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Submission to the Technical Assessment component of the first Global Stocktake – Drugs for Neglected Diseases initiative

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This submission is prepared by the Drugs for Neglected Diseases initiative (DNDi), an international R&D organization that discovers, develops, and delivers new infectious diseases treatments for neglected patients. DNDi was established in 2003 by public research institutions in Brazil, France, India, Kenya, and Malaysia, in collaboration with Médecins Sans Frontières and the World Health Organisation. Using an alternative, collaborative, open science, not-for-profit research and development model, DNDi has developed 12 new and improved treatments for six deadly diseases, that have reached millions of people.

This submission responds to q*uestions 6: How adequate and effective are the current adaptation efforts and the support provided for adaptation towards achieving the goals defined in Articles 2.1(b) and 7.1 of the Paris Agreement? and Question 10: In order to achieve the goals defined in Articles 2.1(b) and 7.1 of the Paris Agreement: a) What further action is required? b) What are the barriers and challenges, and how can they be overcome at national, regional and international levels? c) What are the opportunities, good practices, lessons learned and success stories?*

Climate change will impact the epidemiology and geographical range of climate-sensitive infectious diseases, including the most neglected tropical diseases, many of which lack effective, safe and affordable health tools to prevent or treat them. **DNDi focuses these comments on how the Global Stocktake can best reflect the current inadequate level of preparedness to tackle the spread of infectious diseases, and how research and development for new health tools to prevent and treat such diseases should be considered as an explicit outcome for the collective work of Parties within adaptation efforts.**

1. Impact of climate change on climate-sensitive infectious diseases

Despite ongoing global coordination to mitigate the impacts of climate change, progress to date has been insufficient, and data shows that 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 (1).

Nearly half (11 out of 25) of the vector or waterborne diseases listed by the WHO are also classified as neglected tropical diseases (NTDs)[1] and affect 1.65 billion people, mostly in the least developed economies and most impoverished communities, almost half of them children. They can bring financial devastation to those affected, feeding a vicious circle of ill-health and poverty (2). These neglected tropical diseases kill, disfigure, stigmatize, or debilitate millions of people every year – often the poorest of already impoverished communities.

[1] 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

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, climate change effects 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 (3) (4). Climate change also affects the virulence of the disease, in some cases making it more severe.

Examples of climate-sensitive diseases

Dengue: Rising global temperatures encourage the expansion of breeding grounds for vectors that carry arboviral diseases such as dengue, yellow fever, Zika, and chikungunya, expanding to higher elevations and latitude. Dengue is the most prevalent mosquito-borne viral disease worldwide and in 2019, was named by WHO as one of the ten threats to global health (5). Dengue outbreaks are now occurring worldwide with an 85% increase in the global number of dengue cases from 1999-2019. Endemic countries are facing longer dengue outbreaks along with increased incidence. The population at risk from dengue infection is predicted to increase to 60% of the world's population by 2080, compared to 2015 as a result of climate change, rapid urbanization and population growth (6). Treatment consists primarily of supportive care, with no effective treatment yet available. With the predicated increase in incidence and geographical spread of dengue noted above, the current state of adaptation efforts to prevent or treat such diseases are inadequate.

Leishmaniasis: Transmitted by sandflies**,** Leishmaniasis is also climate-sensitive as the ambient temperature directly affects the vector's development and geographical distribution. The disease epidemiology will therefore be affected by rising temperatures and changing rainfall patterns, transmission might spread to areas not previously endemic to the disease (7). According to a study estimate, the number of people exposed to leishmaniasis may double by 2080 (8). For visceral leishmaniasis, which already places 600 million people at risk each year, treatments are inadequate as they require either hospital stays or complex infusions, while medicines for cutaneous leishmaniasis are more than 60 years old, costly, and often require weeks of painful injections of toxic, heavy metal-based drugs with severe side effects.

Chagas: Climate change will impact the distribution and transmission risk for Chagas disease, a potentially fatal parasitic illness transmitted by insects known as 'kissing bugs" or through mother- to-child, and can cause irreversible, life-threatening damage to the heart and other vital organs. This will vary geographically throughout the Americas where chagas is endemic in 21 countries (9). In recent decades, a dramatic increase in the number of Chagas Disease cases in non-endemic countries has also been observed. By allowing more habitats to become suitable for vectors and reservoir host species of Chagas disease, climate change threatens to transform the disease from a Latin American challenge to a global one (10).

Sleeping sickness: Current models predict that increases in mean annual temperatures are likely to significantly shift the distribution of the T. b. rhodesiense strain of sleeping sickness upwards into the East African highlands where there are high population densities and large livestock populations as reservoirs. Even if the size of the geographical range does not increase significantly, range shifts can lead to changes in the number of people at risk of exposure and disease incidence. One source predicted an additional 46-77 million people at risk by 2090 (11).

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Other considerations

Extreme weather conditions and events are also causing **climate migration or climate internal displacement**[2,3], which can lead to changing profiles of infectious diseases (12). It is estimated that by 2050 there will be 200 million climate migrants, which means one out of every 45 people would be displaced by climate change (13). Malaria and dengue pathogens often move with people. Similarly, schistosomiasis (for which water snails are the intermediate host organism) is spread by population movement, and this will be of concern in areas of increased rainfall and flooding.

While many infections once labelled as "tropical diseases" are now leading to outbreaks worldwide, as illustrated by the recent emergence of dengue and other tropical diseases in areas such as the United States of America (14), Europe (15) and the re-emergence of dengue in Japan (16), **countries in the Global South are the ones that will continue to carry a disproportionate burden due to impacts of climate change on infectious diseases**

2. Status of adaptation efforts to combat climate-sensitive diseases

Adaptive strategies present solutions to reduce the potential impact of climate change on health**.** One of the 10 recommendations of the WHO in the COP26 Special Report on Climate Change and Health is to "Build climate-resilient and environmentally sustainable health systems and facilities, and support health adaptation and resilience across sectors". Another recommendation of this report supports "..stepping up surveillance and research…" and "addressing inequalities that lie at the root of so many global health challenges" to "Prevent and prepare for the next pandemic" (17).

Enhanced health systems investments for disease surveillance, epidemiological investigation, virus testing and vector control are needed to underpin the adaptation efforts- but they will not suffice. **Availability of and equitable access to tools to diagnose and treat climate-sensitive diseases are a key part of building resilient communities and health systems.**

I. Lack of investment into research and development of health tools to tackle climate-sensitive diseases

For many of these climate-sensitive infectious diseases, inadequate investment in medical research and development (R&D) threatens the world's ability to adapt to the effects of climate changes on these diseases. Current tests and treatments for most climate-sensitive neglected tropical diseases (NTDs), should they exist at all, have serious limitations that hamper the provision of lifesaving medical care and impede disease control and elimination efforts. The world lacks tools for prevention, diagnosis, and treatment that are simple, safe, and effective – and that can be easily integrated into already overburdened health systems (18).

The Special Rapporteur on the right of everyone to the enjoyment of the highest attainable standard of physical and mental health recognised the adverse impacts of climate change on infectious diseases

[2] The World Bank's Groundswell report finds that climate change, an increasingly potent driver of migration, could force 216 million people across six world regions to move within their countries by 2050. Hotspots of internal climate migration could emerge as early as 2030 and continue to spread and intensify by 2050.
[3] The International Federation of the Red Cross estimates that there are more environmental refugees than political refugees trying to avoid wars and conflicts.

which puts at risk the right to health as part of the right to an adequate standard of living, as stated in the Universal Declaration of Human Rights. Additionally, the right to essential medicines is embedded in the right to health and includes an obligation for State Parties to ensure the development and availability of safe, affordable and effective health tools with an emphasis on marginalised populations.

Most of these climate-sensitive diseases historically affecting the poorest communities in LMICs, have not attracted the interest of the global biopharmaceutical private sector. To counter the lack of investments in this area by the for-profit pharmaceutical sector, due to limited profit potential, not-for-profit product development partnerships (PDP) - such as DNDi - now play a crucial role in pharmaceutical innovation for these infectious diseases. PDPs use a collaborative model aiming for equitable access to treatment, involving public research institutions, pharmaceutical companies, academia and communities, including in endemic counties, in the development process, and operating with the support of government agencies, development banks, foundations and trusts (19).

Despite successes driving the development of safe effective adapted and affordable new health tools, more needs to be done to address the existing and future needs for drugs, diagnostics and vaccines to treat and control climate-sensitive diseases. Funding also remains scarce, especially for the climate-sensitive diseases endemic mostly to low- and middle-income countries and there is a lack of global and regional mechanisms to support the clinical development and access of the most urgently needed drugs, vaccines and diagnostics.

Innovation for climate-sensitive diseases is a collective responsibility.

No single country or organisation can address the multiple aspects of discovering, developing and ensuring access to new health tools for climate-sensitive diseases. Collaborative approaches, with endemic countries in the lead, that ensure the development of new health tools from bench to bedside are needed that: draw on the experience of communities, clinicians in endemic countries, the scientific power of academia, the expertise to discover and develop products worldwide, the finance to underpin that development, and build on and strengthen the regulatory and the health systems to ensure safety and access. The experience of PDP driven drug development shows that most countries are able to actively participate and contribute significantly to collaborative approaches. One such collaborative approach involves establishments from four dengue endemic countries - Siriraj Hospital in Thailand, the Ministry of Health in Malaysia, the Translational Health Science and Technology Institute in India, Fiocruz in Brazil and DNDi- for the development of therapeutic solutions for dengue infection. The alliance highlights the commitment of endemic countries to invest, lead and collaborate in dengue research.

The increased incidence of some of these climate-sensitive diseases in high income regions, may eventually spur innovation and investment by the for-profit pharmaceutical sector for those diseases considered as the biggest threat, in those regions. This, however, doesn't guarantee research and development of health tools for climate-sensitive diseases affecting lower-and middle-income countries- where the burden of such diseases are already real and extensive. Furthermore, equitable access to these tools would continue to remain a challenge - as highlighted during the COVID-19 pandemic where the development of new health technologies including those subsidized by public funds, did not lead to equitable access even in the face of an acute public health crisis (20). The R&D biomedical system is already failing neglected populations in low resource settings affected by neglected tropical and infectious diseases.

Without changes to the public policies shaping the R&D ecosystem, including ensuring that public investments in R&D are conditioned on public benefits - such as open sharing of R&D inputs, processes and outputs and equitable access, in addition to utilizing and building on innovation capacity in the Global South - innovation will remain the privilege of the rich whilst populations in already burdened countries in the Global South will be the hardest hit by climate-sensitive infectious diseases. Biopharmaceutical innovation for vaccines, diagnostics and treatments thus needs to be a core part of climate change adaptation strategy.

II. Current state of action to combat climate-sensitive diseases in governmental strategies, NDCs and NAPAs

In 2021, the World Health Organisation undertook a qualitative assessment of 31 health and climate change strategies, 23 of which identified vector borne diseases as climate-sensitive health risks (21). This demonstrates that spread of neglected diseases is increasingly being recognised and acknowledged as a consequence of climate change. However, research and development for neglected diseases treatments, vaccines and diagnostics does not feature prominently in adaptation discourse or action.

A review of Nationally Determined Contributions (NDCs) shows that health is one of the three sectors most often prioritized for adaptation in the NDCs, along with water and agriculture. 84% of NDCs that include health considerations refer to health in relation to adaptation priorities and actions (22). Several countries, in their NDCs, have noted the link between climate change and increased incidence of vector borne diseases, but the need for research and development of treatments for climate-sensitive disease have not been explicitly made. Similarly, National Adaptation Programmes of Action (NAPA) developed and submitted by Least Developed Countries to UNFCCC, have included interventions for vector control and surveillance but do not contain plans to support R&D for climate-sensitive diseases.

Therefore, increased efforts must be given to incorporate strategies to manage such impacts in adaptation efforts for the growing burden of infectious diseases, including the development of appropriate health tools, designed and delivered to meet the needs of vulnerable populations.

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3. Recommendations for the Global Stocktake and for Parties actions

The Glasgow Climate Pact 2021 acknowledges that "*Parties should, when taking action to address climate change, respect, promote and consider their respective obligations on human rights,* ***the right to health.*** Access to medicines is embedded in the right to health and includes an obligation for State Parties to ensure the development and availability of safe, affordable and effective health tools with an emphasis on marginalised populations. WHO's COP26 special report on Climate Change and Health specifically mentions that **"health adaptation and resilience need to be considered** in all planning, implementation, communication, and transparency processes of the adaptation goal, and should be part of the global stocktake process."

DNDI makes four recommendations for action:

I. **Consideration of health in broader adaptation planning is needed and should be reflected in the GST outcomes with a recommendation for collective work of the Parties.** Climate change adaptation strategies, with its ambition to improve well-being, will benefit from greater inclusion of health-related adaptation efforts. Connecting the dots between climate change, climate-sensitive diseases, and the need for biomedical R&D, is one such adaptation strategy. Responding to climate-sensitive diseases would also support the dual objective of meeting SDG target of ending the epidemics of neglected diseases by 2030 and ensuring universal health coverage for all. Successful achievements of SDG3 and SDG 13 targets depend upon countries efforts to meet climate change and health goals in a coordinated and integrated manner.

II. **The GST should recommend a health metric under the Global Goal on Adaptation for measuring progress on the implementation of the Paris Agreement.** Indicators on actions adopted for tackling climate-sensitive infectious diseases, including research and development efforts for the development of appropriate health tools are potential ways of measuring progress on adaptation efforts.

III. **All countries, low-, middle- and high-income countries should include plans to support innovation for appropriate health tools in their NDCs and NAPA**. Additionally, **public, international cooperation efforts** on climate adaptation should also prioritize contributions to climate adaptation in the form of accelerated support to health systems and health tools innovation.

IV. **Support south-south R&D collaboration models**, where countries facing the greatest burden and most affected by climate-sensitive diseases lead R&D priority setting and development. Countries in the Global South share commonalities in terms of challenges faced. This also presents scope and opportunities for South-south and triangular research collaboration and partnerships- building on and enhancing capacities to address health challenges of climate change.

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