

## Drugs for Neglected Diseases initiative

### *Briefing Note for 76th World Health Assembly*

**21-30 May 2023**

#### Overview

The Drugs for Neglected Diseases initiative ([DNDi](#)) is a not-for-profit research and development (R&D) organization, in official relations with the WHO, that discovers, develops, and delivers new treatments for neglected patients. Since our creation in 2003 by public research institutions in Brazil, France, India, Kenya, and Malaysia, Médecins Sans Frontières (MSF), and WHO TDR, we have developed 12 new and improved treatments for six deadly diseases that have reached millions of people utilizing an alternative, collaborative, not-for-profit R&D model. Furthermore, DNDi, in partnership with the World Health Organization (WHO), jointly established the Global Antibiotic Research and Development Partnership (GARDP), now an independent organization playing an essential role in its work with Member States to deliver on the Global Action Plan on Antimicrobial Resistance. DNDi is also a member of the Global Accelerator for Paediatric Formulations Network (GAP-f), which promotes innovation of and access to quality, safe, efficacious, and affordable medicines for children.

This briefing sets out DNDi's comments for consideration by World Health Organization (WHO) Member States on the following agenda items of the 76<sup>th</sup> session of the World Health Assembly:

- **Agenda item 12:** Global Strategy for Women's, Children's and Adolescents' Health (2016–2030)
- **Agenda item 13.1:** Universal Health Coverage
- **Agenda item 15.1:** Strengthening WHO preparedness for and response to health emergencies
  - Strengthening clinical trials to provide high-quality evidence on health interventions and to improve research quality and coordination
- **Agenda item 27.1:** Progress reports
  - WHO global strategy on health, environment and climate change: the transformation needed to improve lives and well-being sustainably through healthy environments

## Agenda item 12: Global Strategy for Women's, Children's and Adolescents' Health (2016–2030)

DNDi welcomes the Director General's progress [report](#) and applauds the progress made in the implementation of the Global Strategy for Women's, Children's, and Adolescents' Health (2016-2030). While the report outlines many of the challenges that remain in prioritizing the health needs of women and children, the need for R&D of health tools to address the health requirements of these populations, whose specific medical needs are often neglected, has not been sufficiently highlighted.

When reviewing the report, we request Member States to take note of the following issues:

**The Impact of poverty-related and neglected diseases on women:** NTDs continue to impact 1.65 billion people worldwide and in some cases affect women disproportionately. For example, dengue causes severe complications such as vaginal bleeding – a complication which only affects women. For pregnant women, dengue leads to a three-fold increase in maternal death. Dengue haemorrhagic fever increases the risk of maternal death by 450 times<sup>1</sup>, and overall, the disease increases maternal mortality to 15.9%.<sup>2</sup> Chagas disease is highly prevalent in women of childbearing age and pregnant women in the Americas, and can be transmitted from mothers to their unborn infants. Social and cultural factors also exacerbate gender inequalities. For example, cutaneous leishmaniasis (CL) places an outsized burden on women. Depending on the severity of the scars or disfiguring skin pathology, CL can lead to painful stigma that influences the quality of life and psychological well-being of the patient.<sup>3</sup> In many contexts, women are more vulnerable to skin disease and suffer greater social stigma than men.<sup>4</sup> Stigmatization can affect all aspects of women's lives, particularly interpersonal relationships, social activities, work capacity, and marriage. In addition, the burden of caregiving often falls on women and girls, which impacts their socio-economic potential and access to health services.

**The need to promote the inclusion of women in clinical trials:** Across disease areas, there are widespread knowledge gaps in understanding the impact of medicines on biological females, especially for people of childbearing potential and pregnant and lactating women, who are often excluded from clinical trials due to concerns that drugs could have harmful impacts on foetuses. This came into further prominence during the COVID-19 pandemic, with women and children underrepresented in clinical trials. The DG's report states that 'poor inclusion of women, children and adolescents in early COVID-19 research, testing and surveillance activities hampered a definitive understanding of the direct effects of COVID-19 on them.' This underrepresentation also results in delays in the availability of medicines. DNDi with its partners has proposed a safe and ethical clinical trial recruitment [framework](#) for women of childbearing potential. These and other proposals to ensure responsible strategies in gender-responsive drug development should be integrated into the implementation of the Global Strategy.

**The need for R&D for children:** The report mentions 'treatment of childhood illnesses' as one of the gaps that hinder the achievement of universal health coverage, particularly for LMICs. We wish to extend this concern to the case of children affected by illnesses not specific to childhood, but for which child-adapted treatment formulations are often not developed. Each year, millions of children's lives

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<sup>1</sup> Paixao, Enny S et al. "Dengue in pregnancy and maternal mortality: a cohort analysis using routine data." Scientific reports vol. 8,1 9938. 2 Jul. 2018

<sup>2</sup> Brar R, Sikka P, Suri V, Singh MP, Suri V, Mohindra R, Biswal M. Maternal and fetal outcomes of dengue fever in pregnancy: a large prospective and descriptive observational study. Arch Gynecol Obstet. 2021 Jul

<sup>3</sup> Bennis I, De Brouwere V, Belrhiti Z, Sahibi H, Boelaert M. Psychosocial burden of localised cutaneous Leishmaniasis: a scoping review. BMC Public Health. 2018

<sup>4</sup> Al-Kamel MA. Impact of leishmaniasis in women: a practical review with an update on my ISD-supported initiative to combat leishmaniasis in Yemen (ELYP). Int J Womens Dermatol. 2016 Jun 16

are prematurely ended or debilitated by diseases that are largely treatable – yet the treatment needs of children have long been an afterthought in profit-driven drug development; globally, most medicines prescribed to children have never been tested in children.<sup>5,6</sup> The needs of children living with HIV illustrate this neglect, where the development of optimal paediatric formulations lagged 20 years behind that for adults.

This neglect persists, even though children are disproportionately more at risk of infection, illness, and death from infectious diseases than adults, particularly if they live in poor and vulnerable communities<sup>7</sup>. Children are excluded from the vast majority of clinical trials that are used to assess the safety and efficacy of medicines, and to determine dosing. A 2019 study of clinical trials for neglected diseases found that across more than 360 late-stage clinical trials, only 17% included people younger than 18 years of age. Of the 47 medications recommended by the WHO to treat neglected diseases, only seven are available in paediatric formulations<sup>8</sup>. As a result, children are more often than not left without safe, effective medicines approved for paediatric use. We welcome the establishment and ongoing work of the Global Accelerator for Paediatric Formulations Network (GAP-f, of which DNDi is a member) as an important step to promote innovation of and access to quality, safe, efficacious, and affordable medicines for children. GAP-f has highlighted paediatric formations and research questions for children in several disease areas. These should be incorporated into the strategy in order to advance action to achieve universal health coverage and ensure that vulnerable segments of the population are not neglected from an R&D perspective.

**We urge Member States to:**

1. Support and implement strategies for R&D to better meet the health needs of women including those of childbearing potential, pregnant and lactating women, for poverty related, neglected and other diseases
2. Support research to understand sex- and gender-based barriers in accessing health care services diagnosis and treatments and promote interventions that address these barriers
3. Promote collection, utilization, and reporting of sex- and age-disaggregated information in ongoing and future programs and research
4. Encourage and support development of approaches to include women and children in clinical trials as soon as possible in the drug development process- to close the evidence gap
5. Support prioritization and investment of the development of age-appropriate formulations for children including support for the Paediatric Drug Optimization (PADO) exercise being undertaken by GAP-f to identify a prioritized drug portfolio of the most needed formulations for children, for several diseases.
6. Encourage the rapid and coordinated development of age-appropriate formulations of any treatments through public health focused collaborations between academic institutions, key paediatric networks, product development partnerships, public and private R&D organizations,
7. Support GAP-f identified priorities

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<sup>5</sup> US Food & Drug Administration. Drug Research and Children [Internet]. 2016. Available from: <https://www.fda.gov/drugs/information-consumers-and-patients-drugs/drug-research-and-children>

<sup>6</sup> Watts G. WHO launches campaign to make drugs safer for children. *BMJ*. 2007 Dec 15. Available from: <https://dx.doi.org/10.1136%2Fbmj.39423.581042.DB>.

<sup>7</sup> UNICEF. Maternal, newborn and child survival: Childhood diseases [Internet]. 2022. Available from: <https://www.unicef.org/health/childhood-diseases>.

<sup>8</sup> Neglected tropical diseases in children: An assessment of gaps in research prioritization by Rees CA et al. *PLoS Negl Trop Dis*, January 2019. <https://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0007111>

## Agenda item 13.1 – Universal Health Coverage

Reorienting health systems to primary health care as a resilient foundation for universal health coverage and preparations for a high-level meeting of the United Nations General Assembly on UHC [EB152\(5\)](#)

DNDi welcomes the UN High-level Meeting on Universal Health Coverage in September 2023 and supports the adoption of the resolution. We ask Member States to take note and include the following issues in preparation for the meeting in September and in the development and implementation of the political declaration.

- **R&D can support achievement of universal health coverage**

As the Director General's [report](#) states, access to appropriate, affordable health tools is a key component of achieving universal health coverage. In addition to ensuring access to existing medicines, in order to support UHC, there must also be innovation for, and access to, the missing health tools needed to address unmet needs and ensure no one is left behind.

The true test of UHC is whether it addresses the needs of vulnerable and marginalized populations. However, these are the people whose needs are often excluded from the current biomedical R&D system. Too often, existing health tools for neglected diseases have serious limitations that hamper the provision of care, can cause catastrophic health expenditure, and impede disease control. This is the case, for example, for mycetoma, leishmaniasis, Chagas disease, and onchocerciasis (river blindness). In addition, as EB152(5) recognizes, climate change has and will continue to affect climate-sensitive diseases, disproportionately burdening already vulnerable and marginalized communities. Although the spread or increased intensity of infectious diseases is viewed as a consequence of climate change, R&D for new health tools to address infectious diseases to contribute to resilient and people-centred health systems to strengthen UHC does not feature prominently in discussions around climate change adaptation.

Research and development can support UHC by developing safe, effective, affordable health tools designed from the start to be patient centred **for use the at primary healthcare level, close to the affected communities – reducing the need for specialist intervention in hospital settings. This reduces complexity and cost not only for patients and families, but also health systems.**

Oral treatments and simpler diagnostic tests are such examples. DNDi and its partners have developed the first all-oral treatment for sleeping sickness, which eliminates the need for systematic hospitalization and treatment requiring injections. Avoiding or limiting hospitalization can be critically important for vulnerable people, including those with NTDs, who are poor or otherwise marginalized. In many settings, all expenses related to hospitalization must be paid out of pocket, often representing a catastrophic expense that feeds vicious cycles of poverty.

**Progress in the development of new health tools for neglected populations depends on sustainable investments in R&D, and on public leadership and commitment to drive such investment.** Without specific interventions by governments, unmet medical needs linked to a lack of commercial return on innovation will not be addressed by the profit-driven biomedical R&D system. Alternative financing mechanisms and new partnership models and incentives that do not depend on the primarily profit-seeking model are needed to address key treatment gaps and meet the needs of the most vulnerable populations.

- **Integration and cross-cutting approaches are necessary across health priorities**

People are often faced with multiple health challenges. For example, the risk of developing active visceral leishmaniasis is more than 100 times greater in people living with HIV. There are opportunities for synergies, shared services, and integration of the development and access processes across disease areas – for example, developing better tools for testing and treatment programmes – that bring transformational benefits for patients and health systems alike. Rapid diagnostic tests and simpler, safer, more effective medications lessen the complexity of treatment and care, reduce waste and inefficiency, and bolster health system reach and resilience. This includes for COVID-19, future pandemics and epidemics, other infectious diseases such as NTDs, HIV, TB, and malaria, noncommunicable diseases such as diabetes and hypertension, and mental health.

To prepare for and provide surge capacity to respond to pandemics, for example, much of the infrastructure that is needed for timely development and delivery of health tools for pandemics must be ‘kept warm’, supported, and therefore utilized during inter-crisis times. This includes clinical trial infrastructure and manufacturing capacity and procurement mechanisms/platforms. COVID-19 research built on decades of investment in infectious disease R&D. The high-level meetings should reflect on the extent to which investments in PPR and other disease areas can support UHC and ensure resources are also leveraged to benefit existing health priorities. This could include mutualizing manufacturing needs across disease areas where feasible, and pooling demand and exploring common delivery and access mechanisms for health tools.

**We urge Member States to:**

1. **Promote a coherent, integrated action plan for public-health-centred R&D across the high-level meetings on UHC, PPR, and TB, as well as the IHR amendments and WHO CA+ negotiations.** The high-level meetings provide an opportunity to make links to solve systemic problems that address multiple health issues. Recognizing and building on the overlaps, Member States should facilitate and promote integration across disease areas by linking R&D needs for UHC and the SDGs with investment in sustainable pandemic preparedness and response infrastructure. This could also be included in the implementation of the Global Action Plan for Healthy Lives and Well-being for All, R&D, Innovation and Access Accelerator.
2. **Commit to sustainably investing in R&D** for effective health tools for use at primary healthcare level, including by investing in not-for-profit R&D models based on patient needs.
3. **Establish mechanisms, or modify existing mechanisms, to accelerate access** to ensure that tools developed reach healthcare workers, communities and patients.
4. Acknowledge the role R&D can play in supporting UHC by **including R&D in national, regional, and global UHC action plans** and including monitoring of the development and access to health tools as part of national UHC action plan indicators and international UHC efforts or roadmaps, including through the WHO Secretariat’s review of an indicator for unmet need for health care services.
5. Acknowledge the critical role that governments can play in ensuring their public investments in R&D are designed to deliver equitable access and **commit to specific, globally agreed norms and binding rules** to facilitate this.

## Agenda item 15.1 – Strengthening WHO preparedness for and response to health emergencies

### Strengthening clinical trials to provide high-quality evidence on health interventions and to improve research quality and coordination

DNDi congratulates the WHO Secretariat for passing resolution WHA75.8 at the 75<sup>th</sup> session of the WHA and welcomes the [report](#) on implementation of the resolution. We also commend the Secretariat for organizing several stakeholder consultations with Member States, Non-State Actors, non-governmental organizations, patient groups, and the private sector to identify and establish the baseline of the clinical trial ecosystem. As the Secretariat moves forward with implementation of the resolution, we suggest the following areas for consideration based on our experience conducting clinical trials for infectious diseases including [ANTICOV](#), a multi-country, adaptive platform trial conducted in 13 African countries to identify treatments for mild-to-moderate COVID-19 outpatients.

**Coordination and connectivity:** The DG report identifies the need for ‘further development of clinical trial networks for coordination and data sharing.’ There is scope for additional clinical trial network development – both through establishing new networks and ensuring better connectivity among those that exist already.

**Sustainability:** For both pandemic preparedness for future threats as well as pandemic response, clinical trial infrastructure and processes put in place must be sustained throughout the peaks and troughs of acute public health crises and address the potential of more than one threat at a time.

**Regulatory and ethical review harmonization:** The report by DG highlighted the need for strengthening national regulatory authorities and ethics committees and the ‘need for harmonization of the many different review procedures between countries and committees’ so that the health tools developed are effective, safe and quality assured, and can reach those in need in a timely manner. For example, the African Vaccine Regulatory Forum (AVAREF) – a network of African regulatory authorities and ethics committees – was formed with the aim to harmonize regulatory processes and expedite timelines for approval of clinical trial applications. Networks like this can facilitate both timely approvals of clinical trials and access to health tools, particularly during health emergencies. In addition, the International Coalition of Medicines Regulatory Authorities (ICMRA) was useful during COVID-19 as a forum for regulators to coordinate COVID-19-related reviews.

**Access equity:** Clinical trials require collaboration between different partners and rely on the national systems in which they operate. It is therefore important that all those that contribute to the process, including participants in clinical trials, have access to the benefits/end products of research they participated in and contributed to. Clinical trial frameworks must ensure that drugs are affordable and accessible in an equitable manner for people who need them.

**Research equity:** Broadening the diversity of populations included in clinical trials whenever possible plays a critical role in improving equity and understanding of health outcomes among populations. The inclusion of underserved populations including women who are pregnant, or of child-bearing age, and children is key to ensuring equitable R&D. Disaggregating clinical trial data by sex and age is another important aspect to facilitate this understanding and learning.

**Transparency:** DNDi welcomes the inclusion of language around making trial results, both positive and negative, publicly available and promoting transparent translation of results. However, if there is no transparency around clinical trial costs, particularly when the research is publicly funded, then it is difficult for governments to accurately estimate if public investment is sufficient, used efficiently, or

helpful in addressing exorbitant prices that hamper access to new health tools. Despite significant public funding, including for late-stage research, pharmaceutical and biotechnology companies often claim that the high costs of R&D – clinical trials, in particular – justify high prices for drugs and other health tools, yet they do not publicly disclose these costs in any detail. What limited information is available indicates that R&D expenditures are outpaced by revenues.<sup>9</sup> DNDi is one of few R&D organizations that publicly disclose R&D costs by stage of development, including clinical trials<sup>10</sup>. We estimate that we can develop and register new treatments for anti-infectives that combine or repurpose existing drugs for €4-32 million and new chemical entities for €60-190 million.

Disclosure of detailed R&D cost data, in a standardized manner, would allow governments to more accurately estimate the cost of clinical trials and provide a basis for calculating and assessing existing and future funding needs. It would also increase the ability of purchasers to negotiate treatment prices more effectively by addressing longstanding information asymmetry.

**We urge Member States to:**

- **Improve coordination and connectivity between new and existing clinical trial networks**, including multi-country adaptive clinical trial platforms, especially those based in and led by LMICs, and seek to standardize trial protocols, data requirements, and processes.
- Ensure **clinical trial ecosystems** that are critical for timely development and delivery of health tools during health emergencies are **'kept warm'** – and used to respond to existing health threats – particularly for diseases that are neglected by the market – therefore utilized **during inter-crisis times** to prepare for and provide surge capacity to respond to pandemics. This could involve working in networks, sharing skills and expertise, and coordinating research nationally to prioritise use of these centres of excellence.
- Support **coordination for regulatory authorities and ethics committees** and promote transnational regulatory cooperation to streamline clinical trial approval and review processes.
- Ensure **clinical research activities include diverse populations**, focus on priority needs, such as evidence to support optimal and appropriate use of antibiotics, and address gaps in data on specific populations by reporting disaggregated data by sex and gender.
- Support the **development of best practices for countries on how to ensure access and benefit-sharing principles are implemented**, including the possibility of a requirement that health tools are registered, available, and accessible, preferentially for the country/geography and community where the clinical trials have been conducted, beyond clinical trial participants, if the health intervention delivers successful results.
- Ensure that links are made to resolution WHA 72.8 'Improving the transparency of markets for medicines, vaccines and other health products', adopted at the 72<sup>nd</sup> session of WHA, which urges Member States to take **necessary steps to mandate public availability of detailed clinical trial cost data** and support dissemination of and enhanced availability of '...costs from human subject clinical trials...', particularly in instances where these trials were publicly funded. One way of mandating disclosure of clinical trials costs is for governments/funders to attach conditions on price transparency and access to the health tools to R&D funding.

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<sup>9</sup> US Congress House Committee on Oversight and Reform. Drug Pricing Investigation: Majority Staff Report. 117th Cong. 2021. Available from:

<https://oversightdemocrats.house.gov/sites/democrats.oversight.house.gov/files/DRUG%20PRICING%20REPORT%20WITH%20APPENDIX%20v3.pdf>

<sup>10</sup> <https://dndi.org/advocacy/transparency-rd-costs/>

## Agenda item 27.1 – Progress reports

### WHO global strategy on health, environment and climate change: the transformation needed to improve lives and well-being sustainably through healthy environments

The [WHO Global Strategy on Health, Environment and Climate Change](#) acknowledges the fact that ‘climate change is... modifying the transmission of food-borne, water-borne and zoonotic infectious diseases, resulting in large impacts on health.’ However, we remain concerned that the need for innovation for new health tools to prevent and combat climate-sensitive diseases is often overlooked.

Climate change is affecting the spread of infectious diseases in three ways: the changing incidence and geographical spread of vector-borne and water-borne climate-sensitive infectious diseases, climate-related migration, and the increased risk of new emerging zoonotic diseases.<sup>11</sup> Nearly half (11 out of 25) of the vector or waterborne diseases listed by the WHO are also classified as neglected tropical diseases (NTDs)<sup>12</sup> and affect 1.65 billion people, mostly in the least developed economies and most impoverished communities. They can bring financial devastation to those affected, feeding vicious cycles of ill-health and poverty.<sup>13</sup>

Climate change is threatening progress towards the control and elimination of such infectious diseases by impacting the geographical range, seasonality, and incidence rates due to changing temperatures and rainfall patterns. Climate change-induced mortality and morbidity from infectious diseases are expected to rise globally in the future: while the incidence of some infectious diseases might be reduced as the environment may become too warm for vector survival, the effects of climate change will mostly propagate infectious diseases. Indeed, additional warming will likely alter pathogen and vector development rates and generation times, shift the geographical distribution of vector or reservoir host populations, alter transmission dynamics, or modify host susceptibility to infection.<sup>14,15</sup>

Many climate-sensitive NTDs lack tools for prevention, diagnosis, and treatment that are simple, safe, and effective – and that can be easily integrated into already overburdened health systems. Where tools do exist, equitable access can remain a challenge – as highlighted during the COVID-19 pandemic, where the development of new health technologies did not lead to equitable access, even in the face of an acute public health crisis.

#### **To ensure well-being and support affected communities in adapting to the adverse impacts of climate change, we urge Member States to:**

- Support **inclusion of R&D for climate-sensitive diseases in climate adaptation discussions** as these are most likely to be neglected by global biopharmaceutical private sector, due to lack of commercial returns.
- Support **South-South R&D collaboration**, where countries that will face the greatest burden of climate-sensitive diseases lead R&D priority setting and development. This also presents scope and opportunities for South-South and triangular research collaboration and partnerships.

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<sup>11</sup> Twin threats: climate change and zoonoses. *The Lancet Infectious Diseases*. 8 December, 2022

<sup>12</sup> WHO list of diseases transmitted by vectors: <https://www.who.int/news-room/fact-sheets/detail/vector-borne-diseases>; WHO list of NTDs: <https://www.who.int/news-room/questions-and-answers/item/neglected-tropical-diseases#:~:text=NTDs%20include%3A%20Buruli%20ulcer%3B%20Chagas,rabies%3B%20scabies%20and%20other%20ectoparasitoses%3B>

<sup>13</sup> World Health Organization. *Global Report on Neglected Tropical Diseases 2023*. 2023

<sup>14</sup> A hot topic at the environment–health nexus: investigating the impact of climate change on infectious diseases. Grobusch, Lena C and Grobusch, Martin P. 29 December, 2021, *International Journal of Infectious Diseases*.

<sup>15</sup> Climate change: an enduring challenge for vector-borne disease prevention and control. Joacim Rocklöv, Robert Dubrow. 20 April, 2020, *Nature immunology*