GAP·f
Global Accelerator for Paediatric formulations
WHO Hosted Network

World Health Organization

Paediatric drug optimization for neglected tropical diseases

Meeting report, September 2023

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The need for paediatric drug optimization (PADO)

The development of medicines for children lags unacceptably behind that for adults by nearly a decade *(1)*. Following the resolution at the Sixty-ninth World Health Assembly on promoting innovation and access to quality, safe, efficacious and affordable medicines for children, the World Health Organization (WHO) and partners have increased their efforts to deliver on this global commitment and have scaled up activities to ensure that age-appropriate formulations are available for children *(2)*.

The Global Accelerator for Paediatric Formulations Network (GAP-f), a WHO-hosted network, works across the life cycle of drug development to accelerate the investigation, development and introduction of optimal formulations for children *(3)*. Priority-setting is the first step to enable a targeted approach to research and development. Developing a priority drug portfolio of the most needed formulations for children is essential to streamline researchers' and supplier's efforts as well as resources around specific dosage forms and formulations that address most urgent needs for children. This is particularly important given that the market for medicines for children is often small and/or fragmented, resulting in limited volumes with potential market failures.

Paediatric drug optimization (PADO) exercises to identify key priority products and their preferred product characteristics for research and development have been successfully undertaken for human immunodeficiency virus (HIV), hepatitis C and tuberculosis, demonstrating their potential and impact to accelerate access to optimal formulations in the context of fragmented, small markets for medicines for children. To provide further guidance to support similar processes for optimizing drugs for children in other disease areas, GAP-f has published a guidance document to undertake a PADO process and adapt it to the specific needs of each disease area *(4)*.

PADO for neglected tropical diseases (NTDs)

In general, due to limited financial incentives, few new drugs are being developed for neglected tropical diseases (NTDs).

Several NTDs disproportionately affect children versus adults and, as for most diseases affecting adults and children, the burden to children is compounded by lack of inclusion of children in clinical trials and/or lack of age-appropriate dosing regimens and formulations *(5)*. There is a severe lack of pharmacokinetic (PK) data for NTD medicines which is required for optimizing doses for children: indeed, only 11% of PK studies for NTD medicines included children, and for most medicines, PK data are not available *(6)*. Research conducted in 2022 showed that, overall, less than half of WHO-recommended medicines for NTDs are approved for children, highlighting the urgent need to increase research activity for NTDs for children, giving priority to diseases that represent a significant burden and lack adequate treatment options *(7)*.

NTDs are a diverse group of infectious diseases that differ in epidemiology, local burdens, WHO control and elimination strategies *(8)* and challenges in terms of availability of paediatric formulations. Since, except for some overlap, each NTD has a specific network of experts and institutions, the PADO for NTDs process comprised specific virtual meetings for priority diseases identified by WHO technical leads and GAP-f.

WHO technical leads and GAP-f gave priority to the following NTDs for the first PADO exercise (PADO founding meeting), based on considerations around disease burden, ongoing research and development efforts, preliminary assessments of the pipeline and knowledge of specific gaps and issues that hinder access to appropriate treatment for children:

- schistosomiasis
- human African trypanosomiasis (HAT)
- scabies and onchocerciasis
- visceral leishmaniasis (VL).

Objectives

The purpose of the four PADO meetings for NTDs was:

- to review drugs and formulations currently recommended by WHO for schistosomiasis, HAT, scabies and onchocerciasis and VL and evaluate their age-appropriateness for children given available evidence;
- to review ongoing studies and efforts to develop paediatric formulations in the four disease areas;
- to review current (and foreseen) market, procurement, access and implementation challenges with a disease-specific lens but also across diseases when drugs are used across diseases; and
- to review the clinical pipeline of agents.

More specifically, the goal of the PADO for NTDs exercise was to develop:

- a PADO priority list – including formulations of NTD medicines to be investigated and developed with a time horizon of 3–5 years;
- a PADO watch list – containing promising NTD candidates for investigation and development for children with a time horizon of 5–10 years; and
- a clear research agenda to support and enable future optimization work, with the goal of ensuring that the unique needs of children are effectively addressed.

Methods

Meeting proceedings

The disease-specific meetings were held over nine months from October 2022 to June 2023, in particular:

- schistosomiasis: 17 October 2022
- HAT: 2 December 2022
- scabies and onchocerciasis: 18–19 April 2023
- VL: 7–8 June 2023.

The PADO for NTDs exercise concluded with a final meeting held on 15 September 2023 with representatives from the four priority disease areas to reach consensus on a final PADO-NTD priority list, watch list and research questions and discuss transversal issues for the way forward.

These meetings brought together academic researchers, clinical experts, product development partnerships, programme managers and other key stakeholders involved in research and development and in initiatives streamlining access to paediatric medicines. Conflict-of-interest declarations were collected for all participants and closely reviewed. Participants with relevant conflicts were asked to participate as observers or resource people.

Available resources published by WHO for managing NTDs in children were reviewed. They included: the WHO Model List of Essential Medicines for Children *(9)*, the 2021–2030 Roadmap for neglected tropical diseases: ending the neglect to attain the Sustainable Development Goals *(8)*, WHO guidelines and management guidance for the NTDs. Other resources published or shared by other stakeholders were also reviewed and are indicated in the disease-specific sections of this report. Updates obtained following disease-specific discussions were considered when finalizing the outcomes of the exercise during the final meeting. Input from meeting participants has been sought for some of the PADO for NTDs meetings on specific aspects and is available in the specific sections below. When deemed necessary, consensus on priority medicines to be further investigated and/or developed for infants, children and adolescents was reached through working group discussions informed by pre-populated frameworks.

Annex 1 has the detailed agenda and Annex 2 has lists of participants of each PADO for NTDs exercise.

PADO for schistosomiasis

Background

Schistosomiasis is a parasitic disease prevalent in tropical and subtropical areas, caused by six species of trematodes of the genus *Schistosoma*. Infection occurs when cercariae penetrate human skin during contact with fresh water contaminated with human excreta containing parasite eggs. Globally, 240 million people in 51 countries (of the 78 where schistosomiasis is endemic) require preventive chemotherapy (mass drug administration (MDA)) for schistosomiasis, of which 90% are in the WHO African Region *(10)*.

The new NTD roadmap 2021–2030 specifically targets the elimination of schistosomiasis as a public health problem, globally *(8)*. WHO has recognized morbidity from schistosomiasis among preschool-age children (PSAC) and has recommended treating and including them in preventive chemotherapy with age-appropriate formulations of praziquantel, the only medicine available for schistosomiasis. An estimated 50 to 60 million PSAC require praziquantel preventive chemotherapy annually *(11,12)*.

PSAC living in high schistosomiasis-endemic areas have levels of infection comparable to school-age children; prevalence of infection exceeding 50% and severe morbidity have been documented in this younger age group. Early signs of morbidity due to schistosomiasis are dysuria and macrohaematuria, abdominal pain, blood in faeces and diarrhoea. Schistosomiasis among PSAC is also associated with anaemia, hepatomegaly and fibrosis, bladder abnormalities and other urinary tract lesions associated with urogenital schistosomiasis among young children.

The 2022 WHO schistosomiasis guidelines recommend annual preventive chemotherapy with a single dose of praziquantel (40–60 mg/kg) in endemic communities with prevalence of *Schistosoma* spp. infection ≥10% for all age groups from two years old *(13)*. WHO also recommends that health facilities provide access to treatment with praziquantel to control morbidity from schistosomiasis among all individuals with schistosomiasis regardless of age, including PSAC younger than two years (40 mg/kg, single dose). The decision to administer treatment to children younger than two years should be based on testing and clinical judgement. In the absence of a paediatric formulation of praziquantel, countries have been implementing this second recommendation by manipulating the available formulations and administering them upon crushing and dispersing in soft food or liquids.

To achieve the goals outlined in the 2021–2030 NTD roadmap, there is a global call to ensure access to paediatric praziquantel once available and to expand preventive chemotherapy to all at-risk groups.

Currently available formulations of praziquantel include a 600 mg tablet from several manufacturers, including two manufacturers prequalified by WHO. These tablets have one to three functional scoring lines, enabling dose increments of 150 mg or 300 mg. The formulation of praziquantel included in the WHO donation programme for schistosomiasis has one functional scoring line, and the manufacturer has committed 250 million tablets per year. This amount covers about half of the needs of praziquantel globally, and the other half is supposed to be procured by national control programmes as well as partners.

PADO priority list

The Paediatric Praziquantel Consortium developed a 150 mg orodispersible tablet (ODT) of L-praziquantel and is expected to receive regulatory approval in 2023 for children aged three months up to six years, but no donation programme will be available for this formulation. This formulation will cover the needs for younger children for preventive chemotherapy and for treatment, therefore it was added to the PADO priority list since. Its clinical development programme is well underway and provides the fastest route to a child-friendly formulation of praziquantel to be rolled-out by country programmes.

An additional formulation of praziquantel – L-praziquantel 300 mg scored ODT – was included in the PADO priority list for schistosomiasis. This formulation was added to reduce pill burden and improve acceptability while accounting for the minimum dose requirement of 300 mg (a 15 kg child will need five 150 mg ODTs for MDA). The priority formulation includes a functional scoring line to enhance dose flexibility for the MDA for schistosomiasis indication (a 10-kg child would need 500–600 mg, corresponding to 1.5–2 tablets), but also considering that this formulation could be used for other indications (such as taeniasis), which may require a 150mg dose increment. Although giving priority to a racemic formulation of a 300 mg scored ODT would facilitate the manufacturing process, potentially reducing the costs, issues have been noted with the dissolution of the racemic mixture versus the L-enantiomer. Although dextro-praziquantel is not active against schistosome species, the racemic mixture has also a more bitter taste than the isolated L-enantiomer.

PADO for schistosomiasis Priority list	
L-praziquantel	150 mg ODT
L-praziquantel	300 mg scored ODT[a]

[a]Pending confirmation of chemistry, manufacturing and controls feasibility.

The group also noted that discussions around optimizing formulations and harmonizing the dosage forms used across age groups (adults and children) and indications would be advisable and should be looked at proactively in the future to avoid market fragmentation and consolidate demand. These considerations should include praziquantel also being used for other indications, including at different doses (such as a 10 mg/kg single dose for taeniasis) and the fact that L-praziquantel is currently being investigated at half dose (compared with what is currently used). If these studies (expected to be completed in 5–6 years) are successful, this may affect the priority formulation to develop for market consolidation. These studies will be closely monitored in the future.

PADO watch list

Forty years after praziquantel was approved as an anthelmintic drug, the pipeline for new schistosomiasis therapeutics is nearly empty, and no other therapeutic alternative has been registered. Even though resistance to praziquantel has not been documented so far, many call for the development of new therapeutic interventions while efforts to improve morbidity control and increase coverage and treatment frequency will inevitably increase the drug pressure, with the risk of selecting and spreading praziquantel-resistant parasites in the future *(14)*.

Some compounds are currently being investigated for schistosomiasis, but they are still in the early stages of development, and thus not enough information is available to indicate whether they are promising for development in children. These compounds will be closely monitored and reviewed once enough information for adults is available (after Phase 1 studies). A preliminary target product profile for medicines against schistosomiasis has also been developed, which will require additional input from the community to define suitable criteria for new treatment *(15)*. Establishing the effectiveness of any new drug on schistosomulae and new infection symptoms should also be considered early on in the development process.

Research priorities

- Study the safety and efficacy of L-praziquantel at half dose compared to the currently recommended one (ongoing).
- Conduct feasibility studies for developing a 300 mg scored ODT formulation of L-praziquantel.
- Investigate the development and feasibility of a racemate of paediatric praziquantel to optimize the cost of the final product.
- Conduct efficacy, safety and acceptability studies with L-praziquantel 150 mg ODT in multiple country contexts, with different endemicity levels and different *Schistosoma* species (partly ongoing).

Considerations on access

With the new paediatric formulation of praziquantel soon becoming available, thinking through the financing and procurement mechanism to accelerate access to the new formulation is imperative.

Whereas pharmaceutical companies donate other NTD medicines through WHO, this new formulation of praziquantel (150 mg ODT) will not be donated and must be procured by countries or partners. Ideally, with a global financing mechanism (funded by donors), countries should access this product for free.

The Pediatric Praziquantel Consortium established the ADOPT programme to identify platforms and approaches for access and delivery and conduct implementation research programmes in three pilot countries (early adopters) to prepare for larger-scale introduction of paediatric praziquantel. As part of this work, engagement with local stakeholders to support policy updates and create demand is being given priority and not-for-profit access models are being explored, including direct procurement by countries, donor-based procurement on behalf of countries and integration in existing children's health programmes.

The establishment of an efficient, coordinated mechanism for procurement will be essential in managing the supply and demand not only for praziquantel but for other NTD products becoming available in the near future.

Moving forward, the group agreed on the following priorities.

- To determine the manufacturing capacity and the need for other generic manufacturers, reliable demand forecasts are needed from countries. Economy of scale can lower the manufacturing cost.
- To identify the most feasible approaches to procurement, options for various procurement models and mechanisms need to be comprehensively analysed, building on experiences from other diseases. The options analysis should carefully look at the operational cost too (how efficient, sustainable and feasible each option will be for countries and manufacturers).
- Options analysis can be taken forward under the leadership of the Working Group on Access of the Strategic and Technical Advisory Group for NTDs with support from other partners and experts.

In general, the group indicated the need for a paradigm shift for procuring medicines for NTDs beyond paediatric praziquantel to ensure procurement sustainability. So far, WHO has coordinated the supply of donated NTD medicines to countries. Participants noted that, in the future, regardless of potential new procurement mechanisms that will be set up, coordinating oversight from agencies such as WHO will be advisable. Finally, it will be important to ensure that any emerging initiative in this area of work builds on and coordinates with the work that other partners will have already done.

PADO for human African trypanosomiasis (HAT)

Background

HAT is transmitted by the bite of a tsetse fly and is a lethal disease if left untreated. The disease has two forms: the chronic form (gambiense HAT), caused by infection with *Trypanosoma brucei gambiense*, found in western and central Africa (93% of the cases in the period between 2018 and 2023); and the acute form (rhodesiense HAT), caused by infection with *T. b. rhodesiense*, in eastern and southern Africa (responsible for the remainder of cases). Only Uganda is affected by both forms of the disease. All age groups and both sexes are at risk of both forms of HAT, although the prevalence is higher for adults than for children.

An estimated 24% of the people diagnosed with gambiense HAT are children and young adolescents younger than 15 years (with 4% younger than five years and 19% 5–14 years old), but with important variation in different settings and highly depending on exposure to tsetse flies. Since, in the general population in sub-Saharan Africa, children and young adolescents younger than 15 years represent 45% of the population (15% younger than five years, 30% 5–14 years old) *(16)*, the infection rate in this subgroup is lower than in adults. This can be explained by a lower exposure to tsetse bites, by the long incubation period up to several years and possibly by differences in health-seeking behaviour. Gambiense HAT can be vertically transmitted, meaning that newborns can also be infected.

For rhodesiense HAT, about 16% of all people diagnosed were reported to be younger than 15 years in Malawi (2012–2021).

In general, the incidence of the disease is declining in response to intensive surveillance and control in endemic areas. As a result, HAT is among the NTDs targeted by WHO for elimination. WHO maintains exhaustive records of all declared cases; since 2018, a historically low number of cases (<1000) has been reported.

The 2019 WHO interim guidelines for gambiense HAT recommend treatment with fexinidazole for everyone six years and older and weighing 20 kg or more with low index of suspicion of severe disease based on clinical judgement and high confidence that the person will have appropriate follow-up to detect relapse early. For people for whom severe HAT is suspected, lumbar puncture is required to decide between administration of fexinidazole or nifurtimox–eflornithine combination therapy (NECT) *(17)*. For children younger than six years or weighing less than 20 kg, pentamidine should be used in first-stage disease and NECT in second-stage disease. A recently completed study (clinicaltrials.gov ID: NCT03974178) explored the use of fexinidazole for rhodesiense HAT, for which WHO currently recommends the use of suramin (intravenous (IV) injection) for first-stage disease and melarsoprol (IV injection) for second-stage disease.

All drugs for HAT are available thanks to donations from manufacturers to WHO under specific agreements that are renewed every five years. WHO estimates the future needs to cover everyone with HAT and works with manufacturers to forecast the production needs with sufficient advance.

Challenges with current treatments

Most medicines for HAT are old, often toxic and with complex, painful IV administration required, which is especially problematic for children (NECT and eflornithine as monotherapy require IV cannulation for seven and 14 days, respectively). This is problematic also since people with HAT are often treated in rural hospitals. Both treatments for rhodesiense HAT (melarsoprol and suramin) are very toxic. They are administered IV, and suramin powder needs to be reconstituted. Doses for children are empirical (not based on studies including children) and are weight-based, with the risk of overdose or underdose. These challenges have been accepted so far because of the benefit–risk ratio, since HAT is often a lethal disease without treatment.

Nifurtimox is an oral medicine available as 120 mg functionally scored tablets, which may be broken to obtain the WHO-recommended dose of 5 mg/kg every eight hours (15 mg/kg daily dose). Tablets can also be cut, crushed and diluted with food or water with sugar to facilitate their intake. However, the dosing of nifurtimox is quite complex and requires administration of ½, ¾ or ¼ fractions of the 120 mg tablets, requiring a pill cutter and risk of dosing errors. A lower-strength formulation (30 mg scored tablets) is available in some markets, but it is not part of the NECT kit donated by manufacturers and distributed by WHO free of charge to countries for gambiense HAT.

Oral fexinidazole was introduced in 2019 but is only indicated for children older than six years or weighing more than 20 kg with gambiense HAT *(18)*. It must be taken with food, once daily for 10 days, with a loading dose over the first four days and a maintenance dose over the last six days and doses depending on the body weight (20–34 kg: 1200 mg (two 600 mg tablets) for four days; 600 mg (one 600 mg tablet) for six days; ≥35 kg: 1800 mg (three 600 mg tablets) for four days; 1200 mg (two 600 mg tablets) for six days). For children, fexinidazole provokes very frequent nausea and vomiting (69%).

PADO priority list

Fexinidazole tablets (600 mg) should not be broken or crushed (must be swallowed whole), since the impact on bioavailability is unknown. Most children in trials or programmatic settings have not reported specific acceptability issues, and a more suitable formulation for younger children was therefore not deemed necessary. This was confirmed after considering the anticipated small market and ongoing development of acoziborole, including for younger children.

Acoziborole is a new, oral benzoxaborole-6-carboxamide that has been studied in a Phase 2/3 trial assessing efficacy, safety and tolerability among adults and adolescents (>15 years old) with gambiense HAT and demonstrated high efficacy and good safety at all stages of disease, removing the need for routine lumbar puncture for most people at diagnosis. The fact that acoziborole is a single oral dose makes it also more accessible to people living in remote areas without easy access to health care. In parallel, the clinical trial for children with gambiense HAT was initiated, with the trial population including children and adolescents 1–14 years old *(19)*. This trial is divided into three steps. The first step of the trial conducted among children weighing 30–40 kg dosed with two 320 mg tablets confirmed the population PK modelling and the good safety profile of acoziborole. Considering the good PK profile and clinical data, the dose regimen could be adapted for people weighing 20.0–29.9 kg (640 mg instead of 480 mg) as a step 2 of this trial while work on a specific formulation for children (granules) has continued for children 1–6 years old, step 3 of this trial. In parallel, 320 mg tablets for adults have been proposed to resume step 2 so that the clinical trial is not delayed. As soon as the paediatric formulation is available, step 3 will include children 1–14 years old dosed with this formulation. The paediatric formulation used in this trial is expected to be 320 mg granules.

Feasibility studies on mini-tablets are being undertaken in parallel with an industrial partner as a contingency plan. Approval for acoziborole for adults with gambiense HAT is expected in the second quarter of 2026 versus the third or fourth quarter of 2027 for children 1–14 years old with gambiense HAT.

Acoziborole was added to the PADO priority list, noting that accelerating its paediatric development plans (including formulation development) is a priority.

PADO for HAT Priority list	
Acoziborole	320 mg paediatric oral dosage form *(to be confirmed)*

Research priorities

Since acoziborole is currently being developed (including plans for paediatric development), and since, based on available data, it is expected to be superior to fexinidazole in efficacy and safety, studying fexinidazole among children younger than six years for gambiense was not considered a research priority.

For rhodesiense HAT, it was noted that current treatments are extremely toxic and that the production of melarsoprol would be discontinued in the near future, leaving people to whom fexinidazole would not be indicated for rhodesiense HAT without treatment tentatively from 2027. Fexinidazole is currently being evaluated also for rhodesiense HAT, with an expansion of the indication expected in the first quarter of 2024, but the indication for children will cover the same population as the gambiense indication: children older than six years (and weighing more than 20 kg).

Considering the expected timelines and challenges of investigating fexinidazole among younger children for rhodesiense (small population and potential challenges in developing a paediatric formulation), which may ultimately approximate the timelines of acoziborole's first approval, it was noted that studying fexinidazole in children younger than six years for rhodesiense was not a priority. However, studying acoziborole for rhodesiense HAT after understanding regulators' minimum requirements for the expansion of indication was noted as a research priority. In vitro data suggest that acoziborole has promising activity against rhodesiense HAT and further preclinical studies are in progress *(20)*.

In the absence of a suitable treatment for younger children for rhodesiense HAT, clinicians would be left with no alternative but using fexinidazole off label (for children younger than six years) because of the life-threatening nature of the disease. Collecting data on this kind of use would be important to inform clinical practice. It should also be explored (such as by asking for scientific advice at the European Medicines Agency (EMA)), if and to what extent such data could potentially support a label update and, more broadly, what type of data should be generated to prompt such label update, including by learning from similar experiences in other disease areas.

The need to conduct crush studies (studies to evaluate the bioavailability of tablets when administered after crushing versus when taken whole) with the current available formulation of fexinidazole (600 mg) was noted as a research priority, to fill gaps in special situations, including the off-label use for children with rhodesiense HAT when melarsoprol will not be available anymore. These studies can be conducted with healthy volunteers and can support administration for younger children who cannot swallow tablets whole.

The paediatric development plan for acoziborole will include children down to one year of age included (weighing more than 10 kg). Children younger than one year will likely be breastfed and there are plans to develop a breastfeeding study to investigate the concentration of acoziborole in milk (data from preclinical studies in animal models have shown that acoziborole is present in milk from breastfeeding mothers), trying to assess the exposure to the drug and thus indirectly evaluate safety during breastfeeding.

Even though no data exist on the transmission of resistance parasites, the emergence of resistance to fexinidazole and acoziborole was indicated to be unlikely and this was therefore not considered a research priority.

Research priorities

- Complete the ongoing development of acoziborole for gambiense HAT, including the paediatric development.
- Study acoziborole for rhodesiense HAT, after understanding regulators' minimum requirements for expanding the indication when enough data for adults and children are available for the gambiense indication.
- Conduct a PK crush study with fexinidazole 600 mg tablet with healthy (adult) volunteers to understand the effect of manipulation and crushing on bioavailability.
- Understand what information should be collected to inform a label update to extend the use of fexinidazole to younger children with rhodesiense HAT (this off-label use is expected when melarsoprol is discontinued).
- Conduct breastfeeding studies to understand acoziborole exposure among breastfed children.

PADO for scabies and onchocerciasis

Scabies

Scabies is an infectious disease caused by infestation with the parasite *Sarcoptes scabiei* var. *hominis*. It is one of the most common skin conditions, accounting for a substantial proportion of skin disease in low- and middle-income countries *(21)*. Infestation occurs by skin-to-skin contact, including sexual contact or, less commonly, by contact with infested fomites (such as clothing and towels) *(22)*.

Available estimates indicate globally between 100–200 million cases of scabies at any point of time, with 455 million incident cases annually. Scabies is estimated to cause the loss of about 3.8 million disability-adjusted life-years. Even though scabies occurs worldwide, it is most common in hot, tropical countries, especially resource-poor settings. The risk of being infected with scabies is considerably higher among people living in crowded, impoverished conditions, with limited or no access to effective treatment and in areas of high population density *(8)*.

Young children in resource-poor communities are especially susceptible to scabies and the secondary complications of infestation. The estimated average prevalence of scabies in children is 5–10%. In some regions, especially the WHO Western Pacific Region, a general population prevalence of 20–30% has been reported, with a prevalence among children exceeding 50% *(23)*.

People affected by scabies infestation typically have linear burrows, vesicles and severe itching that may result in breaks in the skin and crusts. Children with scabies have a more widespread rash, including involvement of the palms, soles of the feet, ankles and sometimes the scalp.

Scabies infestation is also known to be a major risk factor for more serious infections, including impetigo, necrotizing fasciitis, bloodstream infections, kidney disease and rheumatic heart disease.

Evidence indicates acute renal damage among up to 10% of children with scabies infestation in resource-poor settings and, for many, acute renal damage persists for years following infection, contributing to permanent kidney damage.

WHO targets for the control of scabies are defined as “reduction of disease incidence, prevalence, morbidity and/or mortality to a locally acceptable level as a result of deliberate efforts; continued interventions are required to maintain the reduction. Control may or may not be related to global targets set by WHO” *(8)*. Primary management of individuals affected with scabies involves applying a topical scabicide such as 5% permethrin, 0.5% malathion in aqueous base, 10–25% benzyl benzoate emulsion or 5–10% sulfur ointment. Oral ivermectin is also highly effective and is approved in several countries. For treating adults and children weighing at least 15 kg with severe and crusted scabies, ivermectin is recommended in an oral dose of 200 µg/kg body weight, repeated once after 1–2 weeks. For mild to moderate scabies, a dose of 200 µg/kg may be given if topical treatment with permethrin is ineffective or not feasible.

Because the regulatory labels for ivermectin limit administration to children weighing ≥15 kg or at least 90 cm tall, ivermectin is not recommended for smaller children.

Because people in the early stage of new infestation may be asymptomatic and because the treatments for scabies do not kill the parasite’s eggs, best results are obtained by treating the whole household at the same time and repeating treatment in the time frame appropriate for the chosen medication.

Experts acknowledge that treatments such as permethrin creams and oral medication (ivermectin) remain difficult to access because of limited availability and cost *(21)*.

WHO recommends preventive chemotherapy (via MDA) with ivermectin or with topical scabicides (for those not eligible for ivermectin treatment) in settings with disease prevalence above 10%.

In the 2021–2030 roadmap, WHO identified the following actions regarding interventions as required to achieve control of scabies.

- Determine whether ivermectin-based single-dose MDA (instead of two doses seven days apart) is effective for programmatic use.
- Identify alternative strategies for MDA including in areas where loiasis is co-endemic.
- Understand whether moxidectin could serve as a treatment.

Onchocerciasis

Onchocerciasis – or "river blindness" – is a disease caused by a parasitic filarial worm (*Onchocerca volvulus*) transmitted by bites of infective blackflies (*Simulium* spp.). Some of the adult worms (macrofilariae) reside in subcutaneous palpable nodules, and the remainder are deep in the body.

Onchocerciasis is an eye and skin disease primarily due to the immune reaction of the body to dying and dead microfilariae in those organs. People with onchocerciasis may show symptoms such as severe itching and various skin changes. They may also develop eye lesions, which can lead to visual impairment and permanent blindness. Onchocerciasis occurs mainly in tropical areas. More than 99% of the people with onchocerciasis live in sub-Saharan Africa *(24)*.

Since the 1930s, *O. volvulus* infection has been suspected to cause epilepsy. Two cohort studies in Cameroon found that the risk of developing epilepsy increased with the skin microfilariae burden in childhood *(25,26)*. Although the mechanism remains to be established, these data and those from many other studies support both the hypothesis that reducing *O. volvulus* transmission will reduce the prevalence of epilepsy and also the call for strategies to reduce the incidence and level of *O. volvulus* infection among very young children.

For onchocerciasis, WHO targets elimination (interruption of parasite transmission) defined as: "reduction to zero of the incidence of infection caused by a specific pathogen in a defined geographical area, with minimal risk of reintroduction, as a result of deliberate efforts; continued action to prevent re-establishment of transmission may be required" *(8)*.

The primary strategy is preventive chemotherapy with a single oral dose of 150 µg/kg ivermectin.

The number of ivermectin tablets (3 mg) to administer for MDA is usually determined based on height rather than weight.

Depending on national policies, preventive chemotherapy is implemented in most endemic areas once a year; in some others, twice or even four times a year.

A major limitation is that ivermectin is not approved for children weighing <15 kg or shorter than 90 cm tall. Since many onchocerciasis endemic areas are loiasis co-endemic, another limitation is that individuals with high levels of *Loa loa* microfilaraemia can have severe and/or serious adverse reactions to ivermectin. This resulted in the standard approach to preventive chemotherapy (community-directed treatment with ivermectin) being restricted to areas where onchocerciasis is meso- or hyperendemic *(27)*. In other areas, alternative treatment strategies are needed *(28)*. This includes lymphatic filariasis endemic areas with any level of *Loa loa* co-endemicity.

In the 2021–2030 roadmap, WHO identified the following actions regarding interventions as required to achieve elimination of onchocerciasis.

- Develop a macrofilaricide-only drug or other treatment strategies to accelerate interruption of transmission; new treatment strategies are particularly needed for loiasis co-endemic areas (such as macrofilaricide or screening for *Loa loa*).
- Develop better understanding of when to use quarterly MDA.
- Improve recommendations about when to use vector control.
- Demonstrate the effectiveness and safety of moxidectin for children and in programmatic setting (moxidectin could replace the need for semi-annual ivermectin MDA).

PADO priority list

Ivermectin was registered for human use in 1987; it is available as a non-dispersible, unscored 3 mg tablet (5 mm diameter) to be administered orally. It has been used extensively for adults and children weighing ≥15 kg or at least 90 cm tall in onchocerciasis and lymphatic filariasis (millions of doses per year). Because the labels for ivermectin by regulatory agencies and WHO limit administration to children weighing ≥15 kg or at least 90 cm tall, ivermectin is not recommended for smaller children. WHO has prequalified generic ivermectin tablets from two manufacturers. Several studies evaluating the PK and safety of ivermectin in smaller children have been published (see Table 1).

Moxidectin, like ivermectin, is a macrocyclic lactone anthelmintic but is a milbemycin, not an avermectin. Moxidectin has been used only in clinical trials so far. It was registered for human use in 2018 and is only approved for adults and adolescents 12 years and older for onchocerciasis. Three post-registration studies designed to support expansion of the United States Food and Drug Administration (US FDA) registration to include children down to four years and to provide additional data for WHO and countries to decide on including moxidectin in guidelines and policies for onchocerciasis control and elimination have been implemented. These included a study conducted in Ghana (MDGH-MOX-1006, NCT03962062) using the 2 mg tablet approved by the US FDA, whose oval shape and small size was chosen in view of potential use down to the age of four years. The study identified moxidectin doses for children 4–11 years old for which additional safety data are now being collected in the large ongoing safety study (MDGH-MOX-3002 (NCT04311671)).

Moxidectin is also currently being investigated for lymphatic filariasis, soil-transmitted helminthiasis, strongyloidiasis and scabies.

Preclinical studies suggest that moxidectin has higher efficacy than ivermectin and could advance scabies control. A Phase 2 dose-finding study among adults has been completed, and a second Phase 2 study evaluating single doses of 8, 16 and 32 mg of moxidectin for adults is currently ongoing. Moxidectin and ivermectin have very different half-lives, which, together with currently available data from preclinical models, suggest that a single dose of moxidectin will cover the whole scabies life cycle, whereas two ivermectin doses (seven days apart) might be needed, which was noted to be difficult to implement at the national level. Data are available on the effect of ivermectin on scabies in large-scale human studies, while only data from a dose-finding Phase 2a study are currently available for moxidectin.

Table 1 summarizes available information, data gaps and additional considerations presented during the meeting.

The group agreed that the formulation of ivermectin that is currently available (3 mg tablet, round, 5 mm) is appropriate for the population for whom the drug is currently recommended. No manipulation is needed to administer the tablet to younger children, and it has good acceptability. Considering a potential expansion of the indication to children <15 kg (or <90 cm) for scabies (and possibly for onchocerciasis on the longer term) based on the results of ongoing and planned studies, the development of a paediatric formulation of ivermectin was considered a priority. Ongoing studies are exploring 1 mg and 1.5 mg ODTs, so this dosage form and strengths were included in the PADO priority list. This also considers the fact that developing a paediatric formulation of moxidectin will still take a few years (and will also depend on the timeline of additional studies that should be undertaken to expand the indication for children younger than four years with scabies).

Since clinical and/or preclinical data indicate that moxidectin is more effective than ivermectin, with a comparable safety profile, and since it is expected to be used in more indications, a paediatric formulation of moxidectin was also indicated as a priority for development.

The specific characteristics of this formulation (dosage form and strength) will depend on ongoing or future studies and would depend on the indications to be investigated.

Generally, the group agreed that, in the medium term, ivermectin and moxidectin can coexist within public health programmes. However, the group also acknowledged that several aspects should be considered when reflecting on anticipated demand for both products in the longer term, including:

- relative efficacy emerging from ongoing and/or planned studies, including final dosing approaches (for example, ivermectin is currently given in two doses, seven days apart, for scabies MDA), which may facilitate programmatic implementation, especially for MDA programmes;
- access and delivery strategies: the innovator is currently donating ivermectin through the Ivermectin Donation Program for onchocerciasis, but the access strategy for other indications has yet to be determined; the moxidectin access strategy has not yet been determined;
- the use of both drugs across different indications pending the results of ongoing studies;
- the final price of the paediatric formulations of both drugs and how this will fit into the current situation in which ivermectin is donated (for onchocerciasis) free of charge; and
- the extent to which scabies and onchocerciasis programmes will be integrated at the country level.

PADO for scabies and onchocerciasis Priority list	
Ivermectin	1 mg or 1.5 mg ODT *(to be confirmed)*
Moxidectin	Oral dosage form *(details of dosage form and strength to cover the full age and weight spectrum for children and adolescents to be determined based on ongoing studies)*

PADO watch list

All compounds currently in Phase 2 are investigated with a focus on onchocerciasis. No compounds in Phase 2 are investigated for scabies, and it is unknown whether they act on scabies. Most treatments being evaluated for scabies are topical (not suitable for MDA) and were not reviewed and discussed in the context of this meeting.

Currently, among the three compounds in Phase 2 for onchocerciasis, two (emodepside and oxfendazole) are new chemical entities and both are direct-acting drugs, targeting the parasite. These compounds were added to the watch list.

WHO will monitor new evidence emerging from ongoing studies and reconvene an expert group when there is enough evidence to reinitiate discussions on whether further priority-setting among these compounds is needed for paediatric development.

Compound ABBV 4083/flubentylosin, an anti-*Wolbachia* treatment, was also considered but not included in the watch list because no activity among humans was observed in a Phase 2 trial.

Investigation of repurposed drugs is ongoing, but none of these regimens were flagged to be given priority for development for children based on existing evidence.

PADO for onchocerciasis Watch list
Emodepside
Oxfendazole

Research priorities

Table 1 lists the priority research gaps for ivermectin and moxidectin.

As mentioned above, one Phase 2 clinical trial investigating efficacy and safety of moxidectin-containing regimens in people with lymphatic filariasis is ongoing (close to completion) and additional Phase 3 studies to generate further clinical data are planned. Noting that adults are the most epidemiologically significant reservoir of lymphatic filariasis infection, with children younger than four years of age having lower exposure to lymphatic filariasis parasites than older age groups (and therefore lowest infection prevalence), studying moxidectin for children with lymphatic filariasis younger than four years was not considered a research priority.

Similarly, considerations around the burden of soil-transmitted helminth infections for children younger than four years would not justify an investment in specific studies exploring moxidectin in this population *(29)*.

In both cases, if a paediatric formulation of moxidectin is developed, there is potential for its use in children below 4 years to facilitate administration of dosing also for these two indications.

Table 1. Summary of available information on ivermectin and moxidectin

	Ivermectin	Moxidectin
Efficacy and safety data available in <15 kg, <90 cm **(depending on effective doses, safety data can apply across indications)**	*Onchocerciasis* • Efficacy data: no • Safety data: no, but safety data for 81 556 µg/kg administered to 1088 children <15 kg with double doses provided to 83% (901 of 1088) are available from academic studies for other indications (such as scabies, scabies MDA, crusted scabies, strongyloidiasis, trichuriasis, phthiriasis and myiasis) *(30)*.	*Onchocerciasis* Moxidectin development has to date based inclusion in studies on age (four years and older) • Efficacy data: no • Safety data: two children aged four years and weighing 14 and 14.6 kg, respectively, received moxidectin 4 mg in MDGH-MOX-1006 (NCT03962062). None of the children in the study were <96 cm. It is anticipated that further inclusion of young children down to four years in clinical studies will potentially generate more data for children weighing less than 15 kg.
	Scabies • Efficacy data: from academic studies conducted with 214–250 µg/kg with 86% (725 of 838) receiving double doses for MDA studies *(31)*. • Safety data: 95% (1028 of 1088) safety data available come from scabies (scabies, crusted scabies, scabies MDA). Among these, 77% (786 of 1088) were obtained for children 12.5 kg to <15 kg. Efficacy, safety and PK data are being generated as part of a Phase 2b trial among children with scabies <15 kg *(32)*.	*Scabies* • Efficacy data: preclinical studies support higher efficacy of moxidectin than ivermectin: in a porcine preclinical model, a single dose of moxidectin was more effective than two doses of ivermectin because of its longer half-life that covered the mite's full life cycle. Clinical data demonstrate mite death in a PK and pharmacodynamic Phase 2a dose ranging trial completed in 2022 (MDGH-MOX-2001, NCT03905265). • A Phase 2b study among adults with scabies is ongoing to assess the dose range from 8 mg up to 32 mg for PK, efficacy and safety (MDGH-MOX-2002, NCT05875441).
Evidence gaps	*Onchocerciasis* • Assessment of available non-clinical safety margins • PK modelling to determine appropriate dose range for clinical evaluation • Determine body of safety data for expanding the onchocerciasis indication to <15 kg/90 cm by stringent regulatory authorities and lower weight and height limit that would be supported by currently available data	*Onchocerciasis* • Additional safety data for moxidectin among children 4–11 years old • PK modelling to determine doses for children younger than four years • Safety data of appropriate moxidectin dose for children younger than four years • Translation of existing clinical data to appropriate height (or weight) criteria for dosing determination if needed

Table 1. Summary of available information on ivermectin and moxidectin (contd.)

	Ivermectin	Moxidectin
	Scabies • Dose selection and safety data for children <15 kg/90 cm suitable for obtaining regulatory approval and WHO prequalification and to inform WHO guidelines and national policy development. • Comparative efficacy and MDA feasibility of single dose versus two doses to cover the whole mite life cycle.	*Scabies* Phase 2 and 3 data for adults and children supporting regulatory approval and WHO prequalification and to inform WHO guidelines and national policy development for using moxidectin for scabies.
Timeline for data generation	Safety data • The Ivermectin Safety in Small Children with Scabies Phase 2b trial planned to be launched in May 2023 in Bangladesh Brazil, the Gambia and Kenya and will include children down to 5 kg *(31)*. The study is expected to be completed within one year. • Plans for submission for regulatory approval and WHO prequalification: unknown.	Safety data • Data to support use in children aged ≥4 years: • Data and modelling generated in children aged ≥4 years to complement available paediatric clinical trial data from MDGH-MOX-1006 (NCT03962062). *Onchocerciasis* • Submission to the US FDA planned by the first half of 2024 (a supplemental new drug application to add children 4–11 years old). • Not yet studied for children younger than four years. *Scabies* • Children with scabies older than four years to be included in the clinical development programme as early as possible after moxidectin dose selection from MDGH-MOX-2002 (NCT05875441) (completion anticipated for the second half of 2024). If the scabies dose is 8 mg, onchocerciasis project safety data can be leveraged to include children with scabies older than four years in studies that follow MDGH-MOX-2002 in 2024–2025. • Submissions to the US FDA (new drug application) and EMA (marketing authorization application) planned for 2027.
Paediatric formulation investigated	A formulation suitable for young children is being developed (1 mg or 1.5 mg ODT)	Available formulation is suitable for children four years and older. Work on an alternative formulation suitable for younger children is ongoing.

Table 1. Summary of available information on ivermectin and moxidectin (contd.)

	Ivermectin	Moxidectin
Timeline for formulation development	• Current projection: unknown • Requires PK modelling of dose for children <15 kg or <five years old • Bioequivalence clinical study needed • Plans for regulatory approval or WHO prequalification: to be defined	• Current projection: 2.5 years (from availability of funding). • Requires physiologically based PK modelling of dose for children younger than four years for both indications (if the dose is different). • Bioequivalence clinical study needed. • Plans for regulatory approval: submission to the US FDA and EMA depending on the indications.
Other indications	• Ivermectin has regulatory approval for strongyloidiasis (dose: 200 µg/kg) • In common use in combination for soil-transmitted helminths (regulatory status unknown) • Some generic ivermectin formulations (WHO prequalified) are used for lymphatic filariasis, and a dose of 150–200 µg/kg is part of the WHO-recommended MDA strategy for eliminating lymphatic filariasis as a public health problem	• In Phase 2/3 for lymphatic filariasis (NCT04410406) • In Phase 2/3 for the soil-transmitted helminths (NCT04726969, NCT04700423) • Phase 2/3 completed for strongyloidiasis (NCT04848688)
Access plans	• The innovator is donating ivermectin to onchocerciasis-endemic countries for elimination. Donations cover use for eliminating lymphatic filariasis as a public health problem. • There is no donation programme for scabies, soil-transmitted helminths or strongyloides. • The price of ivermectin was noted as a major concern, including in the context that ivermectin MDA for scabies might have to include two doses per year versus one dose per year anticipated for moxidectin. • It is anticipated that a paediatric formulation would not be donated for onchocerciasis control (if there is a decision to include children requiring such a formulation in onchocerciasis elimination programmes).	• Moxidectin will be supplied “at cost plus” (cost of manufacturing, shipping and supply support). • Medicines Development for Global Health Limited (MDGH) is working with other stakeholders to support the cost of moxidectin manufacture. • MDGH is implementing a “dual market business model”: selling moxidectin at higher than manufacturing cost to high-income countries for scabies and using the profit to reduce costs for marginalized communities in high-income countries and low- and middle-income countries.

Table 1. Summary of available information on ivermectin and moxidectin (contd.)

	Ivermectin	Moxidectin
Other considerations	*Other* • Ivermectin use in loiasis co-endemic areas is restricted to onchocerciasis meso- and hyperendemic areas due to severe and serious adverse reactions (including death) to ivermectin among severely *Loa loa*–infected individuals. • Concern about suboptimal response of *O. volvulus* to ivermectin emerging in areas under long-term ivermectin-based MDA has been raised and attributed by some to the potential development of resistance, but there are no definitive data.	*Other* • The first study of the safety (and efficacy) of moxidectin among people with loiasis is ongoing and has completed the safety evaluation during the period when severe and serious adverse reactions to ivermectin are observed (NCT04049851). Given current knowledge about the mechanisms behind the severe and adverse reactions to ivermectin, a similar risk profile is anticipated. • There may be an advantage fin using moxidectin in areas with a high prevalence of onchocerciasis-associated epilepsy where biannual community-directed treatment with ivermectin is considered to be difficult to implement. • Post-meeting note: in the moxidectin Phase 3 study (pivotal study for US FDA approval of moxidectin) conducted in ivermectin-naive study areas, suboptimal response to ivermectin was observed for 11–28% of participants treated with ivermectin and 0–3.9% of participants treated with moxidectin *(33)*.

PADO for visceral leishmaniasis (VL)

Background

Leishmania parasites are transmitted to humans through the bites of infected female phlebotomine sandflies.

VL, also known as kala-azar, is caused by parasites of the *L. donovani–L. infantum* complex and is fatal if left untreated in more than 95% of cases *(34)*. An estimated 50 000–90 000 new cases of VL occur worldwide annually, especially in low-resource settings in tropical and subtropical countries across Africa, Asia, America and Europe, with only 25–45% reported to WHO *(35)*. Most cases occur in Brazil, India and eastern Africa, with the highest burden in the last region (Table 2). VL also has outbreak potential.

VL is intrinsically associated with poverty, poor social determinants of health, population movements, environmental and climate change, and weak health systems.

VL is also associated with malnutrition, which is also a symptom of more severe infection and a major risk factor for poorer clinical and treatment outcomes.

Globally, at least 50% of VL cases are reported to be children younger than 15 years, with a higher incidence among males. Many women of childbearing potential are also affected (6–26%) *(36)*. Post-kala-azar dermal leishmaniasis (PKDL) is a skin NTD and mostly a sequela of VL although it can also occur without the history of VL. In eastern Africa, most PKDL cases occur among children, whereas in the Indian subcontinent all age groups are affected, with prevalence of about 18–20% among people younger than 15 years *(37)*.

Table 2. Regional perspectives on VL epidemiology and management, with a focus on children

WHO region	Main observations
Region of the Americas	• Thirteen endemic countries, with an average of 2990 cases per year (and a decreasing trend in cases in 2022, with 1834 VL cases); the majority of cases (92%) occur in Brazil. • VL and HIV coinfection is an increasing problem, with 16% of cases in 2022, most among adults. • The case-fatality rate in 2022 was close to 9,4%. • VL burden is high for children five years and younger (22%), with a fatality rate of 7,3% being reported *(38)*. • Procurement of medicines through the Strategic Fund of the Pan American Health Organization supports countries in the region to procure antileishmanial health products at negotiated prices regardless of the disease burden. • The region has revised leishmaniasis treatment guidelines in 2022. Liposomal amphotericin B is recommended for children and adults, both immunocompromised and non-immunocompromised people, but it is available only in 50% of the endemic countries. In Brazil, which represents 93% of cases, liposomal amphotericin B is not recommended in the national guidelines for children. Furthermore, when available, use is low given the low confidence by clinicians who have extensive experience with the use of pentavalent antimonials.

Table 2. Regional perspectives on VL epidemiology and management, with a focus on children (contd.)

WHO region	Main observations
South-East Asia Region	• In 2013–2022, 60 337 cases were treated for VL. • Most people with VL 0–15 years old were treated with liposomal amphotericin B or miltefosine. Most children with VL are malnourished and have secondary infections, highlighting the importance of ensuring routine nutritional assessment and support. • In Nepal, more than 30% of the total VL cases in 2021 were among children 14 years or younger. • The acceptability of VL treatments is good for children and caregivers, but administration in children is challenging (in particular, administration of IV infusions is challenging and issues with the swallowability of miltefosine capsules and long duration of treatment were noted during the meeting).
African Region	• Eastern African countries in the African Region and Eastern Mediterranean Region (Eritrea, Ethiopia, Kenya, Somalia, South Sudan, Sudan and Uganda) account for the highest VL burden worldwide, with the highest burden being in Kenya, Ethiopia and South Sudan in the African Region. • In Ethiopia (especially the northern part), most people with VL are older than 14 years, whereas in Kenya, South Sudan and Uganda, most people with VL are younger than 14 years of age. • All countries had an increasing number of cases between 2018 and 2022, including increasing trends among younger children. One reason is improved surveillance, interrupted supplies of rapid diagnostic tests and drugs or focal outbreaks etc. • The first-line treatment regimen is the two daily injections of pentavalent antimonials plus paromomycin (PM) for 17 days The second-line regimen is IV infusion of liposomal amphotericin B and is reserved for special conditions, such as pregnancy, young children, very sick people, people who are co-infected with HIV etc. The first-line treatment for people with VL and HIV coinfection is the combination of liposomal amphotericin B and miltefosine. • Most children with VL are malnourished (especially those younger than five years), so administering injections is difficult because of poor muscle mass, and acceptability by children is low because of painful injections and the risk of thrombosis of veins. • Comorbidities are frequently encountered, such as pneumonia and other respiratory infections. • Largely, diagnosis and treatment for VL is free of charge. However, other medications for opportunistic infections, blood transfusions, investigations for other ailments etc are not free of cost. • Médecins Sans Frontières (MSF) has been involved in managing VL in South Sudan since 1993. Between 2014 and 2022, 61% of people with VL treated by MSF were 0–14 years old, with 80% of them experiencing acute malnutrition, with malnutrition especially affecting children younger than two years. Anaemia is also very common among children admitted for VL treatment, with clear improvement observed after treatment (39). MSF has similar projects in other VL endemic countries, such as Ethiopia and Sudan.

Table 2. Regional perspectives on VL epidemiology and management, with a focus on children (contd.)

WHO region	Main observations
Eastern Mediterranean Region (Djibouti, Somalia and Sudan)	• Since 2019, Sudan reports the highest VL burden globally. • In 2021, children and young adolescents 0–14 years old represented about 69% of the VL burden in Sudan (and children 0–5 years old comprise 60% of VL cases in Djibouti), with the mean age of people with VL in the endemic areas being 8.6 years and malnutrition being a major risk factor (Sudan) *(40)*. • PKDL used to have a high incidence in eastern Africa (>50%) and especially in Sudan, but the incidence is declining (12%). An ongoing large cohort study is being prepared in Sudan and will provide more information about the burden of PKDL. • Children prefer oral therapy, but parents prefer that children receive parenteral therapy, believing that they are more effective. • Two treatments are available in Sudan, namely sodium stibogluconate (SSG) and PM. Liposomal amphotericin B is not suitable for endemic areas where storage facilities and cold chain are suboptimal, so the drug is reserved for tertiary hospitals in Sudan or research centres and shortages are very frequent. • The price, availability and supply of VL medicines are challenging, with breach in supply because of last-mile supply chain challenges.

Overview of current treatment for VL – discussion on challenges and opportunities for children

Treating leishmaniasis depends on the form of the disease, the species of infecting parasite, potential coinfections and the person's immune status but also on the eco-epidemiological areas, since treatment responses differ from region to region *(41–43)*.

Current treatments for VL require taking poorly tolerated, sometimes toxic and costly drugs, often over a long period of time with painful injections. Injections need to be administered by experienced and trained health-care providers in hospital settings, require reconstituting lyophilized drugs, and infusions need to be closely monitored for adverse events. For several decades until 1990s, therapeutic options relied mainly on the use of pentavalent antimonials, either SSG or meglumine antimoniate (MA), despite high rates of cardiac, hepatic, pancreatic and renal toxicity. In the past three decades, new drugs were developed, including injectable liposomal amphotericin B, the oral drug miltefosine and injectable PM, giving improved treatment options. However, in eastern Africa, a combination of SSG plus PM is still the first-line treatment due to better efficacy over other antileishmanial drugs. While these injections were noted by caregivers to be mostly acceptable for children and caregivers, administration is painful and considering that many children with VL are severely malnourished, with almost no muscle tissue available for injections (and difficulties to find a vein for amphotericin B), the risk of nerve damage, thrombosis of vein and injection abscess is still high when injecting. Miltefosine remains the only oral antileishmanial drug to date, but it has low dose flexibility and acceptability in younger children (see below).

Most VL drugs are available from a single supplier and are not registered in several endemic countries. Except for AmBisome®, there is no donation programme for other antileishmanial drugs in place.

As mentioned above, recommended treatment regimens for VL are eco-epidemiological region specific. For example, in eastern Africa, first-line treatment includes the combination of SSG and PM or PM plus miltefosine, while second-line treatment includes liposomal amphotericin B. In the South-East Asian Region, the first-line treatment is liposomal amphotericin B (at different doses) alone, or plus miltefosine or PM or a combination of miltefosine plus PM, and the rescue treatment is either higher doses of liposomal amphotericin B or amphotericin B deoxycholate. For the Region of the Americas, first-line treatment was recently revised to liposomal amphotericin B (strong recommendation, low certainty evidence) and/or pentavalent antimonials or other formulations of amphotericin B (conditional recommendation, low certainty evidence). In the Region of the Americas, the use of miltefosine for both children and adults with VL is not recommended due to the high rates of relapse (strong recommendation against the use of miltefosine, with very low certainty evidence).

Despite several improvements in the past decades, treatment options remain limited:

- **Pentavalent antimonials: SSG and MA**
  SSG and MA are both pentavalent antimonials. They are chemically similar, and their toxicity and efficacy are related to their antimonial content: MA solution contains 8.1% Sb5+ (81 mg/ml), whereas SSG solution contains 10% Sb5+ (100 mg/ml). These are available as parenteral drugs administered intramuscularly or IV either by infusion (over 5-10 min) or by slow injection through a fine needle (23–25 gauge; 0.6–0.5 mm) to avoid any risk of subsequent thrombosis. The dose is 20 mg Sb5+/kg/day, and treatment lasts 20–30 days. Unresponsiveness to antimonials is as high as 60% in Bihar, India and in Nepal. Injections are reported to be painful at the injection site.

- **Amphotericin B (as sodium deoxycholate or lipid formulations):** amphotericin B deoxycholate is given daily or on alternate days by IV infusion at a dose of 0.75–1.0 mg/kg per day for 15–20 doses to be 99% effective in India; data are lacking for other endemic regions.

  Liposomal amphotericin B is the most extensively used formulation in VL. It is dosed at 3–5 mg/kg per daily dose by IV infusion, given over a period of 3–5 days, up to a total dose of 15–30 mg/kg by infusion or 10 mg/kg as a single dose by infusion depending on the region of its use. The treatment is effective in India, while response rates registered in Africa vary. In the Americas, the recommended dose is 3 mg/kg/day for seven days up to 20 mg/kg total dose.

  The two formulations of amphotericin B have different safety and efficacy profiles. The liposomal complex has a better safety profile, and it has become the standard of care, whereas deoxycholate is used only as a rescue medicine in case of unresponsiveness or certain conditions. Treatment with liposomal amphotericin B is expensive despite the price negotiated between the WHO and the manufacturer, and the drug requires a cold chain. Most clinical trials have been conducted with a reference liposomal amphotericin B formulation; all other lipid formulations should be evaluated for toxicity, bioequivalence and efficacy before they are used clinically.
- **PM** is available as intramuscular injection at a dose of 15–20 mg/kg per day. The treatment lasts 21 days and has been shown to be effective in India (cure rate of 93–95%) and in Africa (efficacy 85%). In Africa, it is currently used in combination with SSG for 17 days (efficacy of 93%). The use of PM has not been evaluated in the Americas. Injections are reported to be painful at the injection site and bear the risk ototoxicity and renal toxicity.
- **Miltefosine** is available as 10 mg and 50 mg capsules, and it is dosed at 2.5 mg/kg per day for 28 days for children 2–11 years old and for people 12 years and older at a dose of 50 mg/day for those weighing <25 kg, 100 mg/day for 25–50 kg body weight and 150 mg/day for >50 kg body weight. An increased allometric dose has been proposed and clinically evaluated to overcome low exposure and reduced efficacy in younger children when using the conventional 2.5 mg/kg per day regimen. This allometric regimen has shown high efficacy in children with VL in eastern Africa and demonstrated to lead to an equivalent exposure to the one observed in adults *(44)*. Although a lower-strength formulation 10 mg capsules is available, capsules have low acceptability for younger children. Miltefosine capsules also need to be protected from moisture, which is not ideal for using them in low- and middle-income countries. As a monotherapy, treatment with miltefosine is effective and only indicated for VL, for PKDL in the Indian subcontinent and for cutaneous leishmaniasis among adults caused by *L. panamensis, L. mexicana, L. guyanensis* and *L. braziliensis* and cutaneous leishmaniasis among children caused by *L. panamensis, L. guyanensis* and *L. braziliensis* in the Americas (strong recommendation, low-certainty evidence). In combination with other antileishmanial drugs (PM and liposomal amphotericin B), it has also shown good efficacy in South Asia and Africa, and for HIV-coinfected people in Africa. However, miltefosine is expensive and is potentially teratogenic and should not be used by pregnant women or women with childbearing potential for whom adequate contraception cannot be assured for the duration of treatment and for 6 months afterwards. One common adverse event, miltefosine causes anorexia, nausea and vomiting (38%), with the need to readminister the medicine to ensure appropriate dosing. Administering miltefosine with food can reduce this effect, but the availability of regular meals is a challenge in settings with a high burden of VL. Miltefosine may also exacerbate diarrhoea (20%), which is already extremely common among children in VL-endemic settings. Vomiting and diarrhoea may reduce drug absorption.

PADO priority list

In recent years, efforts have been undertaken to study combinations of available drugs to shorten treatment duration, improve efficacy and improve the safety profile, including for children *(45)*. SSG-PM therapy (first-line treatment for VL in eastern Africa) was an improvement over SSG monotherapy, but it still has limitations, including the need for admissions and 17 days of two injections per day, retaining the toxicity related to SSG and having limited utility (lower efficacy and higher mortality among people with VL older than 45 years) *(46)*. Other combinations of available drugs have been studied in Africa and in Brazil, including in children, but target efficacy was not achieved for any of these regimens *(47,48)*.

Since the conventional miltefosine dosing regimen has low efficacy for children with VL in eastern Africa, an increased allometric dosing regimen of miltefosine monotherapy for 28 days has been studied for this population, with a 90% cure rate achieved and treatment safe and well tolerated *(49)*. A Phase 3 clinical trial comparing 14 days of miltefosine and PM (with allometric dosing of miltefosine) versus the standard of care (17 days of SSG+PM) in eastern Africa, with 60% of study participants being children 4–12 years old, showed similar efficacy to the standard of care *(50)*. Despite being a more child-friendly alternative thanks to requiring only one injection per day, reduced treatment duration and reduced risk of SSG-associated life-threatening cardiotoxicity, this combination regimen is still suboptimal for people with VL, especially children.

Although several new chemical entities are being investigated in clinical studies (Phase 1 or 2 studies), it will still take some time before children with VL will benefit from them. Meanwhile, even if current available drugs are limited for the reasons described above, efforts should be undertaken to ensure that age-appropriate formulations are available for their optimal use for children.

An age-appropriate formulation of oral miltefosine was indicated as a priority formulation for development, given the high burden of VL among younger children and given problems noted with administering miltefosine capsules and limited dose flexibility. The specific dosage form to give priority for development was identified in dispersible tablets, given known problems with oral liquid or syrups related to both procurement and supply as well as dosing and stability. Anticipating potential recommendations for allometric dosing of miltefosine, which ranges from 30 mg to 80 mg daily dose for female patients and from 40 mg to 100 mg daily dose for male patients (divided in two daily administrations to reduce vomiting), a 20 mg dispersible, scored tablet of miltefosine was included in the PADO priority list (to allow for (multiples of) 20 mg and 10 mg dosing. Investigating the development of miltefosine dosage forms with reduced gastrointestinal side-effects was also noted as a key aspect.

An oral solid dosage form of amphotericin B was also given priority for development, with the characteristics (dosage form and strength) of this formulation pending based on the results of ongoing studies. A Phase 2 study exploring amphotericin loaded in cochleates (to retard the release in gastrointestinal media) for cryptococcal meningitis *(51,52)* and Phase 1a (single dose) and 1b (multiple dose) human studies to evaluate the safety, tolerability and PK of novel oral lipid-based amphotericin B formulations including capsule formulations are being carried out. These capsules have already been shown to be stable at tropical climates and resulting in greater than 99% efficacy at non-toxic doses in validated animal models of VL *(53–55)*. However, it was noted that more information and additional data are needed to understand the systemic exposure of amphotericin B from these new oral formulations to ensure adequate exposure for desired outcomes.

Although co-formulating amphotericin B and miltefosine in an oral formulation was also noted as an option, this was not indicated as a priority to explore in the short-term. Having stand-alone child-friendly oral formulations of VL drugs enables greater flexibility in the drug combination that can be used, which is especially important considering geographical variation in treatment. Moreover, some studies indicated that the combination of amphotericin B and miltefosine in primary VL had not shown promising results in terms of effectiveness *(56)*, and more studies would be needed to investigate the drug-related toxicity of these drugs formulated together and assess whether the unique route of uptake that is currently being explored for orally-administered amphotericin B (lymphatic transport) could reduce toxicity.

Aspects such as the cost and the need for stability at room temperature (including in a hot, tropical climate) were noted as essential for developing these priority formulations.

PADO for VL Priority list	
Miltefosine	20 mg scored dispersible tablets
Amphotericin B	Oral solid dosage form *(details to be determined based on ongoing studies)*

PADO watch list

Several new chemical entities for VL, with new mechanisms of action, are currently being investigated in clinical phases. Although most of them are still in Phase 1, one compound developed in collaboration between the Drugs for Neglected Diseases initiative (DND*i*) and Novartis, namely compound LXE408 is in a more advanced stage of development (Phase 2).

New treatments that are currently being studied aim to shift from currently existing drugs to new effective, safe and easy-to-use treatment. In particular, these compounds are being studied as oral, well-tolerated treatments with improved efficacy that can be used at primary healthcare level and are affordable. Such new treatments will benefit not only people with VL but also people with cutaneous leishmaniasis, since they have new mechanisms of actions targeting other *Leishmania* species and have the potential to benefit people with PKDL and people co-infected with VL and HIV. A new treatment for PKDL in South Asia and East Africa is also being evaluated in Phase 2b/3 studies.

Although not enough data are available to evaluate whether compounds currently being studied in Phase 1 are promising for development for children, the results from preclinical studies and from the Phase 1 trial of LXE408 completed in August 2022 are promising. This first-in-class compound is a kinetoplastid-selective proteasome inhibitor, showed good tolerability in Phase 1 and was therefore advanced to Phase 2, with a trial site already opened in India and a study planned to start in Ethiopia in late 2023. The paediatric formulation that is being explored for these studies is a mini-tablet. Since there are currently no specific concerns with investigating this compound for children, the group decided to include it in the PADO watch list for VL.

PADO for VL Watch list
LXE408

Preliminary discussion on preferred product characteristics for VL drugs

Since most compounds being investigated for VL are in Phase 1 and one has progressed to Phase 2, a conversation was initiated on the preferred product characteristics with the support of an online survey, to collect views and considerations on minimal and optimal targets to frame preferred product characteristics from PADO meeting participants to guide future research and development activities by GAP-f partners and other stakeholders.

Notably, the lowest age indicated for the VL therapeutic indication was two years, although it was noted that expanding the study population to children down to six months would be relevant for settings where a substantial proportion of people who need VL treatment are children younger than two years such as Sudan, where observations in MSF project sites have shown that among all people with VL, 7,5% of children were younger than 2 years. These studies have also shown that children younger than 2 years are at higher risk of death than older children and adults.

In general, there is consensus around the fact that new VL medicines for children will have to be oral formulations that are acceptable for children across the age spectrum and do not require refrigeration, to facilitate procurement and logistic aspects at the country level.

Further discussions on the preferred product characteristics for VL medicines for children, including on the chemistry, manufacturing and controls characteristics of compounds will be carried forward after the meeting with additional partners, including groups and stakeholders within the GAP-f network.

Table 3. First draft of proposed preferred product characteristics for VL products for use in children

Attribute	Minimum target	Optimal target	Annotations
Lowest age for the VL therapeutic indication	Two years	Two years (expanding the study population down to six months would also be relevant)	
Dosage form	Oral or intramuscular	Oral	
Toxicity	No severe adverse events, no gastrointestinal side-effects, low renal and hepatic toxicity and no food intake necessary	No side-effects	
Frequency of administration	Twice daily	Once daily	
Drug–drug interactions (DDIs)	No DDIs with antibiotics, anti-tuberculosis drugs, antiretroviral drugs and other drugs commonly used	No DDI	
Laboratory monitoring requirement	Basic diagnostic available on the ground (haematological, kidney function test, liver function test, blood sugar, ECG)	No laboratory monitoring required	
Efficacy	Non-inferior to the standard of care (about 90%)	Superior to the existing standard of care (about 95%)	
Geographical coverage	VL-endemic areas Against one of the *Leishmania* species (*L. infantum* or *L. donovani*)	All areas of VL outbreaks Active against *L. infantum* and *L. donovani* (full geographical coverage)	

Table 3. First draft of proposed preferred product characteristics for VL products for use in children (contd.)

Attribute	Minimum target	Optimal target	Annotations
Cost for high-burden countries	Similar to existing treatments	Similar or cheaper than existing treatments	No management cost for patients
Stability and shelf life	Room temperature, 1–2 years of shelf life	No cold chain required, storage up to 40°C and shelf life of 3–5 years	
Resistance barrier[a]	Various opinions: Low-to-moderate in vivo resistance risk documented High Less than 10% Active against one resistant strain	Should be active against any resistant strains and should not induce any resistance; no cross-resistance	
Other characteristics		Use of polymeric and metallic nanocarrier-based strategies such as macrophage targeting, organ targeting, liposomal technology, enhanced oral bioavailability and photodynamic therapy	No contraindication for pregnant and lactating women, no need for contraception in women of child-bearing potential

[a] In this context, resistance is defined as the decrease or absence of activity of a specific drug against a previously susceptible population of *Leishmania* parasites through the acquisition of molecular resistance mechanisms leading to reduced or a lack of clinical efficacy even at the highest tolerated doses.

Research priorities

Following the priority-setting exercise, the group considered some of the research gaps for VL medicines for children and noted various other challenges:

- investigating the effect of the COVID-19 pandemic as well as other epidemics, natural disasters and social and political disruptions on the VL burden for children;
- investigating drug resistance for amphotericin B and any implications for the clinical management of people with VL, including children;
- the need for studies with allometric doses of miltefosine for people with VL that enable pragmatic dosing strategies while achieving target exposure;
- developing a simplified weight band–based dosing table for allometric miltefosine for children, including the evaluation of harmonized weight bands used for other diseases;
- investigating the development of miltefosine dosage forms with reduced gastrointestinal side-effects;
- exploring the value of using anti-inflammatory drugs as co-adjuvant treatment for VL;
- investigating the effect of increased doses of liposomal amphotericin B in children with kala-azar relapses; and
- establishing exposure–response (PK and pharmacodynamic) relationships in VL in relation to the target exposure for children (which has been done for miltefosine but is currently lacking for other VL medicines, limiting dose extrapolation and optimization for children; these studies, including on miltefosine, should be undertaken in all regions where VL is endemic to consider regional specificities and their potential effects on medicine PK.

Conclusions and next steps

The PADO for NTDs meetings brought together academic researchers, clinical experts, product development partnerships, programme managers and other key stakeholders involved in research and development to reach consensus on the first-ever PADO priority list for NTDs, which contains seven priority formulations. Gaps in age-appropriate formulations for children for other NTDs will be discussed in the future as part of a broader exercise on setting priorities for essential medicines.

Two formulations were considered of interest for future investigation and inclusion in the PADO watch list, and several research questions to inform the development and safe use of the priority products were identified.

The overall outcome of the exercise will be widely disseminated via multiple opportunities for engagement with regulators, industry, funders, civil society and the general public. To ensure appropriate dissemination and promote the alignment of key stakeholders, peer-reviewed manuscripts will be developed.

Finally, the WHO Department of Control of Neglected Tropical Diseases will use its existing advisory groups and mechanisms to follow up on some of the technical discussions in the areas given priority. Where needed, the GAP-f network and its working groups will be leveraged to advance and accelerate the investigation, development and introduction of the priority products.

Table 4. Priority medicines for NTDs

	Schistosomiasis	Scabies and onchocerciasis	HAT	VL
Priority list	L-praziquantel 150 mg ODT L-praziquantel 300 mg scored ODT[a]	Ivermectin 1 mg or 1.5 mg ODT[b] Moxidectin oral dosage form[c]	Acoziborole 320 mg paediatric oral dosage form[b]	Miltefosine 20 mg scored dispersible tablets Amphotericin B oral solid dosage form[b]
Watch list		Emodepside Oxfendazole		LXE408

[a] Pending confirmation of chemistry, manufacturing and controls feasibility.
[b] To be confirmed.
[c] The details of dosage form and strength to cover the full age and weight spectrum for children and adolescents are to be determined based on ongoing studies.

References

1. Shaping the global innovation and access landscape for better paediatric medicines. Geneva: World Health Organization; 2022 (https://apps.who.int/iris/handle/10665/352200, accessed 16 October 2023).
2. Resolution WHA69.20. Promoting innovation and access to quality, safe, efficacious and affordable medicines for children. Geneva: World Health Organization; 2016 (https://apps.who.int/iris/handle/10665/252800, accessed 16 October 2023).
3. Global Accelerator for Paediatric Formulations Network (GAP-f) [website]. Geneva: World Health Organization; 2023 (https://www.who.int/initiatives/gap-f, accessed 16 October 2023).
4. Paediatric drug optimization standard procedure. Geneva: World Health Organization; 2021 (https://apps.who.int/iris/handle/10665/349315, accessed 16 October 2023).
5. Rees CA, Hotez PJ, Monuteaux MC, Niescierenko M, Bourgeois FT. Neglected tropical diseases in children: an assessment of gaps in research prioritization. PLoS Negl Trop Dis. 2019;13:e0007111. doi: 10.1371/journal.pntd.0007111.
6. Verrest L, Dorlo TPC. Lack of clinical pharmacokinetic studies to optimize the treatment of neglected tropical diseases: a systematic review. Clin Pharmacokinet. 2017;56:583–606. doi: 10.1007/s40262-016-0467-3.
7. Al-Obaidi I, Krome AK, Wagner KG, Pfarr K, Kuesel AC, Batchelor HK. Drugs for neglected tropical diseases: availability of age-appropriate oral formulations for young children. Parasit Vectors. 2022;15:462. doi: 10.1186/s13071-022-05546-7.
8. Ending the neglect to attain the sustainable development goals: a road map for neglected tropical diseases 2021–2030. Geneva: World Health Organization; 2020 (https://iris.who.int/handle/10665/338565, accessed 16 October 2023).
9. WHO Model List of Essential Medicines for Children – 8th list (2021). Geneva: World Health Organization; 2021 (https://iris.who.int/handle/10665/345534, accessed 16 October 2023).
10. World Health Organization. Schistosomiasis and soil-transmitted helminthiases: progress report, 2021. Wkly Epidemiol Rec. 2022;97:621–32.
11. Faust CL, Osakunor DNM, Downs JA, Kayuni S, Stothard JR, Lamberton PHL. Schistosomiasis control: leave no age group behind. Trends Parasitol. 2020;36:582–91. doi: 10.1016/j.pt.2020.04.012.
12. Report of a meeting to review the results of studies on the treatment of schistosomiasis in preschool-age children. Geneva: World Health Organization; 2010 (https://iris.who.int/handle/10665/44639, accessed 16 October 2023).
13. WHO guideline on control and elimination of human schistosomiasis. Geneva: World Health Organization; 2022 (https://iris.who.int/handle/10665/351856, accessed 16 October 2023).
14. Spangenberg T. Alternatives to praziquantel for the prevention and control of schistosomiasis. ACS Infect Dis. 2021;7:939–42. doi: 10.1021/acsinfecdis.0c00542.
15. Caldwell N, Afshar R, Baragaña B, Bustinduy AL, Caffrey CR, Collins JJ, et al. Perspective on schistosomiasis drug discovery: highlights from a Schistosomiasis Drug Discovery Workshop at Wellcome Collection, London, September 2022. ACS Infect Dis. 2023;9:1046–55. doi: 10.1021/acsinfecdis.3c00081.

16. World population prospects 2022. New York: United Nations; 2022 (https://population.un.org/wpp, accessed 16 October 2023).

17. WHO interim guidelines for the treatment of gambiense human African trypanosomiasis. Geneva: World Health Organization; 2019 (https://iris.who.int/handle/10665/326178, accessed 16 October 2023).

18. Kande Betu Kumesu V, Mutombo Kalonji W, Bardonneau C, Valverde Mordt O, Ngolo Tete D, Blesson S et al. Safety and efficacy of oral fexinidazole in children with gambiense human African trypanosomiasis: a multicentre, single-arm, open-label, phase 2–3 trial. Lancet Glob Health. 2022;10:e1665–e1674. doi: 10.1016/S2214-109X(22)00338-2.

19. Betu Kumeso VK, Kalonji WM, Rembry S, Valverde Mordt O, Ngolo Tete D, Prêtre A. Efficacy and safety of acoziborole in patients with human African trypanosomiasis caused by *Trypanosoma brucei gambiense*: a multicentre, open-label, single-arm, phase 2/3 trial. Lancet Infect Dis. 2023;23:463–70. doi: 10.1016/S1473-3099(22)00660-0.

20. Jacobs RT, Nare B, Wring SA, Orr MD, Chen D, Sligar JM et al. SCYX-7158, an orally-active benzoxaborole for the treatment of stage 2 human African trypanosomiasis. PLoS Negl Trop Dis. 2011;5:e1151. doi: 10.1371/journal.pntd.0001151.

21. WHO informal consultation on a framework for scabies control: World Health Organization Regional Office for the Western Pacific: Manila, Philippines, 19–21 February 2019: meeting report. Manila: WHO Regional Office for the Western Pacific; 2020 (https://iris.who.int/handle/10665/333154, accessed 16 October 2023).

22. Scabies. Geneva: World Health Organization; 2023 (https://www.who.int/news-room/fact-sheets/detail/scabies, accessed 16 October 2023).

23. Romani L, Steer AC, Whitfeld MJ, Kaldor JM. Prevalence of scabies and impetigo worldwide: a systematic review. Lancet Infect Dis. 2015;15:960–7. doi: 10.1016/S1473-3099(15)00132-2.

24. Onchocerciasis. Geneva: World Health Organization; 2023 (https://www.who.int/news-room/fact-sheets/detail/onchocerciasis, accessed 16 October 2023).

25. Chesnais CB, Nana-Djeunga HC, Njamnshi AK, Lenou-Nanga CG, Boullé C, Bissek AZ et al. The temporal relationship between onchocerciasis and epilepsy: a population-based cohort study. Lancet Infect Dis. 2018;18:1278–86. doi: 10.1016/S1473-3099(18)30425-0.

26. Chesnais CB, Bizet C, Campillo JT, Njamnshi WY, Bopda J, Nwane P et al. A second population-based cohort study in Cameroon confirms the temporal relationship between onchocerciasis and epilepsy. Open Forum Infect Dis. 2020;7:ofaa206. doi: 10.1093/ofid/ofaa206.

27. Mectizan Expert Committee and APOC Technical Consultative Committee. Recommendations for the treatment of onchocerciasis with Mectizan in areas co-endemic for onchocerciasis and loiasis. Decatur (GA): Mectizan® Donation Program; 2004 (https://mectizan.org/wp-content/uploads/2018/06/englishmectccloarecs-june04.pdf, accessed 16 October 2023.

28. Boussinesq M, Fobi G, Kuesel AC. Alternative treatment strategies to accelerate the elimination of onchocerciasis. Int Health. 2018;10(Suppl. 1:i40–8. doi: 10.1093/inthealth/ihx054.

29. VizHub – Global Burden of Disease results [online database]. Seattle: Institute for Health Metrics and Evaluation; 2023 (https://vizhub.healthdata.org/gbd-results/?params=gbd-api-2019-public/121f73775fb5827061844f0a058d1bd1, accessed 16 October 2023).

30. Jittamala P, Monteiro W, Smit MR, Pedrique B, Specht S, Chaccour CJ et al. A systematic review and an individual patient data meta-analysis of ivermectin use in children weighing less than fifteen kilograms: is it time to reconsider the current contraindication? PLoS Negl Trop Dis. 2021;15:e0009144. doi: 10.1371/journal.pntd.0009144.

31. Romani L, Marks M, Sokana O, Nasi T, Kamoriki B, Cordell B et al. Efficacy of mass drug administration with ivermectin for control of scabies and impetigo, with coadministration of azithromycin: a single-arm community intervention trial. Lancet Infect Dis. 2019;19:510–8. doi: 10.1016/S1473-3099(18)30790-4.

32. Ivermectin Safety in Small Children (ISSC). Washington (DC): National Library of Medicine; 2023 (https://clinicaltrials.gov/ct2/show/NCT04332068, accessed 16 October 2023).

33. Bakajika D, Kanza EM, Opoku NO, Howard HM, Mambandu GL, Nyathirombo A. Effect of a single dose of 8 mg moxidectin or 150 µg/kg ivermectin on O. volvulus skin microfilariae in a randomized trial: differences between areas in the Democratic Republic of the Congo, Liberia and Ghana and impact of intensity of infection. PLoS Negl Trop Dis. 2022;16:e0010079. doi: 10.1371/journal.pntd.0010079.

34. Regional strategic framework for accelerating and sustaining elimination of kala-azar in the South-East Asia Region 2022–2026. New Delhi: WHO Regional Office for South-East Asia; 2022 (https://iris.who.int/handle/10665/361887, accessed 16 October 2023).

35. Leishmaniasis. Geneva: World Health Organization; 2023 (https://www.who.int/news-room/fact-sheets/detail/leishmaniasis, accessed 16 October 2023).

36. Harhay MO, Olliaro PL, Vaillant M, Chappuis F, Lima MA, Ritmeijer K. Who is a typical patient with visceral leishmaniasis? Characterizing the demographic and nutritional profile of patients in Brazil, East Africa, and South Asia. Am J Trop Med Hyg. 2011;84:543–50. doi: 10.4269/ajtmh.2011.10-0321.

37. Post-kala-azar dermal leishmaniasis: a manual for case management and control: report of a WHO consultative meeting, Kolkata, India, 2–3 July 2012. Geneva: World Health Organization; 2013 (https://iris.who.int/handle/10665/78608, accessed 16 October 2023).

38. Maia-Elkhoury ANS, Sierra Romero GA, Valadas SYOB, Sousa-Gomes ML, Lauletta Lindoso JA, Cupolillo E et al. Premature deaths by visceral leishmaniasis in Brazil investigated through a cohort study: a challenging opportunity? PLoS Negl Trop Dis. 2019;13:e0007841. doi: 10.1371/journal.pntd.0007841.

39. Kämink SS, Collin SM, Harrison T, Gatluak F, Mullahzada AW, Ritmeijer K. A clinical severity scoring system for visceral leishmaniasis in immunocompetent patients in South Sudan. PLoS Negl Trop Dis. 2017;11:e0005921. doi: 10.1371/journal.pntd.0005921.

40. Zijlstra EE, el-Hassan AM. Leishmaniasis in Sudan. 3. Visceral leishmaniasis. Trans Royal R Soc Trop Med Hyg. 2001;95:S27–58. doi: 10.1016/S0035-9203(01)90218-4.

41. Control of the leishmaniases: report of a meeting of the WHO Expert Commitee on the Control of Leishmaniases, Geneva, 22–26 March 2010. Geneva: World Health Organization; 2011 (https://apps.who.int/iris/handle/10665/44412, accessed 16 October 2023).

42. WHO guideline for the treatment of visceral leishmaniasis in HIV co-infected patients in East Africa and South-East Asia. Geneva: World Health Organization; 2022 (https://iris.who.int/handle/10665/354703, accessed 16 October 2023).

43. Guideline for the treatment of leishmaniasis in the Americas. 2nd edition. Washington (DC): Pan American Health Organization; 2022 (https://iris.paho.org/handle/10665.2/56120, accessed 16 October 2023).

44. Palić S, Kip AE, Beijnen JH, Mbui J, Musa A, Solomos A et al. Characterizing the non-linear pharmacokinetics of miltefosine in paediatric visceral leishmaniasis patients from eastern Africa. J Antimicrob Chemother. 2020;75:3260–8. doi: 10.1093/jac/dkaa314.

45. van Griensven J, Dorlo TP, Diro E, Costa C, Burza S. The status of combination therapy for visceral leishmaniasis: an updated review. Lancet Infect Dis. 2023:S1473-3099(23)00353-5. doi: 10.1016/S1473-3099(23)00353-5.

46. Musa A, Khalil E, Hailu A, Olobo J, Balasegaram M, Omollo R et al. Sodium stibogluconate (SSG) & paromomycin combination compared to SSG for visceral leishmaniasis in east Africa: a randomised controlled trial. PLoS Negl Trop Dis. 2012;6:e1674. doi: 10.1371/journal.pntd.0001674.

47. Wasunna M, Njenga S, Balasegaram M, Alexander N, Omollo R, Edwards T et al. Efficacy and safety of AmBisome in combination with sodium stibogluconate or miltefosine and miltefosine monotherapy for African visceral leishmaniasis: Phase II randomized trial. PLoS Negl Trop Dis. 2016;10:e0004880. doi: 10.1371/journal.pntd.0004880.

48. Romero GAS, Costa DL, Costa CHN, de Almeida RP, de Melo EV, de Carvalho SFG. Efficacy and safety of available treatments for visceral leishmaniasis in Brazil: a multicenter, randomized, open label trial. PLoS Negl Trop Dis. 2017;11:e0005706. doi: 10.1371/journal.pntd.0005706.

49. Mbui J, Olobo J, Omollo R, Solomos A, Kip AE, Kirigi G et al. Pharmacokinetics, safety, and efficacy of an allometric miltefosine regimen for the treatment of visceral leishmaniasis in eastern African children: an open-label, Phase II clinical trial. Clin Infect Dis. 2019;68:1530–8. doi: 10.1093/cid/ciy747.

50. Musa AM, Mbui J, Mohammed R, Olobo J, Ritmeijer K, Alcoba G et al. Paromomycin and miltefosine combination as an alternative to treat patients with visceral leishmaniasis in eastern Africa: a randomized, controlled, multicountry trial. Clin Infect Dis. 2023;76:e1177-e1185. doi: 10.1093/cid/ciac643.

51. Boulware D. Amphotericin B, an oral lipid nanocrystal for cryptococcal meningitis, Phase 2 results: David Boulware, ECCMID 2023 [video]. Stockport: touchINFECTIOUS DISEASES; 2023 (https://touchinfectiousdiseases.com/hiv/conference-hub/phase-2-study-of-an-oral-formulation-of-amphotericin-b-in-cryptococcal-meningitis-david-boulware-eccmid-2023, accessed 16 October 2023).

52. Encochleated Oral Amphotericin for Cryptococcal Meningitis Trial 3 (EnACT3). Washington (DC): National Library of Medicine; 2023 (https://classic.clinicaltrials.gov/ct2/show/NCT05541107, accessed 16 October 2023).

53. Wasan E, Mandava T, Crespo-Moran P, Nagy A, Wasan KM. Review of novel oral amphotericin B formulations for the treatment of parasitic infections. Pharmaceutics. 2022;14:2316. doi: 10.3390/pharmaceutics14112316.

54. Wasan EK, Gershkovich P, Zhao J, Zhu X, Werbovetz K, Tidwell RR et al. A novel tropically stable oral amphotericin B formulation (iCo-010) exhibits efficacy against visceral leishmaniasis in a murine model. PLoS Negl Trop Dis. 2010;4:e913. doi: 10.1371/journal.pntd.0000913.

55. Wasan KM, Wasan EK, Gershkovich P, Zhu X, Tidwell RR, Werbovetz KA et al. Highly effective oral amphotericin B formulation against murine visceral leishmaniasis. J Infect Dis. 2009;200:357–60. doi: 10.1086/600105.

56. Goyal V, Das VNR, Singh SN, Singh RS, Pandey K, Verma N, et al. Long-term incidence of relapse and post-kala-azar dermal leishmaniasis after three different visceral leishmaniasis treatment regimens in Bihar, India. PLoS Negl Trop Dis 2020;14(7): e0008429. doi: 10.1371/journal.pntd.0008429.

Annex 1
Agendas of the four PADO-NTD meetings

PADO for schistosomiasis

17 OCTOBER 2022		
Welcoming	Daniel Argaw Dagne (WHO)	13:00–13:05
Introduction (PADO, GAP-f) and objectives of the meeting	Martina Penazzato (WHO)	13.05–13:15
Current and future treatment options for schistosomiasis	Amadou Garba Djirmay (WHO)	13:15–13:25
Discussion	All facilitated by Tiziana Masini (WHO)	13:25–14:00
Access to new formulations – opportunities and challenges	Hye Lynn Choi (WHO) Peter Steinmann (Swiss Tropical and Public Health Institute, Pediatric Praziquantel Consortium)	14:00–14:10
Sustainable financing and supply of NTD medicines	Mark Sullivant and Barbara Roth (Medicines Development for Global Health Limited)	14:10–14:20
Global Access Facility – the concept	Mae Shieh (DND*i*)	14:20–14:30
Break		14.30–14:40
UNICEF model to procure formulations of schistosomiasis medicines	Cynthia Kamtengeni (UNICEF)	14:40–14:50
Discussion	All facilitated by Hye Lynn Choi (WHO)	14:50–15:50
Wrap-up	Martina Penazzato and Amadou Garba Djirmay (WHO)	15:50–16:00

PADO for HAT

2 DECEMBER 2022		
Welcome	Daniel Argaw Dagne (WHO)	9:00-9:05
Introduction (PADO and GAP-f) and objectives of the meeting	Martina Penazzato (WHO)	9.05–9:15
Current and future treatment options for human African trypanosomiasis	Gerardo Priotto and Jose Ramon Franco Minguell (WHO)	9:15–9:30
National programme perspective	Charles Wamboga (National Sleeping Sickness National Control Programmes, Uganda)	9:30–9:40
Clinicians' perspective	Leon Kazumba (Neurology Department, University of Kinshasa, Democratic Republic of the Congo)	9:40–9:50
Updates on ongoing studies: fexinidazole	Olaf Valverde (DND*i*)	9:50–10:00
Updates on ongoing studies: acoziborole	Sandra Rembry (DND*i*)	10:00–10:15
Q&A	All, facilitated by Tiziana Masini (WHO)	10:15–10:30
Break		10:30–10:45
Discussion on priorities and research agenda	All, facilitated by Jose Ramon Franco Minguell and Hye Lynn Choi (WHO)	10:45–12:30
Wrap-up	Martina Penazzato (WHO)	12:30–13:00

PADO for scabies and onchocerciasis

18 APRIL 2023		
Welcome	Daniel Argaw Dagne (WHO)	12:00–12:05
Introduction (PADO and GAP-f) and objectives of the meeting	Martina Penazzato (WHO)	12:05–12:15
Current treatment options for scabies and onchocerciasis, with a focus on children	Maria Rebollo Polo (WHO)	12:15–12:30
Clinician's perspective on scabies	Andrew Steer (Royal Children's Hospital Melbourne, University of Melbourne, IACS)	12:30–12:40
Perspective on *Loa loa*–related adverse reactions to ivermectin and the morbidity burden of *Loa loa*; onchocerciasis-related epilepsy	Sébastien Pion (Institut de Recherche pour le Développement, France)	12:40–12:50
Activity overview on moxidectin for onchocerciasis, lymphatic filariasis and scabies	To be confirmed (Medicines Development for Global Health Limited)	12:50–13:10
An overview of the R&D pipeline	Sabine Specht (DND*i*)	13:10–13:25
Q&A	Moderated by Annette C. Kuesel (independent expert, retired from WHO) and Hye Lynn Choi (WHO)	13:25–13:45
Wrap up	Martina Penazzato (WHO)	13:45–14:00

19 APRIL 2023		
Recap from day 1	Martina Penazzato (WHO)	12:00–12:05
Paediatric formulation of moxidectin	Hannah Batchelor (University of Strathclyde, Scotland)	12:05–12:15
Ivermectin for neglected tropical diseases in children weighing <15 kg	Kevin Kobylinski (Mahidol-Oxford Tropical Medicine Research Unit (MORU), Bangkok, Thailand)	12:15–12:30
The development of a paediatric ivermectin formulation	Joerg Huwyler (University of Basel, Switzerland) and Sabine Specht (DND*i*)	12:30–12:45
Priority setting – methods and scope	Tiziana Masini (WHO)	12:45–12:50
Guided discussion on PADO priority list	Moderated by Maria Rebollo Polo (WHO)	12:50–13:20
Guided discussion on PADO watch list		13:20–13:40
Guided discussion on research questions		13:40–13:55
Wrap-up, closing and next steps	Martina Penazzato (WHO)	13:55–14:00

PADO for VL

7 JUNE 2023		
Welcome and opening remarks	Daniel Argaw Dagne (WHO)	12:30–12:35
Introduction (PADO, GAP-f), objectives of the meeting and conflict of interest assessment	Martina Penazzato (WHO)	12:35–12:45
Current treatment options for visceral leishmaniasis, with a focus on children	Saurabh Jain (WHO)	12:45–13:00
Regional perspective on the treatment of children with visceral leishmaniasis	Ana Nilce Silveira Elkhoury (Pan American Health Organization) Dorcas Lamounier Costa (Ministry of Health, Brazil and Pan American Health Organization) Dhruv Pandey (WHO Regional Office for South-East Asia) Henock Keto (WHO Regional Office for Africa) Ahmed M Musa (Institute for Endemic Diseases, Sudan)	13:00–13:50
Q&A	All (Moderated by Martina Penazzato and Saurabh Jain, WHO)	13:50–14:00

Break	All	14:00–14:10
Clinicians' perspectives	Margriet den Boer (Médecins Sans Frontières) Krishna Pandey (WHO Collaborating Centre, India) Fabiana Alves (DND*i*) Open contributions from participants on clinical perspectives (moderated by Saurabh Jain, WHO)	14:10–15:00
Access challenges for visceral leishmaniasis medicines	Fabienne Jouberton (Médecins Sans Frontières and chair of the leishmaniasis procurement committee)	15:00–15:15
Q&A	Moderated by Hye Lynn Choi (WHO)	15:15–15:25
Wrap-up	Martina Penazzato & Saurabh Jain (WHO)	15:25–15:30

8 JUNE 2023		
Welcome day 2	Martina Penazzato & Saurabh Jain (WHO)	12:30–12:35
Q&A from day 1 – second session	Saurabh Jain and Hye Lynn	12.35–12.45
Optimization of miltefosine dosing	Thomas Dorlo (Uppsala University)	12.45–12:55
Development of an oral formulation of amphotericin B	Wasan Kishor (University of British Columbia, Canada)	12:55–13:05
An overview of the R&D pipeline	Fabiana Alves and Joelle Rodes (DND*i*)	13:05–13:15
Q&A	Moderated by Saurabh Jain & Hye Lynn Choi (WHO)	13:15–13:25
Break	All	13:25–13:30
Priority setting • **Methods** • **Priority List** • **Watch List**	Martina Penazzato (WHO) Saurabh Jain (WHO)	13:30–14:45
Review of preferred product characteristic survey findings	Alessandra Nardone (PENTA/GAP-f)	14:45–14:55
Discussion on preferred product characteristic survey findings and research priority gaps	All (moderated by Martina Penazzato, WHO)	14:55–15:05
Research gaps	All (moderated by Martina Penazzato, WHO)	15:05–15:20
Closing and next steps	Saurabh Jain and Martina Penazzato (WHO)	15:20–15.30

Annex 2
List of meeting participants

Name	Affiliation	Schistosomiasis	HAT	Scabies and onchocerciasis	VL
Mehreteab Abraha	Neglected Tropical Diseases Programme, Ministry of Health, Eritrea				✔
Ellen Agler	END Fund, United States of America (USA)				✔
Gabriel Alcoba	Médecins Sans Frontières, Switzerland			✔	
Markos Ali	The END Fund, USA	✔			
Fabiana Alves	DND*i*, Switzerland				✔
Deependra Amatya	Sukraraj Tropical and Infectious Disease Hospital, Nepal				✔
Sarah Andersson	Murdoch Children's Research Institute, Australia			✔	
Daniel Ariop	Case Management of Neglected Tropical Diseases Department, Ministry of Health, South Sudan				✔
Mike Barrett	University of Glasgow, Scotland		✔		
Hannah Batchelor	University of Strathclyde, Scotland			✔	
Ahmed Be-Nazir	Accelerating the Sustainable Control and Elimination of Neglected Tropical Diseases, Bangladesh				✔
Linsey Blair	Schistosomiasis Control Initiative Foundation, United Kingdom of Great Britain and Northern Ireland (UK)	✔			
Moses Bockarie	The END Fund, USA				✔
Michel Boussinesq	Institut de Recherche pour le Développement, France			✔	
Rachel Broznan	Bill & Melinda Gates Foundation, USA		✔		
Christian Burri	Swiss Tropical and Public Health Institute, Switzerland		✔		
Sakib Burza	Health in Harmony, UK				✔
Mariame Camara	DND*i*, Guinea		✔		

Name	Affiliation	Schistosomiasis	HAT	Scabies and onchocerciasis	VL
Ramananda Chaudhary	Kalikot District Hospital, Nepal				✔
Isaac Chikwanha	Global Health Innovative Technology Fund, Switzerland	✔		✔	✔
Robert Colebunders	University of Antwerp, Belgium			✔	
Gláucia Fernandes Cota	Fiocruz Minas, Brazil				✔
Tim Cressey	Chang Mai University, Thailand			✔	✔
Alysha Croker	Health Canada, Canada			✔	
Wendell Rodrigues Oliveira da Silva	Instituto Federal de Educação, Ciência e Tecnologia do Ceará, Brazil				✔
Gokarna Dahal	Neglected Tropical Disease and Vector Borne Disease Control Section, Nepal				✔
Silvio Fernando Guimarães de Carvalho	Universidade Federal de Minas Gerais, Doutorado em Ciências da Saúde, Brazil				✔
Illian de Freitas e Felix de Sousa	Working Group on Pharmaceutical Assistance in Pediatrics (GT-Pediatrics) of the Department of Pharmaceutical Ministry of Health, Brazil				✔
Margriet den Boer	Médecins Sans Frontières, UK				✔
Ermias Diro	University of Washington, USA				✔
Romain Dissard	Medicines Patent Pool, Switzerland	✔			
Thomas Dorlo	Uppsala University, Sweden				✔
Kathiely Martins dos Santos	Ministry of Health, Brazil				✔
Andrew Edielu	The Medical Research Council/Uganda Virus Research Institute and London School of Hygiene & Tropical Medicine Uganda Research Unit, Uganda		✔		
Darin Evans	United States Agency for International Development (USAID), USA	✔			
Olga Fernandez	Centro Internacional de Entrenamiento e Investigaciones Médicas, Colombia				✔
Fiona Fleming	Schistosomiasis Control Initiative Foundation, UK	✔			
Laura Fregonese	European Medicines Agency, Netherlands (Kingdom of the)		✔	✔	✔
Lobna Gaayeb	Medicines Patent Pool, Switzerland	✔	✔	✔	✔

Name	Affiliation	Schistosomiasis	HAT	Scabies and onchocerciasis	VL
Gideon Giesselmann	Luxembourg National Research Fund, Luxembourg			✔	
Ramya Gopinath	United States Food and Drug Administration, USA			✔	✔
Rama Prosad Goswami	Department of Tropical Medicine, School of Tropical Medicine, India				✔
Kebron Haile	The END Fund, Ethiopia				✔
Michelle Helinski	The European & Developing Countries Clinical Trials Partnership, Netherlands (Kingdom of the)			✔	
Stéphane Hugonnet	DND*i*, Switzerland		✔		
Jörg Huwyler	University of Basel, Switzerland			✔	
Medard Ilunga	DND*i*, Democratic Republic of the Congo		✔		
Caroline Jjingo	United States Food and Drug Administration, USA				✔
Clara Jones	Ministry of Health, United Republic of Tanzania			✔	
Prakash Joshi	Kanti Children's Hospital, Nepal				✔
Fabienne Jouberton	Médecins Sans Frontières, Switzerland	✔		✔	✔
Cynthia Kamtengeni	UNICEF, Switzerland	✔			
Shashi Kandel	Neglected Tropical Disease and Vectorborne Disease Control Section, Nepal				✔
Leon Kazumba	Neurology Department, University of Kinshasa, Democratic Republic of the Congo		✔		
Sally Kinrade	Medicines Development for Global Health, Australia			✔	
Wasan Kishor	University of British Columbia, Canada				✔
Kevin Kobylinski	Mahidol-Oxford Tropical Medicine Research Unit, Thailand			✔	
Angela Kopack	United States Food and Drug Administration, USA			✔	
Ansoumane Kourouma	Programme National de Control de la trypanosomiase humaine africaine, Guinea		✔		
Rajiv Kshirsagar	UNICEF, Denmark			✔	

Name	Affiliation	Schistosomiasis	HAT	Scabies and onchocerciasis	VL
Annette C. Kuesel	Independent expert, retired from the WHO's Special Programme for Research and Training in Tropical Diseases			✔	
Praveen Kumar	Kalawati Saran Children's Hospital, India				✔
Thomson Lakwo	Onchocerciasis control programme, Uganda (retired)			✔	
Marc Lallemant	PENTA, Italy	✔		✔	✔
Patrick Lammie	Task Force for Global Health, USA			✔	
Dorcas Lamounier Costa	Universidade Federal do Piaui, Brazil				✔
Kayla Laserson	Bill & Melinda Gates Foundation, India				✔
Janice Lee	DND*i*, Switzerland	✔	✔	✔	✔
Jane Lillywhite	Oriole Global Health, UK				✔
Rogelio López-Vélez	WHO Collaborating Centre for Clinical Management of Leishmaniasis, Spain				✔
Edward Losio	Ministry of Health, South Sudan				✔
Myrlena Regina Machado Mescouto Borges	Instituto Tocantinense Presidente Antônio Carlos, Brazil				✔
Major Madhukar	Rajendra Memorial Research Institute of Medical Sciences, India				✔
Michael Marks	London School of Hygiene & Tropical Medicine, UK			✔	
Florent Mbo	DND*i*, Switzerland		✔		
Jane Mbui	Kenya Medical Research Institute, Kenya				✔
Alia Meyer	DND*i*, Switzerland				✔
Dinesh Mondal	International Centre for Diarrhoeal Disease Research, Bangladesh				✔
Begoña Monge-Maillo	WHO Collaborating Centre for Clinical Management of Leishmaniasis, Spain	✔	✔	✔	✔
Sébastien Morin	Medicines Patent Pool, Switzerland			✔	
Alfred Mubangizi	Ministry of Health, Uganda			✔	
Ahmed Musa	Institute of Endemic Diseases, Sudan				✔
Francisca Mutapi	University of Edinburgh, UK	✔			

Name	Affiliation	Schistosomiasis	HAT	Scabies and onchocerciasis	VL
Erick Mwamba Miaka	National Program for the Control of Human African Trypanosomiasis, Democratic Republic of the Congo		✔		
Daniel Mwiti	Leishmaniasis National Programme, Kenya				✔
Alessandra Nardone	PENTA, Italy	✔	✔	✔	✔
Francisco Javier Moreno Nuncio	Instituto de Salud Carlos III, Spain				✔
Brian Raphael Nzano	Clinton Health Access Initiative, USA			✔	✔
Duncan Ochol	The END Fund, USA				✔
Mary Atieno Ojoo	UNICEF, Switzerland	✔			
Piero Olliaro	University of Oxford, UK				✔
Joseph Olobo	Makerere University, Uganda				✔
Krishna Pandey	Rajendra Memorial Research Institute of Medical Sciences, India				✔
Khechar Nath Paudel	Provincial Hospital Surkhet, Nepal				✔
Eric Pelfrene	European Medicines Agency, Netherlands (Kingdom of the)		✔		
Sébastien Pion	Institut de Recherche pour le Développement, France			✔	
Yosief Redae	Neglected Tropical Diseases Programme, Ministry of Health, Eritrea				✔
Sandra Rembry	DND*i*, Switzerland		✔		
Joelle Rodes	DND*i*, Brazil				✔
Barbara Roth	Medicines Development for Global Health, Australia	✔		✔	
Victoria Ryg-Cornejo	Medicines Development for Global Health, Australia			✔	
Moussa Sacko	Institut National de Recherche en Santé and Publique, Mali	✔			
Jorge Seixas	Instituto de Higiene e Medicina Tropical, Portugal		✔		
Mae Shieh	DND*i*, Switzerland	✔			
Pere Simarro	DND*i*, Switzerland		✔		
Laston Sitima	Ministry of Health, Malawi			✔	

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Penelope Smith	USAID, USA	✔			
Rebecca Smith	Medicines Development for Global Health, Australia			✔	
Yao Sodahlon	Mectizan Donation Programme, USA			✔	
Sabine Specht	DND*i*, Switzerland	✔		✔	
Andrew Steer	Royal Children's Hospital Melbourne, University of Melbourne, Australia			✔	
Peter Steinmann	Swiss Tropical and Public Health Institute, Switzerland	✔			
Russell Stothard	Liverpool School of Tropical Medicine, UK	✔			
Mark Sullivan	Medicines Development for Global Health, Australia	✔		✔	
Shyam Sundar	Banares Hindu University, India				✔
Joel Tarning	University of Oxford, United Kingdom of Great Britain and Northern Ireland			✔	
Louis-Albert Tchuem Tchuenté	University of Yaoundé, Cameroon	✔			
Bhupendra Tripathi	Bill & Melinda Gates Foundation, India				✔
Michel Vaillant	Luxembourg Institute of Health, Luxembourg			✔	
Olaf Valverde	DND*i*, Switzerland		✔		
Prabha Viswanathan	United States Food and Drug Administration, USA				✔
Richard Wamai	Northeastern University, USA				✔
Charles Wamboga	National Sleeping Sickness National Control Programmes, Uganda		✔		
Brenda Waning	Stop TB Partnership Global Drug Facility, Switzerland	✔			
Monique Wasunna	DND*i*, Kenya				✔

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WHO					
Jane Pita Hilary Ajo	WHO Office in South Sudan		✔		✔
Jamal Amran	WHO Country Office in Somalia				✔
Abraham Aseffa	WHO Department of Control of Neglected Tropical Diseases				✔
Kingsley Asiedu	WHO's Special Programme for Research and Training in Tropical Diseases			✔	
Didier Bakajika	Expanded Special Project for the Elimination of Neglected Tropical Diseases, WHO Regional Office for Africa			✔	
Henock Bekele	WHO Country Office in Ethiopia				✔
Abate Mulugeta Beshah	WHO Regional Office for Africa				✔
Po-Lin Chan	WHO Country Office in India				✔
Hye Lynn Choi	WHO Regulation and Prequalification Department	✔	✔	✔	✔
Daniel Argaw Dagne	WHO Department of Control of Neglected Tropical Diseases	✔	✔	✔	✔
Siddhartha Sankar Datta	WHO Regional Office for Europe				✔
Amadou Garba Djirmay	WHO Department of Control of Neglected Tropical Diseases	✔			
Augustin Kadima Ebeja	WHO Regional Office for Africa		✔		
Ana Nilce Silveira Elkhoury	WHO Regional Office for the Americas				✔
José Ramón Franco-Minguell	WHO Department of Control of Neglected Tropical Diseases		✔		
Asma Hafiz	GAP-f, Research for Health, Science Division	✔	✔	✔	✔
Anupama Hazarika	WHO Country Office in Bangladesh				✔
Saurabh Jain	WHO Department of Control of Neglected Tropical Diseases				✔
Charles Katureebe	WHO Country Office in Uganda				✔
Jonathan King	WHO Department of Control of Neglected Tropical Diseases			✔	
Francis Regis Magombo	WHO Country Office in Eritrea				✔

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Farihah Malik	GAP-f, Research for Health, Science Division	✔	✔	✔	✔
Tiziana Masini	GAP-f, Research for Health, Science Division	✔	✔	✔	✔
Antonio Montresor	WHO Department of Control of Neglected Tropical Diseases	✔		✔	
Denise Mupfasoni	WHO Department of Control of Neglected Tropical Diseases	✔			
Pauline Ngina Mwinzi	WHO Expanded Special Project for Elimination of Neglected Tropical Diseases, WHO Regional Office for Africa	✔			
Khin Pa Pa Naing	WHO Country Office in Nepal				✔
Manaye Nigus	WHO Country Office in Ethiopia				✔
Cécile Ollivier	GAP-f, Research for Health, Science Division	✔	✔	✔	✔
Joyce Kerubo Onsongo	WHO Country Office in Kenya				✔
Mona Osman	WHO Regional Office for the Eastern Mediterranean				✔
Bandana Pandey	WHO Country Office in Nepal				✔
Dhruv Pandey	WHO Country Office in India				✔
Martina Penazzato	GAP-f, Research for Health, Science Division	✔	✔	✔	✔
Maria Rebollo Polo	WHO Department of Control of Neglected Tropical Diseases			✔	
Gerardo Priotto	WHO Department of Control of Neglected Tropical Diseases		✔		
José Antonio Ruiz-Postigo	WHO Department of Control of Neglected Tropical Diseases		✔		
Kazim Hizbullah Sanikullah	WHO Regional Office for the Western Pacific				✔
Mutale Nsakashalo Senkwe	WHO Country Office in South Sudan				✔
Prakash Shakya	WHO Country Office in Nepal				✔
Anthony Solomon	WHO Department of Control of Neglected Tropical Diseases			✔	
Anjali Srivastava	GAP-f, Research for Health, Science Division	✔	✔	✔	

Name	Affiliation	Schistosomiasis	HAT	Scabies and onchocerciasis	VL
Sabera Sultana	WHO Country Office in Bangladesh				✔
Afework Hailemariam Tekle	WHO Department of Control of Neglected Tropical Diseases	✔			
Samantha Valadas	WHO Regional Office for the Americas	✔			
Marie Valentin	WHO Department Regulation and Prequalification	✔	✔	✔	✔
Supriya Warusavithana	WHO Regional Office for the Eastern Mediterranean				✔
Aya Yajima	WHO Regional Office for South-East Asia				✔

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