

From milligrams to megatons:

A climate and nature assessment of ten key health products

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Executive Summary

The risks associated with climate change and degradation of nature pose grave threats to global public health, and affordable, sustainable solutions have not yet been fully developed. It is becoming increasingly imperative for organizations in global public health to meet four objectives:

- Climate resilience. Climate change has been identified as the greatest threat to human health of the twenty-first century.¹ It is expected to worsen a range of medical conditions, including vector-borne diseases, other infectious diseases and maternal and child health. Additionally, disasters will become more frequent and severe, imperiling the capacity of healthcare systems to provide accessible services. Vulnerable populations in Low- and Middle-Income Countries (LMICs) will be disproportionately affected. Unless value chains and health products are climate-proofed made resilient to these shifts - the United Nations' Sustainable Development Goal 3 (SDG3), which is meant to ensure "good health and well-being," will be much more difficult to accomplish.²
- **Decarbonization.** As the source of 4.6 percent of global emissions³, health value chains contribute significantly to climate change. Rapid decarbonization of the sector is thus required to meet the Paris Agreement's objectives on warming.
- Nature positivity. As with climate change, the degradation of the natural environment affects public health. Environmental pollution poses a major risk to health (for example, air pollution leads to 7 million deaths per year⁴), and health value chains have significant effects on the environment through water use, wastewater discharges, and generation of plastic waste.⁵ By making health value chains "naturepositive" – that is, helping to build nature's resilience and restoring it to 2020 levels – actors can avoid unintended, detrimental effects on health and align with global commitments to conserve biodiversity.⁶
- Affordability. To ensure widespread access to life-saving treatments, measures taken to meet sustainability objectives must simultaneously assure affordable healthcare. At present, however, little information is available on the potential trade-offs between cost and sustainability, and how those trade-offs can be managed.⁷

4 https://www.who.int/news/item/22-09-2021-new-who-global-air-quality-guidelines-aim-to-save-millions-of-lives-from-air-pollution.

¹ https://www.who.int/news-room/spotlight/ten-threats-to-global-health-in-2019; https://www.paho.org/en/topics/climate-change-and-health.

² https://documents1.worldbank.org/curated/en/322251495434571418/pdf/113572-WP-PUBLIC-FINAL-WBG-Climate-smart-Healthcare-002.pdf.

³ Romanello et al., Lancet Countdown, The 2023 report of the Lancet Countdown on health and climate change.

⁵ https://www.thelancet.com/journals/lanplh/article/PIIS2542-5196(20)30121-2/fulltext.

⁶ https://www.unep.org/news-and-stories/story/cop15-ends-landmark-biodiversity-agreement#:~:text=The%20GBF%20consists%20of%20four,to%20 people%20are%20valued%2C%20maintained.

⁷ https://noharm-global.org/sites/default/files/documents-files/5961/HealthCaresClimateFootprint_092319.pdf.

These imperatives are particularly essential for health products supply chains, as these are highly complex and global, depend on many physical assets, processes and routes, are known to represent over 70% of healthcare's emissions⁸, and are central to the provision of equitable access to health.



This report describes some of the key sustainability issues affecting health value chains of ten health products, and charts a path toward managing them. Its contribution is threefold. First, the report assesses greenhouse gas emissions, effects on nature, and the climate risks associated with ten strategic products in global public health that are critical in the fight against HIV, Tuberculosis, Malaria, for women and children's health and when dealing with global emergencies in LMICs. This assessment is conducted along the whole supply chain, from raw material acquisition to waste disposal. Second, it sets out an agenda of actions that will mitigate detrimental effects and risks, with a focus on maintaining affordability. Finally, the analysis is presented in a framework that can be applied to other health value chains in accordance with leading standards for risk assessment and disclosure.⁹ Figure 1 below introduces the value chains that are the focus of this study.

Romanello et al., Lancet Countdown, The 2023 report of the Lancet Countdown on health and climate change.

9 TNED website; Official Journal of the European Union (2022) Directive (EU) 2022/2464 of the European Parliament and of the Council of 14 December 2022.

Figure 1. 10 priority health products have been selected based on relevance for & representativeness of the Unitaid portfolio and disease space

| Archetypes | Typical products | Focus products | | | |
|--------------------------------------|--|---|--|--|--|
| Small molecule | Oral medications | & Heat stable Carbetocin | | | |
| medicines | Injectable medicines | X Long-acting injectable Cabotegravir | | | |
| | | Oolutegravir-based first line regimen | | | |
| | | Bedaquiline, Pretomanid, and Linezolid (BPaL) | | | |
| | | Artemisinin-based combination therapy | | | |
| Rapid diagnostics | Lateral Flow Assay products (Rapid tests) | R HIV Self-Testing | | | |
| Point-of-Care diagnostics | Point-of-Care PCR testing platforms | Point-of-Care PCR platform for MTB test | | | |
| Integrated diagnostic platform | Lab-based PCR testing platform | High-throughput PCR platform | | | |
| Vector control products | Insecticide- based vector control products | Long Lasting Insecticide- treated Net (dual active ingredient nets) | | | |
| Others | Production of medical oxygen | Pressure swing adsorption oxygen generating plant (PSA O ₂ plant) | | | |
| & Women & Children | | Tuborculosis (Q) / Malaria | | | |

Emergencies

health

Figure 2. While many factors have been accounted for in the calculation of emissions, it is useful to summarize them as a product of emissions intensity, consumption per patient and patient demand

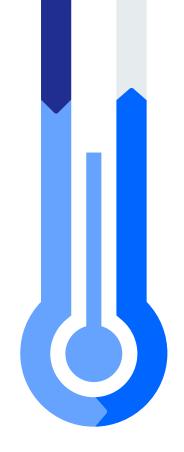
| Products | Product Emission Factor by weight, kgCO ₂ e/kg | Consumption per patient- year, kg/patient | Total GHG emission per patient-year, kgCO ₂ e/patient | Patient demand ¹ in 2030, M | Total GHG emission, ktCO ₂ e |
|--|--|--|---|---|---|
| Heat-stable Carbetocin | 7.4 | 0.03 | 0.2 | 17 | 4 |
| Long-acting Cabotegravir | 9.7 | 0.2 | 2 | 21 | 11 |
| Dolutegravir-based regimen ² | 64.4 | 1.3 | 83 | 32 | 2,657 |
| B-PaL regimen ³ | 57.4 | 0.7 | 41 | 0.1 | 2 |
| Artemisinin-based combination therapy | 6.9 | 0.04 | 0.3 | 480 | 103 |
| HIV Self-Testing | 9.4 | 0.1 | 0.9 | 30 | 27 |
| Point-of-Care PCR testing platform | 4.3 | 0.1 | 0.3 | 30 | 10 |
| High-throughput real time platform for HIV-1 PCR test | 3.1 | 0.1 | 0.4 | 31 | 14 |
| Long-Lasting Insecticide- treated Nets | 7.5 | 0.1 | 0.7 | 115 | 506 |
| Pressure swing adsorption oxygen generating plant | 0.2 kg CO ₂ e/m3 | 101m ³ | 17 | 854 M m ³ | 147 |
| | | | | | ~ 3,480 |

1. Assumptions for patients treated: 3.5 injections of LA Cab per person/year; 1 HS Carbetocin injection per patient/year; DTG 1 tablet per day; 1 cycle of malaria per patient/year; 1 regimen of B-Pal regimen per patient/year; 10 liters per minute of oxygen for 1 week per patient/year. 1 net for 2 people for 3 years.

- 2. The Dolutegravir-based regimen includes three drugs: Tenofovir, Lamivudine, and Dolutegravir.
- 3. The B-PaL regimen includes three drugs: Bedaquiline, Pretomanid, and Linezolid.

Emissions

Despite being usually small in size and weight, health products can be associated with significant footprints, as Figure 2 highlights. This is largely driven by the presence of components that are highly energy intensive to produce, such as Active Pharmaceutical Ingredient (API) in medicines and plastics in diagnostics, the frequent or continuous product use for each patient or individual, and large demand worldwide (up to hundreds of millions of beneficiaries). Dolutegravir-based HIV treatment exemplifies this: despite a daily dose expressed in milligrams of active pharmaceutical ingredient, the analysis estimates that by 2030 it will contribute 2.7 megatons of GHG emissions annually worldwide, due to a particularly emissive set of APIs, the need for daily treatment and a demand expected to reach 30 million People Living with HIV by 2030. The second largest footprint of the 10 products are dual active ingredient LLINs, which are distributed in very large quantities, and where most emissions come from the manufacturing of 57,500 tons of plastic annually. At the other end of the spectrum, heat-stable Carbetocin requires much smaller quantities of an active ingredient that is simpler to manufacture - resulting in a much smaller footprint. The central scenario of this study projects limited use of air freight in value chains, and as a result emissions from transportation are only 1% of the total. If all marine transport were displaced by air freight, transport emissions would rise to 17% of the total.



Forty percent of emissions can be abated without increasing overall costs. As Figure 3

highlights, 70 percent of emissions can realistically be abated by 2030 – of which 40 percent of the total can be removed at cumulative net-zero cost. The remaining 30 percent would increase product costs. Energy efficiency measures and the use of renewable energy can yield savings across the whole portfolio, especially in medicines, while contributing significant abatement (27 percent across the portfolio). The adoption of high-quality recycled PET (rPET) could reduce emissions per net at a cost of \$0.2 to \$0.3 per net.¹⁰

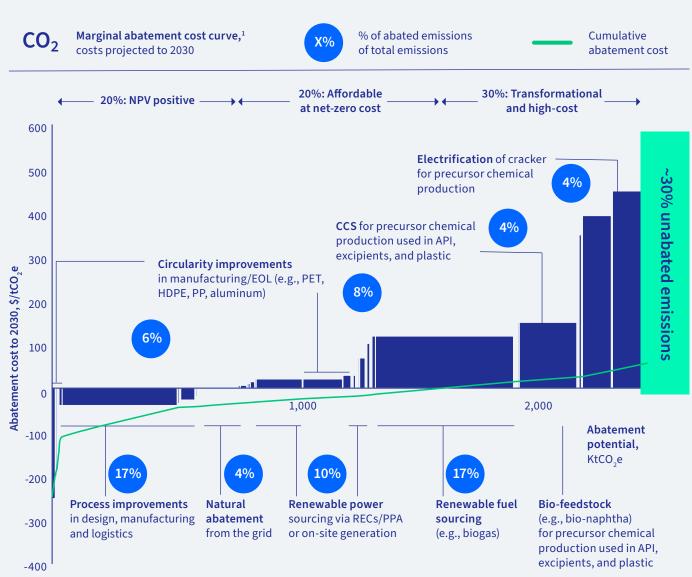


Figure 3. 40% of GHG could be abated without increasing overall costs

1. Shows a non-exhaustive list of abatement levers. Abatement costs are computed as the difference in levelized costs of production between 'from' and 'to' technologies from 2022 to 2030.

Note: All GHG abatement levers cost are assumed as the difference between cost of current technology vs. decarbonization lever net of any benefits. It does not account for any green premium that certain players may choose to apply.

Source: Expert interview, IEA, Mission Possible Partnership.

Nature

The impact on nature from waste materials is notably problematic for health value chains. These effects are a concern across the sector and are likely to be particularly challenging in settings with limited resources for waste management. While medicines tend to have impacts upstream at the point of manufacturing, nature impacts from devices is more concentrated downstream through the creation of waste products.

- Medicine manufacturing processes generate large volumes of harmful waste that require treatment. This waste can include the toxic solvents used to make APIs (e.g., ~400kg of solvents used to create 1kg of DTG API) as well as the APIs themselves, which can cause antimicrobial resistance in the natural environment. While a detailed analysis of waste management practices in the selected value chains was not possible, there is evidence that waste products are not fully treated in regions where production is concentrated. The resulting effects on public health are already significant and could become more severe as discharges accumulate.
- Downstream effects result from generation of waste products in settings without waste management resources. Dual AI LLINs alone are projected to create 57,500 tons of plastic waste by 2030. The expansion of "decentralized" products and delivery models – for example through self-testing – means that waste must increasingly be managed within communities rather than in health facilities.

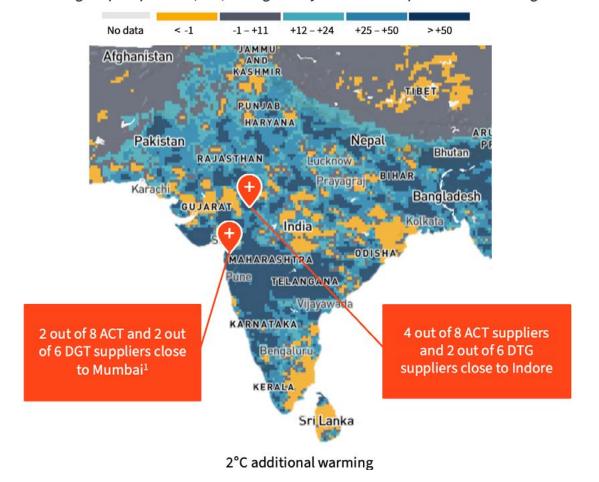
Solutions to manage discharges exist but their costs and feasibility remain untested. Investments include specialist filters for APIs and infrastructure for recycling or treating waste, while lower cost community waste management models or 'product as a service' arrangements with equipment suppliers are promising but untested at scale in target countries.

Green chemistry processes can alleviate damage to nature from synthetic medicines and save costs. While solutions that focus on managing discharges typically require investment, green chemistry approaches can reduce costs, nature damage and emissions by limiting the volume and toxicity of inputs. For TB treatments, initial pilots of green-chemistry practices have already cut raw material use by more than 50 percent¹¹. Expanding the application of these approaches to a wider portfolio of treatments could potentially mitigate detrimental effects on nature and enhance affordability. As capacity is ramped up globally and expanded across regions, there is an opportunity to implement such approaches as it is typically more cost-effective to adopt a new manufacturing process at the time of construction.

Resilience

Upstream climate risks are growing and can threaten health products' availability where value chains are concentrated in clusters. Value chains in all sectors are exposed to increasing risks of outages due to extreme events such as flooding or wildfire. As many health value chains have developed around regional 'clusters', there is a risk that a single extreme event could disrupt a substantial portion of supply. Within the portfolio of products under review, as **Figure 4** highlights, DTG and ACT manufacturers are clustered in flood exposed regions of India. Avoiding the risk of supply outages can involve a range of measures, from strengthening assets along the supply chain to increasing stockpiling; regionalization of value chains can also contribute to resilience provided output can be flexibly exported.

Figure 4. Elevated flood risk upstream due to regional concentration, and severe hazard related disruptions downstream



Change in precipitation (mm) during a 100-year storm compared to no warming

1. Firms are be counted twice if they have multiple locations.

Sources: Expert interviews, Probable Futures, <u>Supply Chain Dive</u>, <u>Times of India</u>, <u>World Health Organization</u>.

Downstream risks can create acute pressure on healthcare, though best practice disaster management and resilient health systems can mitigate this. The 2022 Pakistan floods affected healthcare needs and the ability of systems to manage them: for example, bednet distribution was affected at a point when mosquitos could spread very rapidly, leading to a fourfold increase in malaria cases [ref: "It was just the perfect storm for malaria" - Pakistan responds to surge in cases following the 2022 floods (who.int)]. Emergency management frameworks, including guidance from the World Health Organization (WHO)¹², can be more widely adopted to mitigate impacts without incurring significant investment costs. Greater heat stability of products and temperature control of value chain can also mitigate the risk of lost efficacy in the context of growing extreme heat.

Framework for action

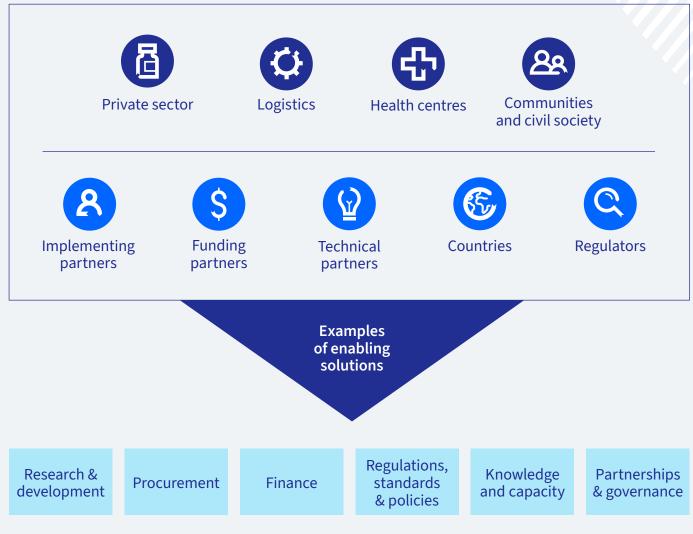
To encourage the implementation of these levers within health value chains, partners across the public health ecosystem can take catalysing steps towards making health products more "climatesmart": less carbon emissive, less harmful to nature, more resilient and responsive to climate and nature risks, and locally adapted with regards to evolving needs from health systems and communities. Several common pathways emerge across groups of key levers:

- For upstream processes such as energy efficiency or pharmaceutical wastewater treatment, multiple challenges need to be overcome in order to support implementation of more advanced processes. This includes generating and disseminating evidence on costs, feasibility and emissions, creating the right incentives through policies, regulations and standards, procurement practices and market-based approaches, enabling access to finance, and increased research on more sustainable technologies such as green chemistry.
- For upstream inputs such as renewable energy and recycled materials, barriers are more likely to be related to cost or the accessibility of sustainable inputs. This requires funders to provide incentives for value chain actors to bear these costs.

- For product design efficiencies, the challenge is to orchestrate a shift from one norm of production to another more sustainable benchmark, in a way that is economically viable and maintains affordability. Further evidence could support a switch to new designs (e.g., confirming bed nets remain stable when bulk packaged).
- For management of waste within health centers and at community level, challenges include a lack of evidence on the most effective approaches, and a lack of funding and capacity to implement them. Procurement models that combine capital and operational support, underpinned by sufficient funding and capacity building, and efforts to study new waste management models, can ensure such approaches are increasingly deployed.
- To support resilient access to products, barriers center more on information on risks (e.g. geospatial exposures to physical risks), and best practices. Improvements in tools and metrics for assessing resilience of health products supply chains, supported by capacity building efforts, can empower practitioners to do more. Further research on the efficacy of climate risk management practices in health systems could support better targeted responses.

All of these interventions require partnerships to drive progress towards climate-smart health products. As value chains expand rapidly over the course of this decade, cost-effective progress requires an alignment on priorities and supporting funding, standards, practices and policies. Only strong partnerships across the ecosystem can deliver this.

Figure 5. Critical enablers and solutions across the partner ecosystem



Source: Unitaid.

1. Introduction

Context and objectives

Global public health partnerships play an essential role in preventing and treating diseases in low- and middle-income countries (LMICs). Millions of people in LMICs die every year from preventable, treatable diseases because they cannot access the health products they need.¹³

Global health institutions such as Unitaid save lives by making medicines and treatments affordable, fit-for-purpose, and rapidly available for populations in LMICs. Over 170 million people in LMICs benefit from treatments, tests, and tools supported by Unitaid every year: this provides a critical boost to the response of countries and partners, accelerating progress by more than three years.^{14,15}

Healthcare needs are growing due to climate change and nature degradation. Climate change has been identified as the greatest public health threat of this century.¹⁶ It affects human health through many different pathways, including direct exposure to extreme heat and weather events, indirect exposure through habitats with vectorborne diseases, unsafe food and water systems, and systemic effects from economic development, poverty, and geopolitical conflicts. The impact of climate change is expected to be consequential and far-reaching. It has dramatically affected the transmission season of malaria, for example, lengthening it by around 14% in regions of Africa.¹⁷ The season is projected to extend even further, and the World Health Organization (WHO) projects an additional 250,000 deaths per year by the 2030s in part due to climate change impacts on diseases like malaria.¹⁸ Heat-related deaths are projected to increase by 370% by 2050 under a 2°C scenario. The degradation of nature, including the pollution of air, water and soil, as well as destruction of habitat, can also have a major impact on public health, with around 7 million premature deaths annually resulting from air pollution alone.¹⁹ This is comparable to the 8.9 million deaths caused by the world's biggest killer, ischaemic heart disease, in 2019.20

- 14 https://unitaid.org/assets/GF-Unitaid_EN.pdf.
- 15 <u>https://unitaid.org/assets/Impact-Story_Accelerating-access-to-se</u>.
- 16 https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(23)00056-5/fulltext.
- 17 The Lancet medical journal notes that the length of the malaria transmission season increased by around 14% in the highlands of Africa between 1951 to 1960 and 2012 to 2021: https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)01540-9/fulltext#seccestitle90.
- 18 https://www.who.int/news-room/fact-sheets/detail/climate-change-and-health#:~:text=The%20WHO%20conservatively%20projects%20250,like%20 drought%20and%20migration%20pressures.
- 19 https://www.who.int/health-topics/air-pollution#tab=tab_2.

20 https://www.who.int/news-room/fact-sheets/detail/the-top-10-causes-of-death#:~:text=The%20top%20global%20causes%20of,birth%20asphyxia%20 and%20birth%20trauma%2C.

¹³ https://unitaid.org/about-us/#en.

Climate and nature risks affect people in LMICs disproportionately because they are more exposed to these risks and healthcare systems lack the capacity to manage them.

To moderate these adverse outcomes, health value chains must adapt to climate risks and reduce their own greenhouse gas emissions and effects on nature. Health value chains, which encompass all activities required to source raw materials, then manufacture, distribute, use and dispose of products, must become more resilient. With healthcare accounting for around 4.6% of global net emissions,³ health value chains can help directly curb climate change and reduces its health impacts by taking measures to reduce their emissions. These value chains directly affect nature too; for example, many pharmaceutical manufacturers discharge toxic wastewater, which can threaten the health of nearby communities.²¹ Recognizing the need to reduce environmental impacts and adapt to climate change - in a context of complex and fragmented upstream supply chains, which represent over 70% of healthcare's emissions – Unitaid has committed to advancing health products that are less harmful to the environment, more resilient, and better adapted to climate and environmental risks. This study aligns with that commitment.²²

This report examines how actors in the global healthcare system can reduce health value chains' carbon emissions, mitigate their impact on nature, and adapt to climate change while also safeguarding the critical public health outcomes they support.

The report's contribution is threefold. First, because evidence is scarce on the climate- and nature-related impacts and risks of health value chains in LMICs,²³ the report holistically assesses the emissions, impact on nature, and climate risks associated with ten key health products in global public health. These products play a crucial role in combating HIV, Tuberculosis and Malaria, improving Women's and Child's Health, and responding to Global Emergencies. Second, the report outlines a framework for alleviating major effects and risks, including levers that could be pulled within health value chains and enabling actions that other healthcare actors could take. Finally, the analysis is presented in a framework that can be applied to other health value chains in accordance with leading risk assessment and disclosure standards, such as the standards set by the Task Force on Naturerelated Financial Disclosures (TNFD) or the Corporate Sustainability Reporting Directive (CSRD).24

²¹ For example, pharmaceutical residues have been found in drinking water, surface and ground waters, soils and animal tissues across the European Union. Studies have demonstrated that these residues are adversely impacting ecosystems and could have detrimental effects on public health by facilitating antimicrobial resistance https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:52019DC0128.

²² Unitaid (11 Nov 2021) Unitaid launches Climate Action Roadmap as UN Climate Change Conference urges action; Unitaid, Strategy 2023-2027.

²³ https://noharm-global.org/sites/default/files/documents-files/5961/HealthCaresClimateFootprint_092319.pdf.

²⁴ TNFD website; Official Journal of the European Union (2022) Directive (EU) 2022/2464 of the European Parliament and of the Council of 14 December 2022.

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The report is structured as follows:

- Section 2 details the framework used to identify the potentially harmful interactions between climate/nature and health value chains. It also describes how key health products were selected for the detailed assessment.
- Section 3 synthesizes the assessment's findings on the climate- and nature-related risks and impacts of the ten key health products.
- Section 4 provides an overview of the key levers for mitigating these risks and impacts.
- Section 5 concludes by setting out a framework for supporting the development of less harmful, more resilient health value chains throughout the global public health system.

The report includes a number of thematic case studies included as Boxes. In order of their appearance, these are: Decentralization, Green Chemistry, Circularity, Regionalization, Disaster preparedness.

Additional detail on the technical approach is provided in an accompanying annex.

2. Methodology

This section summarizes the approach used to (1) assess climate- and nature-related risks and impacts and (2) identify the levers to address them. As well as following the technical steps described in this section, the project team benefited from extensive input from an Expert Sounding Board, whose members are acknowledged in the front matter of this report.

Assessment scope

The assessment looked at the value chains of 10 selected products to determine their effects on, and risks to, climate and nature. Drawing from desk research, expert interviews, and syndication among stakeholders, the following dimensions were prioritized based on the materiality of risks and impacts that are most relevant to health value chains:²⁵

- Climate impact: Greenhouse gas (GHG) emissions
- Nature impacts: Non-GHG air pollution, water consumption, water pollution, non-hazardous waste, and hazardous waste
- Climate and nature risks: Water scarcity, mean temperature increases, precipitation changes, extreme heat, storms, wildfires, rises in sea levels, floods, and scarcity of materials.

The assessment's components align with established standards in other assessments of sustainability risks and impacts, such as the Greenhouse Gas Protocol for climate impacts, the Task Force on Climate-related Financial Disclosures (TCFD) and TNFD for nature impacts as well as climate and nature risks.²⁶ A full assessment of the risk involved in the transition to net zero emissions is not included in the scope of work, though the evaluation of material scarcity risk considers gaps in the supply of essential materials. A case study on the transition's potential impact on the price and availability of key raw materials is included in **Section 3**.

²⁵ Exploring Natural Capital Opportunities, Risks and Exposure (ENCORE) database; the Intergovernmental Science-Policy Platform on Biodiversity and Ecosystem Services (IPBES).

²⁶ Greenhouse Gas Protocol (GHG Protocol) - Product Lifecycle Accounting and Reporting Standard; TCFD website; TNFD website.

The focus products assessed were chosen from a list of 30 strategic products, based on an initial review of their individual impacts and risks and their representativeness for products and supply chains with similar characteristics. The selection of health products is based on Unitaid's "30 by 2030" list of essential new innovations outlined in Unitaid's 2023-2027 Strategy. These innovations were grouped into six product "archetypes", as illustrated in Figure 6. These archetypes encompass small molecules medicines for treatment and prevention, diagnostics products used for testing interventions, vector control products employed in Malaria prevention, and O₂ production equipment. These products were mapped to Unitaid's programmatic focus areas, addressing conditions such HIV, tuberculosis (TB), malaria, global health emergency response, and women's and child's health. Ten products (shown in Figure 1) were then prioritized based on the following considerations:

- The magnitude of their impacts and risks related to climate and nature so that the most effective mitigation and adaptation levers could be identified. These impacts and risks were assessed using high-level data and expert interviews.
- The expected demand for the product to ensure that the analysis focused on the products with the most potential for positive outcomes in public health, with consideration of climate risks' possible effects on demand, where possible.
- The products' representativeness of product archetypes and included health conditions to ensure the findings could be relevant to a wider set of products.

Features of the assessment approach

Risk and impacts were assessed in 2030, under a business-as-usual scenario. That is, they were assessed using volumes projected to 2030 and assuming current trends in policies and actions.

The approach was designed to be high-level and to prioritize the general over the specific. This assessment is intended to serve as a starting point for understanding the key climate and nature risks and impacts in the context of health product value chains. The products and value chains are therefore defined in a way that captures the product features that cause the greatest risks and have the most impact on climate and nature, while also ensuring that these insights apply to products with similar features. This approach allows the results to be replicated. The disadvantage of this approach is that it does not capture variation between products from specific manufacturers.

Additional methodological details are in a separate annex accompanying this report.

| Archetypes | Small molecule medicines | Rapid diagnostics | POC diagnostics | Integrated diagnostics platform | Vector control products | Others |
|---|--|--|---|---|--|--|
| Description | Medical interventions that are swallowed or directly administered into the bloodstream or muscle | Rapid technologies used to detect and diagnose diseases | Professionally administered diagnostic platforms which integrate assessment steps | Instrument platforms that automates steps to measure large samples of DNA and RNA variation | Basic and non-electronic devices used to identify and prevent diseases | All other products |
| Sample products from "30 by 2030 list" | Heat stable Carbetocin LA Cabotegravir | POC CD4 test | OC testing platform | PCR based testNGS based test | Long Lasting Insect- icide-treated Net Indoor residual spray ¹ | Thermal ablation device Pulse Oximeter |
| | 3HP - based Dolutegravir-based first line regimen MDR TB Nitromidazole/ diarylquinoline² ACT | COVID test | | | Spatial repellent | Medical oxygen plar |
| Key characteristics which influence risk and impact | Room temperature storage Combination air and maritime transport Exposed to climate hazards Water use important in manufacturing Professional use Environmentally harmful waste (chemicals, plastic) Other waste (e.g. cardboard) | Room temperature storage Maritime transport Exposed to climate hazards Water use important in manufacturing Self-administered Environmentally harmful waste (plastic) Other waste (e.g. cardboard) | Maritime transport Exposed to climate hazards Water use important in manufacturing Professional use Environmentally harmful | Maritime transport Exposed to climate hazards Power required for operation Professional use Other waste | Sea transport Exposed to climate hazards Water use in manufacturing Self-administered Environmentally harmful waste Other waste | Sea transport Exposed to climate hazards Power required for operation Professional use Other waste |

. х. . . _ . .





Respond to Global Health Emergencies ৰ্জ



1. Indoor residual spray requires professional application.

2. Consideration of B-PaL (Bedaquiline, Pretomanid, Linezolid).

Source: Unitaid.

The risks and impacts of each product were assessed along eight supply chain steps. The assessment considers characteristic inputs and activities for each value chain step,²⁷ as well as key geographies for these activities. These factors (such as raw materials used, production method, and transport mode) were determined based on extensive research and interview with health experts. A product's characteristics and the location of related activities are based on a broad view of the average product and are not supplier-specific, which allows the findings to be more generally applicable.

This approach comes with limitations. Using an "average" product to elucidate key risks and impacts ensures that key insights from the analysis can be applied to a broad group of products that share the same characteristics. However, this approach may have limitations in comparison to a bottom-up, product and supplier specific assessment. The approach identified the general levels of climate and nature risks and impacts which can be used to understand main areas of concern. The GHG analysis takes a more detailed approach. However, credible, publicly available data sources are scarce. The assessment therefore relies on proxies where data were not available. Additionally, the results depend strongly on where each supply chain activity was assumed to take place as, for example, a detailed analysis of risks requires geospatial analysis at the asset level to understand the underlying vulnerability.

This analysis thus used regional averages to provide a high-level view of risks and impacts. Lastly, this analysis focused on ten health products and has not studied their relative strengths or weaknesses compared to alternative or competing products (for instance, impacts and risks associated to the LLIN vector product haven't been compared to alternative vector control products such as spatial repellents).

The product analysis quantitatively assessed the climate impact of the selected product value chains and was enhanced by a qualitative assessment of nature impacts and of climate and nature risks. GHG emissions were evaluated in line with the GHG Protocol Product Lifecyle Accounting and Reporting Standard, which involves calculating GHG emissions from the production, use, and disposal of products. GHG emissions were calculated using available data on production volumes and associated emission factors. A review of data quality, consistent with an approach developed by the GHG Protocol, allowed an assessment of the relative degree of confidence in each emissions estimate. Nature impacts and climate and nature risks were evaluated gualitatively based on reputable data sources with global coverage, academic research articles, extensive expert input, and syndication among stakeholders.²⁸ This provides a systemic view of "hot spots" or areas of concern that any detailed assessment of specific cases can start from.

²⁷ The value chain consists of the following standardized steps: acquisition and pre-processing of materials, inbound transportation, production, assembly and packaging, outbound transportation, last-mile transportation, product use, and end-of-life and waste in operations.

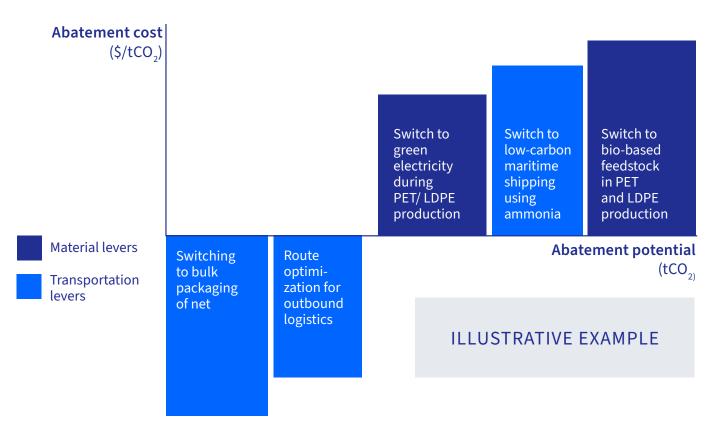
²⁸ Data sources for evaluating the magnitude of nature impacts and climate and nature risks include the IPCC, the World Resources Institute, and Climate Analytics: Aqueduct 4.0 Current and Future Global Maps Data (World Resources Institute), 1979-2019 Historical Baseline; ISIMIP, Climate Analytics 2022 (Climate Impact Explorer), 2030 1.5 degree global warming scenario (NGFS current policies).

Identification and prioritization of levers for mitigation and adaptation

Mitigation and adaptation levers were identified based on extensive research and expert review.

 For levers that mitigate GHG emissions, a quantitative approach was used.
 Decarbonization levers are prioritized using marginal abatement cost curves (MACCs) for each selected product. MACC curves represent present the least cost way of achieving any level of decarbonization by ordering available levers and associated levels of abatement in order of their cost of implementation. Figure 7 below illustrates. The MACC curves presented in this project represent estimates of the costs and levels of abatement that can be achieved in relevant countries in 2030 under conservative projections of policy action and technological progress.

• Levers that mitigate nature-related impacts and adapt to climate- and nature-related risks were identified based on a qualitative assessment, leveraging public sources and expert inputs.



Source: Unitaid.

29 Each block represents one abatement lever. The width of the block reflects the lever's emissions reduction potential in a given year. The height of the block reflects the annual abatement cost to reduce emissions by 1 tCO_2 with this lever. The abatement cost is the cost difference between the mitigation lever and the conventional technology, divided by the total abatement over the technology's lifetime. Levers are typically sorted by increasing abatement costs for the reduction of emissions by 1 tCO_2 e.

Figure 7: Illustrative MACC for long-lasting insecticidal nets in 2030²⁹

3. Synthesis of overarching impacts and risks

This risk and impact assessment exposes issues concentrated at the top and bottom of health value chains, as **Figure 8** summarizes Emissions, which are driven by energy-intensive acquisition of raw materials and product manufacturing, are concentrated upstream in value chains. Effects on nature, which are mainly caused by unmanaged waste products, are concentrated upstream and at the end of product life. All stages of the product value chains are exposed to climate risks; the resulting effects are present both upstream, where production is geographically concentrated, and downstream, where hazards interrupt the delivery of care.

Figure 8. Emissions are concentrated upstream, while nature impacts and climate risks are at both ends of the value chain

| High nat | ure impact | High clir | nate and nature | risk E | missions intensit | y High | Medium | Low |
|---------------------------------------|--|-------------------------------------|-----------------|-----------------------------------|--------------------------------------|---------------------------------------|------------------------|-----------------------------|
| | A Material acquisition & pre- processing | B Inbound transport- ation | C Production | D Assembly and packaging | E Outbound transport- ation | F Last mile transport- ation | G Product use | H End of life & waste |
| Medicines | Ŷ | | Ŷ€ [₿] | | | 6 | € [}] | |
| Rapid diagnostics | Ŷ€ [₽] | | Ŷ | | | € [₽] | | φ |
| Point of care diagnostics | ¢& | | (E) | | | €€ [↓] | 65 ¹ | Ŷ |
| Integrated diagnostics platform | Ŷ€ [₽] | | E ! | | | €€ [↓] | 65 ¹ | Ŷ |
| Vector control products | Ŷ€ [₽] | | Ŷ€ [₽] | | | 65 ¹ | | Ŷ |
| PSA O ₂ plant | Ŷ | | | | | 65 ¹ | S | |

3.1 Climate impact: GHG emissions concentrated upstream and comparable to other health product value chains

GHG emissions across the selected products' value chains are largely concentrated upstream.

1. Materials acquisition:

Materials acquisition, pre-processing, and manufacturing activities account for around 95 percent of the selected products' total GHG emissions. Materials acquisition and pre-processing activities, which are primarily concentrated in China and India, contribute ~80 percent to the total emissions.

- a) Active pharmaceutical ingredients: APIs used in medicine manufacturing account for most of these emissions (around 70 percent). API production is highly emissive, largely due to extraction from hydrocarbons and to processing these hydrocarbons into the base chemicals needed for API synthesis. These processes generally require high temperatures of about 450°C generated from fossil fuels. Drivers of variation in emissivity between different medicines are discussed in more detail below.
- b) Others: Within the portfolio of products reviewed, plastics and metals account for 8 percent and 2 percent of materials acquisition emissions, respectively.

2. Manufacturing:

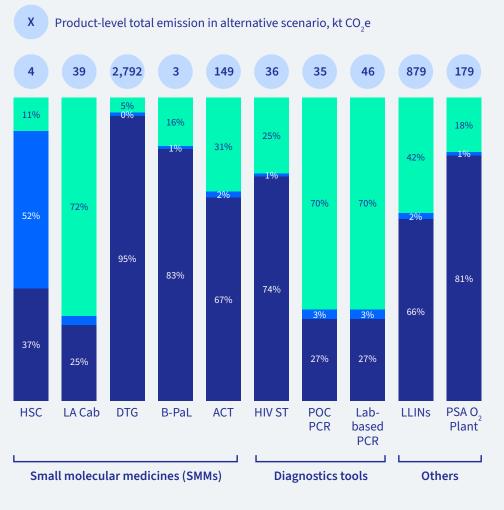
Manufacturing is responsible for around 10 percent of the selected health products' value-chain emissions. The main driver of manufacturing emissions is electricity use, particularly in producing the Dolutegravir-based regimen and LLINs products. Emissivity of electricity is higher in China and India, largely due to higher shares of fossil fuels in these countries' grid-mix. Additionally, variations in industrial practices related to energy efficiency, along with differing regulations and environmental policies, significantly influence the amount of emissions generated by manufacturing.

3. Transportation:

Transportation's share of emissions in the supply chain is only 1 percent of total emissions in the current scenario with mix use of sea, road, and air transportation. This finding is based on an assumption that all ten products will be deployed at sufficient volume to be transported to usercountries by sea, although around 60% of heatstable Carbetocin will continue to rely on air freight. However, if air freight were to replace all marine transportation, logistics emissions would increase by 17-fold to account for around 17 percent of total emissions. As Figure 9 shows that emissions from diagnostics products (i.e., PCR and POC-PCR) and LA Cabotegravir will increase most (by two to three times), because ~8-9 percent of product-level emissions originate from marine shipping.

Most GHG emissions are generated by the Dolutegravirbased regimen and LLINs.





Comments

- If air freight is extensively used and replaces all marine transportation in our analysis scenario, it causes transport to account for 17% of all emissions.
- Air freight emission for LA Cabotegravir products will make up ~72% of total emissions in the alternative scenario, primarily due to marine transportation accounting for approximately 9% of its total emissions in the current scenario (the highest logistic emission contribution at the product level).

Additional emission from air freight in the alternative scenario: switching all marine transportation to air freight

Emission from transportation based on current scenario (mix of marine, road, and air)

Emission from other value chain

1. Using an average of India-Africa and China-Africa cases, it is assumed that switching from sea freight to air freight results in a 40% decrease in distance.

Figure 10. Overview of the ten products' total GHG emissions

| | | | Ð | 5 | , | e | |
|-----------------------------------|--|--|--|---|--|--|---|
| Archetypes | Small molecule medicines | Total GHG emission, ktCO ₂ e | Percentage out of total product portfolio GHG emission, % | Patient demand ¹ in 2030, M | Total GHG emission per patient-year, kgCO ₂ e/patient | Consumption per patient-year, kg/patient | Product EF by weight, kgCO ₂ e/kg |
| Small molecule medicines | Heat-stable Carbetocin | 4 | 0.1% | 17 | 0.2 | 0.03 | 7.4 |
| | Long-acting Cabotegravir (CAB-LA) | 11 | 0.3% | 21 | 2 | 0.2 | 9.7 |
| | Dolutegravir-based regimen ² | 2,657 | 76% | 389 | 83 | 1.3 | 64.4 |
| | B-PaL regimen ³ | 2 | 0.06% | 0.1 | 41 | 0.7 | 57.4 |
| | Artemisinin-based combination therapy (ACT) | 103 | 3% | 300 | 0.3 | 0.04 | 6.9 |
| Rapid diagnostics | RIV Self-Testing | 27 | 0.8% | 30 | 0.9 | 0.1 | 9.4 |
| Point-of-Care diagnostics | Point-of-Care PCR testing platform | 10 | 0.3% | 30 | 0.3 | 0.1 | 4.3 |
| Integrated diagnostic platform | High-throughput real time platform for HIV-1 PCR test | 14 | 0.4% | 31 | 0.4 | 0.1 | 3.1 |
| Vector control products | Long-Lasting Insecticide- treated Nets (LLINs) | 506 | 15% | 115 | 0.7 | 0.1 | 7.5 |
| Others | Pressure swing adsorption oxygen generating plant (PSA O ₂ plant) | 147 | 4% | 854 M m ³ | 17 | 101 m³ | 0.2 kgCO ₂ e/m ³ |
| | | ~3,480 | | | | | |
| Major emission contributor | Women & Children's health | HIV & Co-infection | s 🚺 T | uberculosis | Respond to Health Emer | | Malaria |

1. Assumptions for patients treated: 3.5 injections of LA Cab per person/year; 1 HS Carbetocin injection per patient/year; DTG 1 tablet per day; 1 cycle of malaria per patient/year; 1 regimen of B-Pal regimen per patient/year; 10 liters per minute of oxygen for 1 week per patient/year. 1 net for 2 people for 3 years.

2. The Dolutegravir-based regimen includes three drugs: Tenofovir, Lamivudine, and Dolutegravir.

3. The B-PaL regimen includes three drugs: Bedaquiline, Pretomanid, and Linezolid.

Figure 11. Overview of the ten products' GHG emissions per patient year

| | | | | | · · · · · · · · · · · · · · · · · · · | • | × | | |
|-----------------------------------|----------|--|---------------------------------|---|--|---|--|---|-------------------------|
| Archetypes | Small | l molecule medicines | Top emission category | Emission from top emission driver per patient-year, kgCO ₂ e/patient | % of emission from top emission driver | Total GHG emission per patient-year, kgCO ₂ e/patient | Top emission driver consumption or activity per patient-year | Top emission driver emission factor | Main driver |
| Small molecule medicines | 8 | Heat-stable Carbetocin | Outbound air freight | 0.1 | 57% | 0.2 | 239 kg*km | 0.001 kgCO ₂ e/ kg*km | Air freight distance |
| | 8 | Long-acting Cabotegravir (CAB-LA) | API | 1 | 66% | 2 | 0.002 kg | 572 kgCO ₂ e/kg | API emission factor |
| | 8 | Dolutegravir-based regimen | API | 73 | 89% | 83 | 0.2 kg | 314 kgCO ₂ e/kg | API emission facto |
| | | B-PaL regimen | API | 33 | 82% | 41 | 0.2 kg | 190 kgCO ₂ e/kg | API consumption |
| | | Artemisinin-based combination therapy (ACT) | API | 0.2 | 60% | 0.3 | 0.003 kg | 47 kgCO ₂ e/kg | API emission factor |
| Rapid diagnostics | 8 | HIV Self-Testing | Natural gas in manufacturing | 0.6 | 66% | 0.9 | 0.1 CCF | 6 kgO ₂ e/CCF | Natural gas usage |
| Point-of-Care diagnostics | | Point-of-Care PCR testing platform | Plastics for consumables | 0.2 | 49% | 0.3 | 0.1 kg | 3 kgCO ₂ e/kg | Plastic consumption |
| Integrated diagnostic platform | 8 | High-throughput real time platform for HIV-1 PCR test | Plastics for consumables | 0.3 | 69% | 0.4 | 0.1 kg | 3 kgCO ₂ e/kg | Plastic consumption |
| Vector control products | A | Long-Lasting Insecticide- treated Nets (LLINs) | PET for nets | 0.4 | 52% | 0.7 | 0.1 kg | 4 kgCO ₂ e/kg | PET consumption |
| Others | Ø | Pressure swing adsorption oxygen generating plant (PSA O ₂ plant) | Electricity for product use | 9 | 52% | 17 | 0.2 MWh | 56 kgCO ₂ e/MWh | Electricity consumption |
| Major emission contributor | | Women & Children's health | HIV & Co-infe | ctions | Tuberculosis | Ś | Respond to Global Health Emergencies | Mala | ria |

Differences in emissions between the products depend on the emissivity of key ingredients, volumes required for treatment, and overall patient demand, as Figures 10 and 11.

The Dolutegravir-based regimen, which accounts for around [76 percent] of GHG emissions from the ten products, has high emissions due to all three factors: its API is highly emissive, involving a complex synthetic process with low yield; the treatment regimen requires high annual doses of API; and demand for treatment is projected to be high with 32 million People Living with HIV. Dual AI LLINs, by contrast, involve a moderate emissions-intensive input of treated plastic, with one net sufficient to protect a person for three years, but high levels of demand with 115 million LLINs projected to be supplied in 2030³⁰ driven by continuous adoption of the new generation of nets (i.e., dual active ingredient) in regions where mosquitos have developed resistance to the insecticide from the previous generation.

Among small molecule medicines, variation in perpatient emissions is driven by API consumptions.

From **Figure 10**, the BPaL regimen – the product with the second-highest GHG emissions per patient ([41] kgCO₂e/patient per year) – has an emissive API and requires large doses for treatment.³¹ By contrast, long-acting Cabotegravir, a preventative treatment, requires a much lower dosage (~0.2 kg/ patient-year) than the Dolutegravir-based regimen (~1.3 kg/patient year), and the naturally derived ACT has a less emissive API than other small-molecule medicines. Both have lower emissions per patient as a result. Among other non-medicine products, the most emissive per patient is the PSA O_2 plant which requires significant energy input (0.2 MWh/ patient-year), equaling to the annual household electricity consumption in rural eastern Africa³².

The emissions analysis is subject to some uncertainty, especially for APIs. Scientific literature on the emissivity of APIs in representative manufacturing conditions remains scarce. A topdown approach was developed to tackle this challenge. The approach builds upon key synthesis metrics, including solvent usage, yield rate, and synthesis steps to estimate APIs' emissivity (~50-825kg CO₂/kg APIs). It has also been validated against a bottom-up Life cycle analysis (LCA) approach, which is based on material/energy input in each synthesis step (see Lumefantrine case study, Figure 13). A further challenge is that manufacturing processes are closely guarded intellectual property, with publicly available data sources on API synthesis mainly focus on emissions in product development, during which processes are expected to be less efficient than when APIs are manufactured at scale. In reflection of this, emissions estimates apply an efficiency assumption of 10%-40% as highlighted in Figure 12 below.33

³⁰ https://dashboards.endmalaria.org/forecastingCommodities/long-term-forecast.

³¹ Although GHG emissions per patient per year were estimated to facilitate comparisons among products, these are challenging due to heterogeneity across products (such as acute versus chronic treatments, SMM versus diagnostic platforms, different product units, and dissimilar demand volumes). Given this heterogeneity, emissivity among products was estimated in different ways (such as per unit or per patient), but each approach has its own limitations.

³² https://www.nature.com/articles/s41598-023-40021-y#:~:text=Projected%20household%20electricity%20demand%20for.of%20South%20Africa%20in%202030

³³ From about 40 percent in waste improvements from late development to the commercial phase in 97 API manufacturing processes, <u>https://pubs.acs.org/</u> <u>doi/10.1021/acssuschemeng.1c01940</u>.

Figure 12. Outside-in proxy approach for API emission factors

| | | | High impacts | ← → | Low impacts | Lab-to-con | nmercial conversion | Es | timated emi | ssion factor |
|---|------------|--|--|--|--|--|--|---|---|---|
| SMMs | APIs | | Solvent usage (kg /kg API produced)More usage, higher emission | Steps of synthesis More steps, higher emission | Yield rate Higher yield rate, lower emissions | Conversion from lab- scale to commercial scale | Rationale | Scaling factor to benchmark API (based on weighted average multiple of three metrics) | Emission factor (kg CO ₂ e/ kg API produced) | Comments/rationale |
| Artemisinin- based | Q 0 | Lumefantrine ¹ | 6 | 5 | 48% | 10% | Efficient process | | 45 | Emission factors of Lumefantrine and |
| combination therapy (ACT) | Q 0 | Artemether ² | 5 | 4 | 19% | 10% | Efficient process | | 79 | Artermether are calculated based on bottom-up value chain analysis |
| Dolutegravir- based first | Q 0 | Tenofovir Disoproxil Fumarate³ | 83 | 5 | 27% | 0% | Already a commercial procedure | 1 | 367 | |
| regimen | ٩ | Lamivudine ⁴ | 75 | 4 | 37% | 40% | Based on academic research ¹⁰ | 0.9 | 188 | • A scaling factor was calculated based on three |
| | ٢ | Dolutegravir⁵ | 394 4 22% 40% | 3.2 | 707 | scaling metrics: 60% weight of solvent usage, 30% weigh of yield rate, and 10% steps | | | | |
| 3PaL regimen | ٢ | Bedaquiline ⁶ | 137 | 12 | 5% | 40% | | 2.3 | 496 | of synthesis • Emission factors of other |
| | ٩ | Pretomanid ⁷ | 20 | 3 | 31% | 40% | | 0.4 | 91 | APIs are scaled based on the scaling factor to the EF of Tenofovir Disoproxil |
| | ٢ | Linezolid ⁸ | 10 | 7 | 73% | 10% | Already an efficient reaction | 0.5 | 174 | Fumarate (TDF), which is from a bottom-up life cycle |
| Long-acting Cabotegravir (CAB-LA) | ٢ | Cabotegravir ⁹ | 317 | 4 | 42% | 40% | Based on academic research ¹⁰ | 2.6 | 572 | analysis. |
| Heat-stable Carbetocin | Q 0 | Octreotide | 225 | 7 | 80% | 0% | Commercial process | 1.0 | 716 | • Emission factor of Carbetocin is scaled based |
| | ٩ | Carbetocin | 250 | 9 | 80% | 0% | | 1.2 | 825 | on the scaling factor to the EF of Octreotid |
| Value-chain LCA based approach Chemical proxy approach | | <u>https://</u> <u>https://</u> | doi.org/10.1021/op doi.org/10.1021/op doi.org/10.1021/ac: doi.org/10.1021/ac: | <u>300037e</u> . ssuschemeng.2 | | | | /doi/full/10.1021/acs.op wiley.com/doi/epdf/10.1 | r <u>d.3c00187</u> . 002/ange.201 | |

- 4. https://doi.org/10.1021/acs.oprd.0c00083.
- 5. <u>https://doi.org/10.1080/17518253.2022.2057200</u>.
- 6. Note: starting materials of different synthesis may vary in complexity.
- 10. https://www.researchgate.net/publication/359643561_Three-step_synthetic_ procedure_to_prepare_dolutegravir_cabotegravir_and_bictegravir.
- 11. https://doi.org/10.1021/acssuschemeng.1c01940.

Figure 13. LCA vs. chemical proxy approach for Lumefantrine API

| | LCA approach ¹ | Chemical proxy approach ² | | | | |
|--|--|---|--|--|--|--|
| Methodology | A bottom-up approach to calculate the carbon emission based on material/energy input in each synthesis step to create 1kg pure API | A top-down approach to estimate emission factor based on the similar synthesis process of other APIs with readily available baseline data | | | | |
| Key assumptions | API name: Lumefantrine Synthesis steps: 5 steps Solvent usage: ~6 kg solvent per kg API produced Yield rate: ~48% overall yield | API name: Ephedrine HCL Synthesis steps: 4 steps Solvent usage: ~5 kg solvent per kg API produced Yield rate: ~15% overall yield | | | | |
| Estimated emission factor, kg CO ₂ e/kg Lumefantrine produced | 45 | 48 | | | | |

Details to follow

1. <u>https://doi.org/10.1021/op060244p</u>.

2. https://doi.org/10.1021/acssuschemeng.8b05473.

3.2 Effects on nature: Prevalent at both ends of the value chain and exacerbated by the concentration of activities in lowerand middle-income countries (LMICs)

The selected products negatively affect nature through water pollution and hazardous waste, which are prevalent at both ends of the value chain. The selected products' detrimental effects on nature are typical of value chains in the lifescience sector. Upstream, raw material-sourcing and manufacturing activities cause air and water pollution and hazardous waste that contaminate ecosystems, especially bodies of water.³⁴ Hazardous waste includes, for example, toxic solvents, which account for as much as 90 percent of material weight in chemical reactions during the manufacturing of APIs for the smallmolecule medicines assessed. When these solvents are improperly disposed of, they contaminate ecosystems.³⁵ Some active ingredients themselves are also toxic, such as insecticide chemicals used in the production of LLINs and Bedaquiline, which is classified as environmentally toxic. Improper disposal of active ingredient can also contribute to resistant bacteria, viruses and parasites. This is particularly an issue for antibiotics such as the components of the B-PaL regimen.

Downstream product use and disposal generate significant plastic waste. This waste can accumulate in the environment and degrades, causing the formation of contaminated microplastics and potential leaching of harmful substances into the environment.³⁶ Many health products, such as HIV self-tests, are made of plastic and for single use. LLINs have a longer lifespan of two to five years but are still expected to generate 57,500 tons of plastic waste annually by 2030.³⁷ The corresponding figure for the wider bed net market, of which dual-AI LLINs are projected to have around a 50% share, is expected to be larger still. The growing decentralization of healthcare, as discussed in Box 1, means that plastic waste will often be dispersed into communities rather than at healthcare centers, requiring different management solutions.

The selected products' downstream effects on nature are concentrated in LMICs, where many ecosystems are already facing considerable stress and the capacity for mitigation is more limited.³⁸ This applies both upstream and downstream:

³⁴ Air pollution results from raw material-sourcing, such as mining of iron ore, production processes, and road transportation.

³⁵ Solvents are the main ingredient in chemical reactions by weight and are often highly toxic. One hundred kilograms of chemical waste can be produced in the manufacturing of one kilogram of finished pharmaceutical products. Sources: <u>Nqeketo and Watts 2023</u>, Expert Interviews, <u>Constable 2020</u>, <u>Jessop 2011</u>, <u>Byrne et al 2016</u>, <u>https://pubs.acs.org/doi/10.1021/op060170h</u>.

³⁶ https://www.unep.org/resources/report/chemicals-plastics-technical-report.

 $^{\,}$ 37 $\,$ Estimated based on demand for 30 million LLINs and the plastic weight of one LLIN.

³⁸ WWF Living Planet Report; World Economic Forum: "Scaling Investments in Nature: The Next Critical Frontier for Private Sector Leadership," February 2022.

- Most upstream activities take place in Asian LMICs, where the uptake of waste management processes in industry tends to be lower than in OECD countries. This, combined with geographic concentration of some manufacturing activities, can lead to significant discharges of harmful waste products into the natural environment. For example, a 2016 study of Hyderabad, a city home to over 170 pharmaceutical manufacturers, found that water in all sampling sites was contaminated with antimicrobials, and 95 percent of the samples had concerning levels of fungi and bacteria that were resistant to antibiotics.³⁹
- Downstream activities of the selected products - from last-mile transportation to products' end-of-life - are concentrated in Africa and South and South-Eastern Asia. LMICs often lack infrastructure or regulatory frameworks to prevent or mitigate the selected health products' potential effects on nature. For example, a 2018 report from the United Nations Environment Programme (UNEP) stated that over 90 percent of waste generated in Africa was disposed of at uncontrolled dumpsites and landfills. The report forecasted that mismanaged plastic waste would grow by 2025.40 Although some policies to reduce plastic waste are in place, capacity and mechanisms to monitor their effectiveness are in early stages of development or non-existent.⁴¹ More generally, studies have highlighted links between mismanaged solid waste and adverse health outcomes from infectious diseases, including malaria.42

Further research is needed to better understand the full scope and extent of healthcare products' impact on nature. Although some substances such as Bedaguiline and insecticides are known to be toxic to the environment, the impact of up to 88 percent of pharmaceuticals on nature is not understood.⁴³ Negative effects can result from persistence, bioaccumulation, or toxicity, especially over the long term, though there is little product-specific information available on this. The Pharmaceutical Strategy for Europe, released in 2019 by the European Commission, aims to address this deficit and was updated in 2023 to improve environmental protection, including strengthening environmental risk assessments and increasing their transparency. This step will advance understanding of the environmental effects of pharmaceuticals.44

- 39 https://pubmed.ncbi.nlm.nih.gov/28444620/.
- 40 https://wedocs.unep.org/bitstream/handle/20.500.11822/25515/Africa_WMO_Summary.pdf?sequence=1&isAllowed=y.
- 41 https://www.afro.who.int/news/tackling-health-impacts-plastic-pollution-africa.
- 42 https://www.unep.org/ietc/resources/publication/africa-waste-management-outlook.
- 43 https://www.sciencedirect.com/science/article/pii/S0160412019309493?via%3Dihub; https://enveurope.springeropen.com/articles/10.1186/s12302-019-0256-3.
- 44 https://www.sciencedirect.com/science/article/pii/S0273230023001058.

Box 1: Healthcare decentralization is critical to health outcomes in LMICs but has implications for waste management.⁴⁵

Health systems are increasingly shifting prevention and treatment towards primary care, community level care and in some cases self-care. This has been shown to substantially improve health outcomes for many interventions. For example, point-of-care (POC) testing for HIV in infants between 2017 and 2019 enabled most anti-retroviral therapies (ARTs) to be initiated within one day, instead of the median wait-time of 39 days for lab-based diagnostics. Diagnostic decentralization has the strongest momentum as more threats of disease emerge and demand rises in LMICs. For example, sales of Genexpert POC tests for tuberculosis increased from around 6 million in 2015 to 12 million in 2018. Similarly, the HIV self-testing market is growing fast.

The decentralization of healthcare means waste management approaches need to be adapted to the level at which health care is delivered. A consequence of this evolution is that waste ends up being generated at lower levels of health systems: for instance 600 tons of plastic waste will be generated from HIV self-testing in 2030⁴⁶. POC testing also generates significant quantities of medical waste, including hazardous chemicals and plastics. In some cases, a reverse supply chain approach may be needed to collect hazardous waste and return it to a central point at which it can be more effectively managed. This challenge is exemplified by POC test cartridges that integrate materials that cannot be separated, limiting their recyclability. Circularity levers could help to mitigate the effects of waste in decentralized systems, as discussed further in **Box 3**.

Decentralization of care also has implications for the vulnerability of healthcare to climate and nature risks. Decentralization means that patients need to travel shorter distances to access treatment. For example, in Malawi, the median travel time for socio-economically disadvantaged patients to an ART facility decreased from 120 to 30 minutes.⁴⁷ With shorter travel distances and decentralized treatment designs, patients' access is less likely to be compromised by climate hazards. Moreover, POC testing reduces the need to transport test samples. This increases the system's resilience to extreme heat and temperature changes, as cold-chain transport for heatsensitive samples is no longer needed. However, a decentralized system also relies more on local distribution and storage of treatments and testing kits, which may be more vulnerable to climate hazards than centralized levels.

- 46 Calculated based on ~20g of plastic per test multiplied by 2030 demand of 30 million tests.
- 47 https://pubmed.ncbi.nlm.nih.gov/29329396/.

⁴⁵ Ongaro et al 2022, Boeke et al 2021, Abongomera et al 2018, Odhiambo et al 2021, Celis 2021, MSF.

3.3 Risks: Production and use are concentrated in high-risk regions, with the greatest risks downstream

The effect of climate and nature risks on health value chains increasingly threatens to disrupt both upstream production and downstream access. Climate hazards can hinder raw material-sourcing and manufacturing upstream, particularly when these are concentrated in specific, hazard-prone regions with few suppliers. Weather-related events can interrupt transportation and prevent access to the selected health products by damaging critical infrastructure.

Climate change is increasing the frequency and intensity of hazards worldwide, particularly in regions that are most vulnerable to them. The frequency and intensity of major weather events – such as extreme temperatures, heavy precipitation, floods, and droughts – are increasing due to climate change.⁴⁸ According to the Intergovernmental Panel on Climate Change (IPCC), vulnerability to climate hazards is highest in regions such as West, Central and East Africa as well as South Asia. Vulnerability is highest in regions experiencing poverty, political instability, and limited access to basic services and infrastructure, which also tend to be the focus of global health interventions. Projected changes in key geographies include a doubling of economic losses from flooding in China as warming increases from 1.5 to 2 degrees,⁴⁹ increases in extreme precipitation in India over levels that have already risen 85% since 2012,⁵⁰ and a doubling in heatwaves in regions of Africa if warming reaches 2 degrees.⁵¹

Climate and nature hazards can disrupt the selected products' upstream supply chain activities, particularly when these activities are concentrated in one region. Hazards could interrupt upstream value-chain activities by affecting manufacturing facilities, raw materials, and workforces. Products such as heat-stable Carbetocin and long-acting Cabotegravir are currently only produced by the originator and therefore are regionally concentrated, although they will become more dispersed as generic manufacturers enter the market. For other products, although global supply is produced globally, public health procurement may be limited to a specific region, increasing the risk of disruption by climate hazards. Production of medicines predominantly sourced from India, such as anti-retroviral medicine DTG, are concentrated in Hyderabad and Mumbai. These regions are often exposed to climate risks as well. For example, flooding interrupted production in Hyderabad in 2020, which affected the city's transportation infrastructure and thus production.⁵²

⁴⁸ https://www.ipcc.ch/report/ar6/wg1/downloads/report/IPCC_AR6_WGI_Chapter11.pdf.

⁴⁹ https://nhess.copernicus.org/articles/22/1577/2022/.

⁵⁰ https://www.worldbank.org/en/news/feature/2023/08/17/india-managing-the-complex-problem-of-floods-and-droughts.

⁵¹ https://onebillionresilient.org/extreme-heat-inflames-gender-inequalities/#nigeria.

⁵² https://india.mongabay.com/2020/11/hyderabad-floods-highlight-the-need-for-a-disaster-mitigation-and-climate-resilience-plan/.

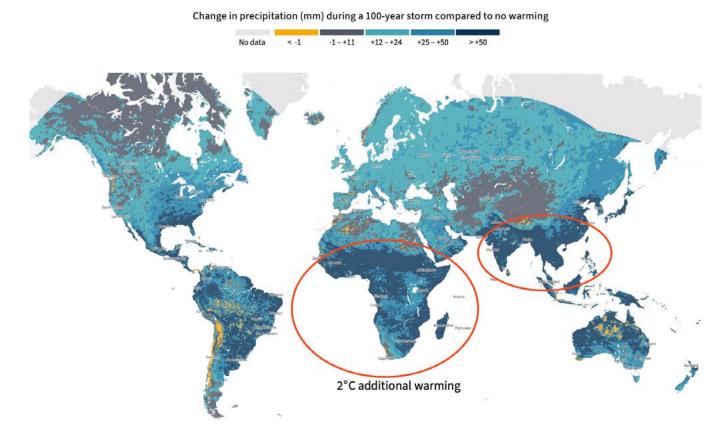


Figure 14: Flood risk is increasing with global warming, especially in regions with public health burdens

Source: Probable Futures

The selected products' downstream valuechain activities are concentrated in regions with high and increasing exposure and vulnerability to climate hazards. Most of the selected health products are used in Sub-Saharan Africa, a region that is highly exposed to climate hazards, particularly prolonged droughts and seasonal floods. In addition, the region is especially vulnerable to climate hazards due to poverty, political instability, and a less climate-resilient infrastructure.⁵³ Climate hazards therefore pose a considerable risk to the downstream value-chain activities of the selected health products. Climate hazards can, for example, disrupt transportation and restrict patient access, which is particularly problematic for products that are required for time-sensitive interventions, such as heat-stable Carbetocin, or those that require regular contact between patients and healthcare providers, such as B-PaL for multi-drug-resistant (MDR) tuberculosis. The IPCC has noted that extreme events are already disrupting health services. Multiple examples are evident:54

- Flooding in Namibia prevented delivery of medication to healthcare centers, depriving many patients of HIV medications.⁵⁵
- In Zimbabwe in 2019, low water levels in Lake Kariba, the source of the country's main power supply, disrupted health services due to electricity shortages, especially in rural and suburban areas.⁵⁶
- In Kampala, Uganda, 8 percent of main roads are at risk of flooding, which can greatly increase the time required to reach healthcare facilities. Certain neighborhoods are cut off almost completely from health services during heavy floods.⁵⁷
- Floods in South Sudan in 2021 restricted local populations' access to healthcare services.⁵⁸

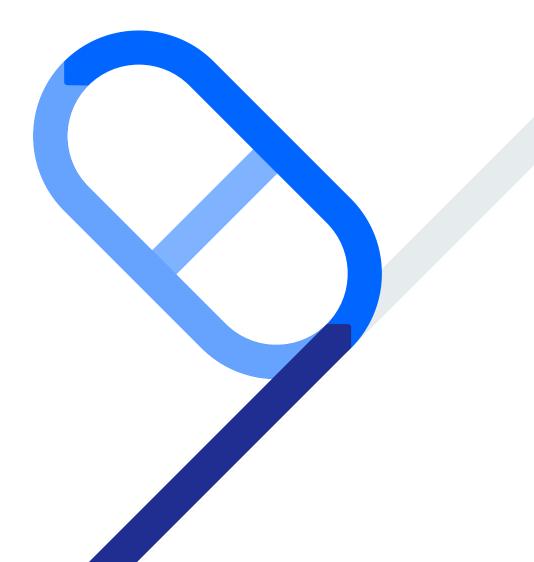
Climate hazards can increase the incidence of diseases, especially in regions with less resilience. In regions with under-developed infrastructure, disasters such as floods can multiply the incidence of water-borne diseases such as cholera, thus increasing the burden on healthcare systems. In Dar es Salaam, cholera outbreaks during rainy seasons are concentrated in areas with poor infrastructure – including drainage, water supply, and sanitation systems – which exacerbates the effects of flooding and the spread of disease. A 10mm increase in weekly accumulated precipitation led to a 1.5 to 3.5 percent increase in cholera numbers in areas lacking sufficient infrastructure.⁵⁹

Product efficacy can also be affected by increasing heat. Extreme heat events are projected to increase in frequency and severity across much of the world: for example, the average annual number of heat wave days could increase 2.5 times by 2050 in Nigeria.⁶⁰ This poses a specific risk to heat-sensitive health products, such as Dolutegravir and ACT, which have been shown to lose efficacy at high temperatures, especially when combined with high humidity.⁶¹ This can be problematic in transportation and storage, where reliable cooling may be unavailable. However, other products such as heat stable Carbetocin, LA Cabotegravir and HIV self-tests have shown high levels of stability to high temperatures⁶² and expert consultees pointed towards potential variation between "labelled" temperature tolerance and actual performance for other products.

- 54 https://report.ipcc.ch/ar6/wg2/IPCC_AR6_WGII_FullReport.pdf.
- 55 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4375215/.
- 56 https://openknowledge.worldbank.org/entities/publication/4857132b-6dfe-578f-b8d0-95fb63246e96.
- 57 https://openknowledge.worldbank.org/entities/publication/4857132b-6dfe-578f-b8d0-95fb63246e96.
- 58 https://www.afro.who.int/photo-story/who-delivers-crucial-health-supplies-flood-affected-communities-south-sudan
- 59 https://openknowledge.worldbank.org/entities/publication/4857132b-6dfe-578f-b8d0-95fb63246e96.
- 60 https://onebillionresilient.org/extreme-heat-inflames-gender-inequalities/#nigeria.
- 61 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4856632/#:~:text=Furthermore%2C%20the%20forced%20degradation%20study,were%20stable%20under%20these%20conditions.

62 For example, HS Carbetocin is resilient to temperatures of 60C for one month, LA is heat stable at 50C for 30 days CAB if packaging is in tact and direct sunlight avoided. HIV ST has been shown to retain accuracy after one month stored at 37 degrees (compared to the officially recommended limit of 30 C): https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4918937/.

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4. Synthesis of potential levers

This section presents evidence on potential levers to mitigate risks and impacts set out in Section 3 (Synthesis of overarching impacts and risks). It highlights the potential to significantly reduce product emissions at low cost, with a focus on manufacturing process improvements, sourcing of sustainable inputs and product redesign. It then considers opportunities to reduce impacts on nature through upstream and downstream waste management, as well as through green chemistry approaches to reduce both waste and emissions. Finally, it reviews options to enhance resilience to climate and nature risks, with a focus on securing downstream access to products.

4.1 Climate mitigation: Around 40 percent of value-chain emissions can be mitigated without increasing costs

Around 20 percent of GHG emissions from the selected products can be mitigated by adopting levers with a positive net present value (NPV⁶³). The adoption of these levers can both reduce GHG emissions and save costs. Most of these cost-saving levers are concentrated upstream and include:

Process improvements in manufacturing

Increasing energy efficiency, reducing fuel demand by improving heat recovery and temperature control, and adopting continuous manufacturing can reduce manufacturing emissions among all products. Moreover, green chemistry principles (see **Box 2**) can reduce or eliminate the use and generation of hazardous substances during chemical synthesis processes.⁶⁴ Today these principles can also help to reduce GHG effects with solvent recycling and reuse and adoption of green solvents (derived from agricultural crops/ plant matter) and biocatalysts (naturally occurring or engineered enzymes). For example, some pharmaceutical companies have already developed a solvent selection guide so that their chemists can choose less toxic, less flammable solvents that have less effect on the environment and better production yield and efficiency.

Packaging and product redesign

Product and packaging redesign could achieve the dual mission of reducing carbon emissions and lowering costs. In packaging redesign, switching

63 Net present value: a financial metric that evaluates the profitability of an investment by comparing the present value of expected cash inflows with the present value of outflows.

64 The 12 Principles of Green Chemistry were developed in 1998 and have been adopted by many members as a means of embedding sustainability in process design: <u>https://www.acs.org/greenchemistry/principles/12-principles-of-green-chemistry.html</u>.

to bulk packaging to reduce single-use plastics (for LLINs, for example) or redesigning medical consumables through "lightweighting" – for instance, the thin-walled plastic pipettes used in assays for the POC PCR testing platform and the high-throughput, real-time platform for HIV-1 PCR tests – can likewise save costs while cutting emissions. In product redesign, optimizing the product's form-factor/structure by refraining from using high-emission materials (for example, the plastic emission factor is ~2 kgCO₂/kg, while the paper emission factor is ~1.4 kg CO₂/kg) can help to mitigate GHG impact, especially in diagnostic products like HIV self-testing kits.

Natural abatement in the national grid

Some of the selected products are manufactured in countries with power grids that still rely heavily on fossil fuels, such as China and India. For example, 70 percent of India's electricity came from coal in 2020.⁶⁵ Projected abatement of these power grids will reduce manufacturing emissions linked to electricity use (assumed 'natural abatement', which depends on uncertain levels of uptake of clean energy). Enerdata forecasts renewable energy to account for 33 to 54 percent of India's power mix in 2030.⁶⁶

A further 20 percent of emissions can be abated by levers with cumulative neutral NPV. These levers may be NPV-negative, but their cost can be partially offset by the benefits gained from implementing previous NPV-positive levers. These levers include:

Circularity improvements in manufacturing

Recycled materials such as plastic, glass, and aluminum can be used for non-sterile medical product components, primary packaging, and/or secondary packaging. For example, the Sustainable Medicine Partnership (SMP), aims to develop closedloop recycling for pharmaceutical packaging (PVC blister packaging, for example), which contains materials that have previously been difficult to recycle.⁶⁷ In some cases, the proportion of recycled or reused content in raw materials will be limited by the need for products "clean" enough for the life-sciences industry. Industry-wide regulations can help to establish stringent compliance guidelines so that high-quality recycled materials can be used without compromising medical products' safety and effectiveness.

Circularity improvements in End of Life

At the end of the value chain, improving the recycling rate for plastic packaging materials and sterilized, medical, consumable waste – if possible – can further reduce and avoid the end-of-life emission that is otherwise landfilled or incinerated. This can be achieved by implementing eco-design principles to bolster the recyclability of medical products (by using mono-materials to enable easy recycling, for example) and improving sorting, decontamination, and/or recycling infrastructures, especially in Africa.⁶⁸

Renewable power

Renewable power such as solar, wind, hydroelectricity, and geothermal power play a crucial role in reducing GHG emissions from energy sources used. Companies can use different

⁶⁵ https://www.iea.org/countries/india.

⁶⁶ https://www.enerdata.net/.

⁶⁷ https://www.agilyx.com/agilyx-joins-the-sustainable-medicines-partnership/.

⁶⁸ BioPhorum environmental sustainability roadmap 2022 - BioPhorum.

procurement options for renewable electricity – including on-site renewable installation, renewable energy certificates (RECs), and power-purchase agreements (PPAs) – based on regional availability and technological feasibility.

In upstream manufacturing renewable power is particularly relevant as the industry shifts to electrified boilers, furnaces, and crackers and adopts heat pumps, meaning it can play a role in providing energy or heat in all chemical production processes (such as API, excipients, plastic, and glass).

On the downstream product-use side, electricity is essential for powering air conditioning and refrigeration, providing oxygen to patients, and operating PCR digitalization systems. In addition to reducing emissions, it can have an important role in supporting resilience.

The case of SEforALL, a partnership between a utility company and energy management company, in Dakwa, Nigeria, illustrates the relevance of developing decentralized renewable energy systems. SEforALL has implemented a solar energy system with photovoltaic panels at the Dakwa Primary Health Centre (PHC). This system provides 3 kWp using 12 solar panels and four batteries, storing energy accumulated during the day to meet needs in the evening. Additionally, refrigerators and fans have been installed at the Centre, and the lighting system has been replaced with a more energy-efficient one, thereby improving overall energy efficiency.

Renewable fuels

Renewable fuels can also be adopted by various upstream supply players – including chemical, glass, and metal manufacturers – to provide lower carbon industrial heat/steam for medium-to-high temperatures. However, these sources of energy derived from more sustainable fossil fuels (such as biomass, biogas, and green hydrogen) may face barriers to adoption based on feedstock availability, regulatory applicability, and load-profile applicability. Furthermore, as this energy source still involves combustion, GHG emissions persist.

However, an additional [30 percent] of emissions can be abated by adopting transformational but high-cost levers. These levers include more costly technologies that have yet to be commercialized at large scale, including carbon capture and storage (CCS), the use of sustainable feedstock, and the electrification of crackers for all precursor chemical (ethylene, etc.) production at tier-n suppliers. For CCS, several U.S.-based oil & gas companies are already announcing CCS projects in plastic and packaging production. Additionally, these companies are planning a CCS hub in Houston, where 95 percent of US ethylene production is concentrated.⁶⁹ As a potential sustainable feedstock solution, a few companies have already demonstrated bio-ethylene production from bioethanol, but questions remain about its commercialization potential.⁷⁰ Since these longterm transformation technologies are still nascent, capital investment, market demand, and regulatory measures will be needed to accelerate their adoption worldwide.

70 https://www.lummustechnology.com/news/releases/lummus-and-braskem-announce-partnership-for-green.

⁶⁹ https://corporate.exxonmobil.com/news/news-releases/2022/0120_industry-support-for-large-scale-carbon-capture-and-storage-gains-momentum-in-houston.

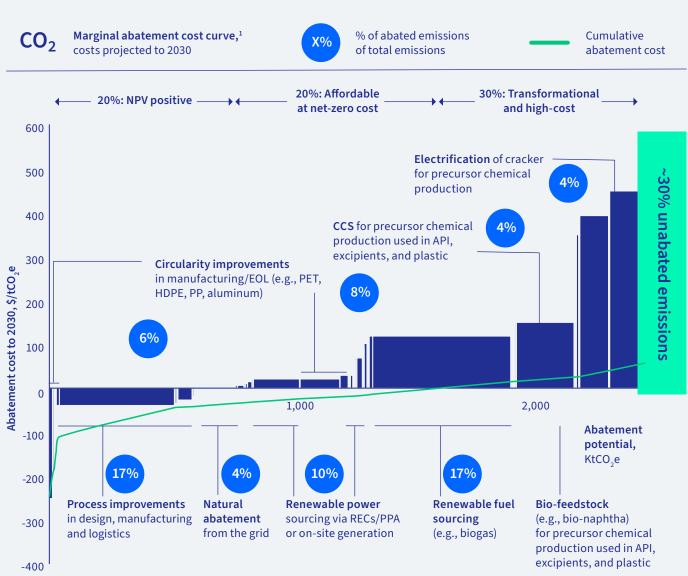


Figure 15. 40% of GHG could be abated without increasing overall costs

1. Shows a non-exhaustive list of abatement levers. Abatement costs are computed as the difference in levelized costs of production between 'from' and 'to' technologies from 2022 to 2030.

Note: All GHG abatement levers cost are assumed as the difference between cost of current technology vs. decarbonization lever net of any benefits. It does not account for any green premium that certain players may choose to apply.

Source: Expert interview, IEA, Mission Possible Partnership.

Key insights

Process improvements

to reduce fuel/material

HS Carbetocin has a high

NPV-positive abatement potential, due to the

continued use of air freight

Diagnostics have 10–20%pt

less abatement potential than SMMs, reflecting

products

Lower rate of CCS,

 Limits to recycled plastics used in sterile medical

sustainable feedstock,

e-cracker in India/China

for plastic manufacture

demand across API/plastic drive ~15% NPV savings across all products

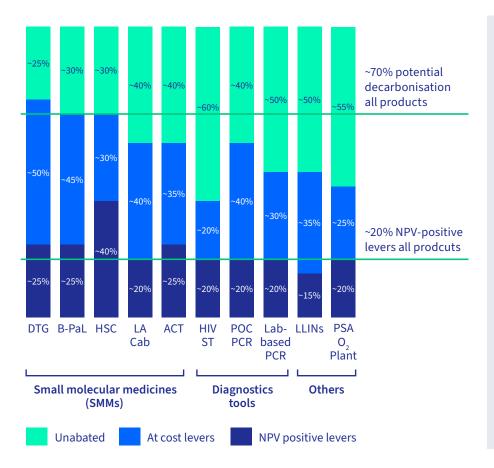


Figure 16. Abatement potential across products based on lever implementation scenarios, %

Source: Unitaid

Across 10 selected products, NPV-positive levers can abate at least 15% of emissions for all products. As Figure 16 indicates, abatement potentials for most products with NPV-positive levers range from 20%-25% due to comparable process improvements during API/plastic manufacturing to reduce fuel/material demand. However, HS Carbetocin has the highest abatement potential (~40%) with NPV-positive levers because the modal shift from air to marine can address ~25% of total emission without increasing additional cost. When looking at abatement potentials with all levers, Diagnostics tools tend to have~10%-20% lower abatement potential than small molecule medicines with all levers, due to lower feasibility to reduce the key material (i.e., plastic) emission in the near term. This is mainly driven by the limitation of recycled plastics used in sterile medical products and lower adoption rate of low-carbon plastic production technology using CCS, sustainable feedstock, e-cracker in India/China.

4.2 Nature impact mitigation: approaches to managing discharges are not yet adopted at scale in LMIC, while green chemistry approaches may reduce impacts and costs

Upstream approaches to waste management are established but costly. Manufacturers can reduce hazardous and non-hazardous waste by improving waste treatment. For example, advanced wastewater filtering on APIs and improved incineration of toxic solvents could curb the leakage of hazardous materials into the environment.

These processes have been widely adopted in higher-income countries, but in several locations where the selected products are manufactured, adoption has been less robust – partly due to cost.⁷¹ Opportunities to reduce impacts of waste by controlling upstream inputs hold significant promise. Product manufacturers could also lessen their impact on nature by sourcing more sustainable plastics. For instance, bio-based or carbon-capture-based alternatives to plastic can reduce hazardous waste and water use from the raw-materials stage of plastic-heavy products, such as LLINs and HIV self-tests. Over the medium term, green chemistry approaches hold significant promise for mitigating damage to nature while lowering costs (see **Box 2** below).



*Box 2: Green chemistry principles can mitigate detrimental effects on nature and improve efficiency*⁷²

The use of green chemistry in product manufacturing could reduce discharges of harmful waste products while increasing raw-material efficiency. "Green chemistry" refers to a variety of innovations that make chemical processes more sustainable. Green chemistry principles can be applied across the life cycle of a chemical product to prevent pollution, lower or eliminate hazardous waste, boost efficiency, and reduce raw-material usage. Simplifying chemical processes, which generate waste at each chemical-reaction step, can diminish waste. For example, decreasing the number of steps needed to synthesize and purify APIs typically improves efficiency and lowers costs. Similarly, biocatalysis, which uses gene-modified yeast cells to produce APIs, has the potential to eliminate hazardous waste. Re-engineering processes to use inputs that are less toxic, such as green solvents, can alleviate toxicity.

Green chemistry principles are already being adopted in pharmaceutical production.

For example, Virginia Commonwealth University's Medicines for All (M4ALL) research has significantly reduced raw material costs in TB drugs using green chemistry principles to improve manufacturing processes. M4ALL has achieved a 55 to 66 percent reduction in raw materials and an 18 to 43 percent increase in yields in the manufacturing of bedaquiline, pretomanid, and sutezolid.

At-scale adoption of green chemistry principles in pharmaceuticals will require additional investment in research and development and further stakeholder engagement. Green chemistry has been gaining in popularity. Certain green processes, such as solvent recycling and replacement, are relatively mature and could be used in pharmaceutical production.⁷³ However, other processes, such as biocatalysis, are less mature. Targeted R&D support for green chemistry innovations and investment in new technology and equipment could help to improve public health outcomes, particularly in LMICs. For instance, green chemistry could be encouraged and supported (through research, funding and/or technology transfer) when new manufacturing capacity is being installed (e.g., in a context of a growing market, regionalization of manufacturing or expansion of the generic market through voluntary licensing).

72 M4ALL experts, Ngeketo and Watts 2023, Expert Interviews, Constable 2020, Jessop 2011, Byrne et al 2016.

73 For example, over 12,000 green chemistry-related patents were granted in the US between 1990 and 2019.

Health products' downstream impact on nature can be curbed through lower-cost actions that have yet to be proven at scale. Waste can be minimized by adopting the circularity levers discussed in **Box 3** below. These levers could reduce raw-material needs upstream and waste downstream. Raising awareness about correct product disposal and building capacity within healthcare systems may also reduce waste.

Lower-cost measures, yet to be demonstrated on a large scale, have the potential to diminish the downstream environmental impact of health products on nature. Waste occurring at products' end-of-life could be minimized by improving waste management capabilities and infrastructure in LMICs. For example, public-private partnerships or direct investments in recycling, co-processing, and high-temperature incineration could significantly reduce the hazardous waste that ends up in community landfills. Developing water, sanitation, and hygiene (WASH) infrastructure could decrease waste as well. For example, improved solid waste treatment can prevent hazardous waste from increasing anti-microbial-resistant (AMR), anti-viralresistant (AVR), and drug-resistant parasites. AMR is of particular concern for antibiotics and significantly threatens human health.

Box 3: Circularity levers can reduce downstream waste⁷⁴

Adopting circularity levers across public health value chains could significantly reduce their environmental impact upstream and downstream. Circularity levers decrease the need for raw materials and minimize waste by, for example, improving product design, re-using and recycling materials and products, and/or extending the lifetime of products. Improving material efficiency and re-using materials would reduce health products' adverse effects on nature from both rawmaterial sourcing and product disposal, which cause significant harm to nature in health value chains.

However, the adoption of circularity levers across global health supply chains is mainly constrained by health and safety restrictions, and decentralized use of health products. Health and safety restrictions specific to health products can prevent the adoption of certain circularity levers. Currently, health products that have direct contact with patients must be made from virgin plastics to ensure patient safety, medication purity, and reagent validity in tests. The plastics used in health products are difficult to recycle, as WHO guidance advises the incineration of any waste that has come into contact with patients. Some products used in decentralized settings and self-testing are physically designed in a way that makes them difficult and costly to recycle; for example, POC testing cartridges combine bio-hazardous, chemically hazardous, and plastic into one product.

(Continues on following page)

(Box 3 continued)

Nevertheless, circularity levers have been adopted in health systems through changes in business and contracting models. Levers such as take-back schemes can be used to collect the devices distributed in home settings, such as LLINs and HIV self-tests. All-inclusive pricing contracts, where payments are made based on patient outcome, can also encourage material efficiency by inducing manufacturers to extend product lifetimes and provide effective maintenance. Such contracts could be implemented for suitable health products, such as highthroughput testing platforms, POC PCR testing platforms, and/or PSA oxygen plants. Some companies, such as Hologic, have already proposed them.

The broader adoption of other circularity levers in health product supply chains – such as innovative product design and waste processing – will require further investment. Innovative product design and material choice can alleviate the need for virgin plastic and hazardous substances in products, thereby limiting upstream adverse environmental impact and simplifying waste management. It is estimated that plastic-free devices could enable a 100 percent abatement of polystyrene emissions, and 50 percent reduction of virgin material overall.⁷⁵ Waste processes have also been re-designed to enable recycling of single-use products. A number of commercial systems already offer a waste-to-pellet solution to transform medical plastic waste into a sellable by-product (so far limited mainly to polypropylene). Such innovative circularity levers could be implemented for suitable products such as high-throughput and POC testing kits and self-tests.

4.3 Climate and nature risks: Low-cost operational levers can mitigate key downstream risks

Efforts to strengthen resilience in value chains can focus on levers within the control of actors in the global health system. While a host of measures can enhance resilience – such as investment in resilient infrastructures and effective, national planning for disasters – this study focuses on levers that can be influenced by actors in health value chains. Diversification can enhance upstream resilience. Since the production of some products is concentrated in hazard-exposed regions, climate risks can be decreased by diversifying geographic sources of supply. As discussed in **Box 4** below, regional manufacturing that is close to end-markets could play a key role.

Box 4: The growing push for regional manufacturing capabilities could improve efficiencies and increase resilience, but there are significant barriers in the way⁷⁶

Strengthening and diversifying health related regional manufacturing capabilities presents significant opportunities to enhance the availability, affordability, accessibility and marketability of health products, despite the challenges that need to be overcome. At the same time regional manufacturing can also contribute to more efficient and climate-smart health product manufacturing and supply. Currently, a significant proportion of health products are manufactured in North America and Asia, despite their extensive use in Africa. At present, Africa imports at least 70 percent of its consumed health products, and the dependence on imports is much more pronounced in some countries within the continent. Dominant health product markets in Africa and other underserved regions are catered to by imports, but smaller, context-specific needs are often overlooked, leaving many without access to life-saving health products.

In reaction to the shortages of healthcare products induced by the COVID-19 pandemic, many regions are striving to augment their healthcare manufacturing capacity. Enhancing regional value chains presents an opportunity to lower transportation costs and carbon emissions while improving alignment with local needs. There is also evidence of opportunities to improve accessibility and affordability through regional manufacturing. Regionalization of production, moreover, can bolster supply-chain resilience by diversifying supply sources and mitigating the risk of disruptions in upstream logistics – including those caused by extreme climate events - thereby enhancing health security.

Several elements are crucial to cultivate regional manufacturing of health products, including research and development, regulatory and quality control capacity, enabling trade and procurement policies and demand generation to allow production at scale.

Regulatory institutions are indispensable to ensuring the high quality of manufactured products for both public and private markets. Africa currently suffers 42 percent of counterfeit drug cases reported by the WHO, largely in the private market and there is evidence many of these are from imports. Effective regulation is also key to promoting climate smart manufacturing and reducing mismanagement of waste that results in contamination of ecosystems. Enhancing regional manufacturing capacities is expected to play a crucial role in regulatory systems strengthening, including harmonization and reliance.

Integrating climate related opportunities and risks into regional manufacturing initiatives can contribute to making investments in this area more sustainable and competitive. Furthermore, adopting strong climate and nature standards and approaches from the start also offers opportunities to "leapfrog", enabling acceleration, optimization, and efficiency of manufacturing essential health products in Low-and Middle-Income Countries. Investing in relatively costly but highly effective solutions, such as temperature-controlling equipment or on-site renewable power, could improve supply chains' resilience. Investing in efficient temperature control – air-conditioned delivery trucks and storage units, for example – across the value chain could extend the efficacy of heat-sensitive health products, thus making them more resilient against extreme heat. Similarly, investing in on-site renewable power supply at regional health centers could prevent adverse effects from power outages caused by climate and nature hazards.

Downstream resilience of supply chains can be improved by adopting relatively low-cost, readily implementable levers, such as local disaster-

planning. The WHO has published guidelines for a climate-resilient, low-carbon healthcare system. The guidelines address disaster-planning strategies, which include integrated risk-monitoring and early warning systems, as well as climate-related emergency preparedness and management.⁷⁷ Following these guidelines will help healthcare systems prepare and build the capacity to respond to climate disasters by implementing climaterelated risk management and climate-smart policies and protocols, establishing climateinformed health-emergency management and disaster-risk management, and supporting community engagement. The WHO has also established the Health Emergency and Disaster Risk Management Framework (2019), a comprehensive approach that all actors can adapt and apply. Its key components include policy, planning, communication, and infrastructure, amongst others.⁷⁸ Effective disasterplanning strategies are discussed further in **Box 5**.

Effective disaster-planning ensures continuity of care and supports positive health outcomes. Policy-planning must be holistic in its approach and offer a clear governance structure for coordinating disaster response. This includes developing disaster and emergency policies that address healthcare provision and cover a range of hazards and responses relevant to the local context. In the Philippines, for example, the Disaster Act requires municipalities to coordinate local disaster risk management offices that conduct risk assessments, handle early warning systems, train first-responders, and coordinate response and recovery efforts. During the COVID pandemic, this requirement allowed essential services to coordinate and communicate effectively and deploy a multi-sector response.⁷⁹ In India in 2018, for example, flooding in Kerala disrupted delivery of TB medication to healthcare centers, causing shortages, but a realtime, case-based patient management system helped to preserve patient information and provided multi-purpose, frontline health workers to ensure continuity of treatment.⁸⁰

⁷⁷ https://iris.who.int/bitstream/handle/10665/373837/9789240081888-eng.pdf?sequence=1.

⁷⁸ https://iris.who.int/handle/10665/326106.

⁷⁹ https://openknowledge.worldbank.org/entities/publication/4857132b-6dfe-578f-b8d0-95fb63246e96.

⁸⁰ https://pubmed.ncbi.nlm.nih.gov/32183921/.

Box 5: Disaster preparedness enables quick and effective responses that mitigate disruption to healthcare access during climate events

Natural hazards can significantly and adversely affect health outcomes. Natural hazards impact health directly (through physical and emotional trauma, for example) and indirectly (such as by limiting access to healthcare due to damage to roads and hospitals). Some natural hazards also have widespread effects by accelerating the spread of diseases; for example, stagnant water and heat can contribute to the spread of infectious diseases like malaria.

Disaster risk management efforts can help avoid, reduce, and manage the risks from natural hazards at a relatively low cost. Disaster risk management solutions include improved data systems, disaster response protocols, training in disaster preparedness, and community engagement. Data solutions can help safeguard important patient data and provide patients with timely information. Disaster planning and protocols across healthcare centers allow frontline workers to respond and make decisions quickly. Resources such as training and funds are required to support disaster responses, particularly in LMICs. Finally, community engagement and partnerships with trusted local organizations to provide relief and improve patient outcomes can alleviate the impact of environmental hazards.

Effective disaster management and partnerships allowed the Unitaid-funded endTB trials to continue during severe flooding in Pakistan. In 2022, monsoon rain caused severe flooding across provinces of Sindh and Balochistan in Pakistan, impacting 33 million people and damaging health, transportation, and communication infrastructures. Moreover, stagnant water from the flooding facilitated the spread of malaria, putting vulnerable patients at further risk. At the time, the endTB partnership was conducting trials to treat multi-drug-resistant TB (MDR-TB). These trials require frequent contact with patients to monitor their response to medication.⁸¹ The flooding displaced 65 trial participants, but endTB's disaster management strategy prevented them from dropping out. This strategy included:

- Comprehensive and mandatory first-aid training, which equipped all employees with the skills to provide immediate assistance in their communities during emergencies.
- Fulfilling the most vulnerable participants' essential needs, such as food and hygiene products, so that treatment could be prioritized. Psychological First Aid guidelines offered to both patients and healthcare workers via a mental health hotline.
- Data solutions and tele-health models to obtain patient information securely and to connect with patients.
- Partnerships with trusted local organizations to support relief action, good patient outcomes, and community preparedness strategies.

5. Framework for action

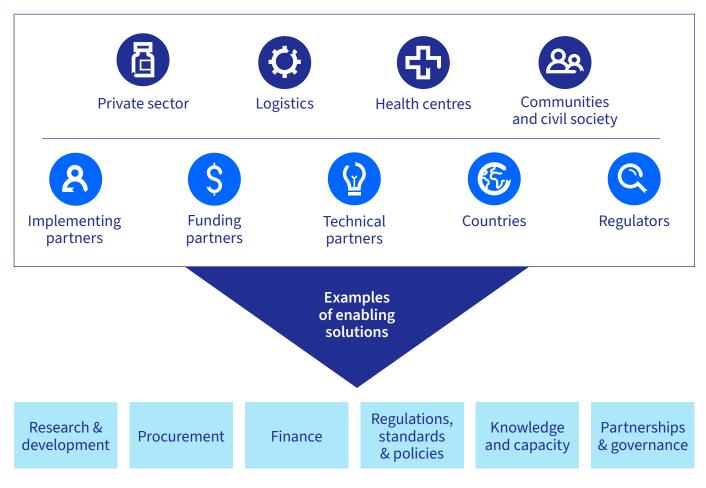
This chapter considers how stakeholders throughout the global health ecosystem could help to implement the key levers set out in Chapter 4. It frames the potential set of actors, their contribution areas, and how they might come together to promote the levers for advancing health products supply chains that are less harmful and more resilient to environmental risks, while ensuring they remain affordable for underserved and vulnerable populations.

While the proposed framework for action does not provide specific recommendations for any individual stakeholders, Unitaid will look forward to harnessing the full potential of such levers as part its climate and health strategy and through its partnerships towards introducing and shaping markets for climate-smart health products.

Actors in the value chain could implement the mitigation and adaptation levers. These actors – grouped in Figure 17 as private-sector manufacturers, logistics providers, health centers and programs, and communities – can directly implement means to decarbonize, reduce naturerelated effects, and adapt to climate- and nature-related risks.

A second group of actors in the ecosystem can have an enabling role. These groups are represented in Figure 17 as implementing partners (such as international development agencies and global public health agencies), funding partners (donors and multi-lateral development banks/ MDBs, for example), technical partners (such as universities and researchers), country-specific health systems, and regulators. They can either directly incentivize actors in the value chain to implement levers or take actions that create an environment more conducive to this. The actions they can take include setting procurement processes or regulatory standards, providing finance or capacity building, knowledge sharing or research and development, or establishing partnerships or frameworks through which stakeholders can collaborate.





Source: Unitaid.

Models of collaboration to support the levers depend on which actor implements them and what the likely barriers are. Around 20 of the most important levers can be grouped into five categories, based on the implementing actor and type of action required, as represented in Figure 17. Groups A-C are implemented by upstream actors, either through purchasing decisions (A), process changes (B), or output changes (C), while Groups D and E are implemented largely by health programs in the areas of waste management (D) and resilient access (E). (A) For upstream processes – where value chain actors may be unfamiliar with the more advanced processes – providing accessible information on business cases, technical training, and partnerships between funders and technical partners to jointly scale new processes can facilitate cost-effective implementation. Research on the broader application of green chemistry approaches can yield significant gains over the medium term. (B) For upstream inputs, barriers are more likely to pertain to cost or accessibility to sustainable components. Funders must provide incentives for upstream actors to bear these costs, recognizing that markets for recycled materials or sustainable energy may be less developed in some regions than in others.

(C) For product design, the challenge is orchestrating a shift from one method of production to another, more sustainable method in a way that maintains economic viability and affordability. This action will require strong coordination among the private sector, technical partners, funders, and implementation partners to develop standards, manage implementation risks related to new approaches (e.g. the storage of bed nets in bulk packaging), and provide technical support for the transition. (D) For downstream waste, challenges include a lack of funds and of capacity for implementation – for both the initial installation of equipment and its ongoing operation and maintenance. Procurement models that bundle these equipment costs and are underpinned by sufficient funding and capacitybuilding can ensure that equipment is used effectively.

(E) For resilient access, there is a lack of accessible information on adequate risks management approaches and best practices; demonstrating new community-centered care models that are more resilient can contribute to expanding the breadth and relevance of available solutions.

Illustrative actions – upstream levers:



- Implement catalytic market shaping interventions to incentivize product manufacturers to abate materials and energy related emissions in line with net zero goals, while minimizing financial impact on product costs
- Introduce climate and nature impacts and risks related considerations in regulatory standards
- Foster adoption of climate and nature requirements in international procurement tools and practices applicable to health products
- Expand research on green chemistry and eco-design product alternatives

Illustrative actions – downstream levers:

by extreme weathers

- Design market-based interventions to stress-test product designs and supply chains to make them more resilient and responsive to service disruptions caused
- Demonstrate community-based takeback program to reduce waste and nature impacts and increase circularity
- Develop product-specific regional manufacturing models that foster increased resilience to climate and nature risks

Underpinning all the levers is a need for enhanced data and partnerships.

A key learning from this analysis is the fact that data to understand the true environmental risks and impacts related to the health sector are not always available, particularly in LMICs. Data can be advanced through the continued development of industry standards, such as the GHG Protocol sector guidance⁸², and through further research into the emissions intensity of pharmaceutical ingredients when synthesized at commercial scale. Partnerships can drive the collection and dissemination of data, and the adoption of standards to track progress in mitigating risks and impacts. And given the wide range and systemic nature of the challenges and solutions outlined in this report, strong partnerships will be essential to drive progress – building on existing networks and initiatives, as well as new alliances and partnership models.

82 https://ghgprotocol.org/sites/default/files/tools/Summary-Document_Pharmaceutical-Product-and-Medical-Device-GHG-Accounting_November-2012.pdf.





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