured rollout plan. Without identifying target locations and contexts, progress would remain stalled. To accompany this statement, participants pointed to two planned pilot programs using moxidectin in mass drug administration (MDA) settings in Africa as key examples:

- A randomized controlled trial (RCT) in Angola, which will feature two arms—one using moxidectin and the other ivermectin for MDA[6].
- A programmatic rollout in Ghana, the first onchocerciasis-endemic country to recently grant regulatory approval for moxidectin[7].

These pilots will be pivotal, offering the first data on moxidectin's programmatic use. Such studies are critical, as current data gaps hinder efforts to model and optimize use cases. Discussions also emphasized the importance of coverage surveys to inform pilot site selection. Participants debated whether coverage requirements for moxidectin align with those for ivermectin and stressed the need to establish clear thresholds for the use of moxidectin.

What are the necessary elements for enabling moxidectin adoption?

Participants emphasized that the successful adoption of moxidectin will depend on addressing several critical factors to ensure programmatic effectiveness. Stakeholders stressed the importance of building a solid foundation that encompasses accurate data, strategic guidance, financial planning, and operational capacity. These elements are essential to laying a strong foundation for integrating moxidectin as a complementary tool in onchocerciasis elimination efforts. The discussions reinforced several key enablers:

1. **Accurate data:** Reliable data on coverage and endemicity is essential for defining thresholds for moxidectin use. High coverage rates are crucial for success. Participants noted that while some implementation units report ivermectin coverage rates above the 80% threshold, actual coverage can fall as low as 30-40% because of low program performance. Introducing a new drug without addressing these gaps could undermine its impact.

> *"New drugs can't solve a coverage issue"*

2. **Addressing epidemiological barriers and knowledge gaps:** There is limited knowledge regarding moxidectin's interaction in areas co-endemic with Loa loa, particularly among individuals with high Loa loa microfilarial densities, where adverse effects may pose significant challenges. Furthermore, although moxidectin has received regulatory approval for the treatment of onchocerciasis in individuals aged 12 years and older, clinical studies assessing its efficacy and safety in younger populations (e.g., children aged 4–11 years) remain incomplete. Lastly, field trials are needed to better characterize the community acceptability as well as patterns of intra- and inter-individual variation in treatment responses over multiple rounds of moxidectin mass drug administration.

6 A randomized controlled trial in Angola
7 Community pilot treatment implementation program

3. **WHO guidance:** Field data from pilot studies will provide critical evidence for the feasibility of moxidectin's programmatic use. While scientific and modeling data strongly demonstrate greater potency compared to ivermectin, stakeholders emphasized the need for World Health Organization's (WHO) recommendation. Such a recommendation will be essential to facilitate regulatory approvals and the integration of moxidectin into national programs.
4. **Cost modeling:** Participants called for detailed cost-effectiveness studies to justify the higher initial costs. Currently, the estimated price of procuring moxidectin tablets represents a significant portion of last-mile budgets, underscoring the need for economic analysis to ensure sustainability.
5. **Capacity building:** It was also stressed that training for health workers and community drug distributors (CDDs) will be crucial. This includes training on the delivery of moxidectin doses.
6. **Learnings from other programs**. Participants suggested drawing lessons from the IDA rollout for LF to better understand the introduction process[8]. These insights could inform strategies for rolling out moxidectin, avoiding potential pitfalls, and streamlining implementation.

What are the potential barriers? What would be needed to address these?

The discussion identified several barriers to moxidectin adoption, many of which mirrored the enablers but highlighted critical gaps that go beyond technical and operational challenges:

1. **Challenges of transitioning to a new product:** The introduction of moxidectin as a non-donated product represents a significant shift in the current paradigm. Unlike ivermectin, which has been donated by Merck through Mectizan Donation Program since 1987, moxidectin requires countries to adopt a procurement model. This shift from the established donation framework raises questions of affordability and sustainability. Participants noted the urgent need to rethink the current "business-as-usual" approach to drug distribution in onchocerciasis elimination and explore alternative models that can sustain long-term use of moxidectin.
2. **Lack of demand visibility:** Another barrier is the uncertainty around demand for moxidectin. Producing a drug requires significant lead time and potentially investment in equipment, and the absence of clear, quantified demand makes it challenging for manufacturers to plan production, ensure sufficient stock, and provide accurate pricing as cost of production is volume dependent. Like all medications, moxidectin has a limited shelf life, making accurate forecasting is essential to avoid waste and ensure availability. Countries' hesitancy to express interest in moxidectin further exacerbates this uncertainty, creating a cycle of hesitation on both supply and demand sides.

How can moxidectin be effectively integrated into national strategic plans? How soon will this happen?

This question is crucial, but discussions revealed that there is still a significant journey ahead before moxidectin can be widely integrated into national plans. Several factors need to be addressed to pave the way for its adoption:

1. **There is a need for an endorsement by WHO:** Participants emphasized that many countries are unlikely to include moxidectin in their national strategies without a formal endorsement from WHO. The treatment guideline development process has been triggered and will review all the latest clinical data as well as the implementation data collected in the pilot projects.
2. **There is still uncertainty of adoption timelines:** The process of integrating moxidectin into national plans is like a "chicken-and-egg" situation. Countries hesitate to adopt the drug without WHO's guidance, but WHO's endorsement depends on comprehensive data. Participants noted that while moxidectin has already been recognized by WHO as a potential tool and is expected to be included in the updated Essential Medicines List (EML), significant gaps (such as funding, support of implementing partners) remain.
3. **There needs to be a clearly articulated vision for future procurement models:** Countries require

8 Accelerating the uptake of WHO recommendations for mass drug administration using ivermectin, diethylcarbamazine, and albendazole

clarity on drug price and the procurement models that will replace the donation process. Without this understanding, governments will remain hesitant to commit to integrating moxidectin into their strategies.

From the discussions, it emerged that unless these key issues are adequately addressed, the adoption of moxidectin into national strategic plans may face significant delays.

RECOMMENDATIONS AND NEXT STEPS

To effectively advance the adoption and integration of moxidectin, participants emphasized the need for a multifaceted approach. Key actions should focus on generating robust evidence, identifying strategic pilot sites, and addressing operational and logistical challenges. These efforts aim to build confidence in moxidectin's feasibility and impact while setting the stage for broader implementation. Key recommendations include:

1. **Generate evidence:** Continue generating evidence on cost-effectiveness and operational feasibility, and programmatic outcomes to support WHO recommendations and guide decision-making.
2. **Pilot rollouts:** Identify and expand pilot programs in sites where National Onchocerciasis Elimination Committees (NOECs) already recommend biannual ivermectin, using these locations to evaluate moxidectin's potential as a substitute or complement.
3. **Focus on high-cost areas:** Prioritize high-cost and hard-to-reach areas where moxidectin's extended treatment interval could reduce operational and logistical expenses.
4. **Develop the supply and procurement mechanisms** where countries and partners can access drug information, pricing, and delivery timelines for planning and inclusion in national strategic plans.
5. **Demand planning and system readiness:** Develop a clear strategy to quantify and communicate demand, ensuring adequate production and supply planning.
6. **Monitor and evaluate success:** Establish robust monitoring and evaluation frameworks to assess moxidectin's impact on transmission and elimination progress.

CONCLUSION

The roundtable underscored the critical role moxidectin could play in accelerating onchocerciasis elimination. However, stakeholders acknowledged the complexities of transitioning to a new tool, from addressing cost barriers to ensuring operational readiness. While significant challenges remain, the shared commitment among participants to generate evidence, pilot innovative strategies, and foster collaboration offers a promising path forward. Identifying high priority use cases can help define demand and supply planning. Securing funding to support the early implementation of moxidectin would help gather real-world data and experience, driving further investment and ensuring its sustained availability. With these efforts, moxidectin can become an integral component in the global onchocerciasis elimination efforts.

APPENDIX

Agenda

Presentation	Objective	Time
Opening	Welcome participants, outline the objectives of the roundtable, and set the tone for collaborative discussion.	5 min
Overview of the context	Moxidectin development update, policy initiatives, and introduction strategy.	20 min
Discussion with all participants Open the floor for an interactive discussion with participants	Potential guiding questions will include: [For all partners] • Where would moxidectin be helpful to accelerate achieving the elimination goals for your country or the countries you support? • At what scale do you anticipate using it? • What are the necessary elements to enabling moxidectin adoption? • What are the potential barriers? • What would be needed to address these? [For country representatives]: • How can moxidectin be effectively integrated into national strategic plans? • How soon could that happen? [For implementing partners] • How do you envisage supporting countries with the introduction of moxidectin?	50 min
Wrap-up and Next steps	Summarize key takeaways from the discussion and outline the next steps for advancing moxidectin's role in onchocerciasis elimination. This could include action points, commitments from stakeholders, or potential partnerships	10 min
Closing		5 min

List of Participants

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Bridges to Development
Bruyère Health Research Institute
Centre de Recherche en Maladies Tropicales (CMRT)
Gates Foundation
Ghana Health Service
Global Institute for Disease Elimination (GLIDE)
Health & Development International
Higher Institute for Scientific and Medical Research
Imperial College London
Medicine Development for Global Health
MMGH Consulting Gmbh
Sightsavers
Task Force for Global Health
The Carter Center
The END Fund
The Kirby Institute, UNSW Sydney
USAID