

FIGHTING MALARIA

I. A GLOBAL PUBLIC HEALTH CHALLENGE

Malaria is a parasitic disease transmitted to humans through the bite of the *Anopheles* mosquito. The *Plasmodium* parasite colonizes and destroys red blood cells, causing malaria attacks with the sudden onset of fever, fatigue, headache, shivering, vomiting, etc. Attacks may be very serious, leading to severe anemia, convulsions, coma, permanent damage, and even death.

In the last 15 years, unprecedented resources have been committed to improving the coverage of preventive and curative interventions among malaria-affected communities. The R&D community has studied malaria in depth as a disease, its causes, its disease processes, its transmission, and the interventions that are needed to prevent and treat it. This has brought tremendous positive results. The incidence rate of malaria declined globally between 2010 and 2017, from 72 to 59 cases per 1000 population at risk. This represents an 18% reduction over the period.¹

In 2017, an estimated 219 million cases of malaria occurred worldwide, compared with 239 million cases in 2010 and 217 million cases in 2016.. The global tally of malaria deaths reached 435 000 deaths. In 2017, five countries accounted for nearly half of all malaria cases worldwide: Nigeria (25%), the Democratic Republic of the Congo (11%), Mozambique (5%), India (4%) and Uganda (4%).

National-level surveys in the WHO African Region show that only about one third (34%) of children with a fever are taken to a medical provider in this sector. The pace of progress must be greatly accelerated if the global malaria targets for 2020 and beyond are to be reached and many challenges threaten continued progress. They include emerging parasite resistance to antimalarial medicines, mosquito resistance to insecticides and unmet financial needs.

Malaria response is at a cross-roads and the global health community urgently needs to find another approach, resulting in a boost in funding for malaria programmes, expanded access to effective interventions especially for children and underserved population and greater investment in the research and development of new tools, as defined in 2015 by the World Health Assembly in the WHO Global Technical Strategy for Malaria, a 15-year malaria framework for all countries working to control and eliminate malaria.² . Those ambitious but attainable goals for 2030 require speeding-up innovation and intensifying partnerships.

Malaria stakeholders must continue working together to eliminate malaria for good.

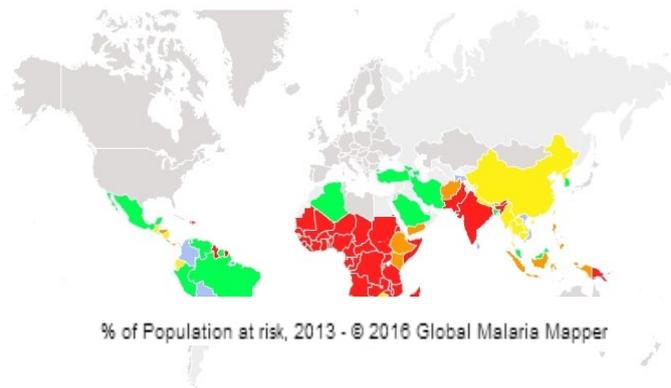
II. SANOFI GLOBAL HEALTH

Sanofi Global Health is dedicated to conduct, in collaboration with its partners, initiatives for the most vulnerable populations in low and middle income countries, to provide sustainable solutions to unmet medical needs in malaria, neglected tropical diseases, tuberculosis, diabetes, cardiovascular diseases, mental health and epilepsy.

¹ World Malaria report 2018

² WHO Malaria draft global technical strategy post 2015: http://apps.who.int/gb/ebwha/pdf_files/WHA68/A68_28-en.pdf?ua=1

Active since the 1930s in the research, production and distribution of anti-malarial drugs, Sanofi created a malaria program within its Global Health Division³ in 2001, strengthening Sanofi's role as a major player in the fight against malaria.



For more information about malaria, see:

- WHO, *Malaria Factsheet*, updated November 2017
<http://www.who.int/mediacentre/factsheets/fs094/en/>
- *Global Malaria Mapper*, created by MMV and WHO
http://www.who.int/malaria/publications/world_malaria_report/global_malaria_mapper/en/

The management of malaria is complex and requires many different types of know-how. Sanofi's malaria strategy supports the WHO and the global malaria community's vision of a world free of malaria through a portfolio of high-quality medicines, both existing and future, as well as information, education and communication initiatives and surveillance programs.

By mobilizing Sanofi's resources in support of our partners (health authorities, ministries, non-governmental organizations, experts, and universities), Sanofi Global Health is stepping up by committing to:

- Continue to provide the only hemi-synthetic quality assured artemisinin combination therapy (ACT) with a sustainable pricing and safety stock for all patients with uncomplicated *Plasmodium falciparum* malaria infection
- Develop a prequalified primaquine formulation suitable to children
- Provide the first prequalified artemether injectable for patients with severe malaria not having access to first line treatment
- Strengthen disease awareness efforts with innovative and efficient programs and tools targeting children

III. MALARIA INITIATIVES

Because drug alone is not enough, Sanofi supports a holistic approach to defeat malaria, for the appropriate prevention, diagnosis and treatment of the disease. Many different stakeholders must be involved to achieve success: scientific experts, National Malaria Control Programs (NMCPs), doctors, field nurses, community health workers, logisticians, teachers, and communities.

Success in this field requires the development of educational tools designed to meet a range of different needs, and adapted to different audiences. Along with scientific experts and NMCPs, Sanofi develops training and medical information tools to provide the most complete information possible about the prevention, diagnosis and treatment of malaria.

Targets and activities

Education manuals and training tools developed by the Sanofi Global Health Programs team are provided to public health authorities and non-governmental organizations (NGOs), so that they can be adapted to fit the specific characteristics of each country, and used in the field by legitimate stakeholders (public officials, NGOs, school teachers, etc.).

³ Formerly called Access to Medicines department

1. ASAQ Winthrop®, an affordable, high-quality anti-malarial medicine

Artesunate Amodiaquine Winthrop® (ASAQ) is an anti-malarial medicine developed by Sanofi and the Drugs for Neglected Diseases *initiative* (DNDi), within the scope of their innovative public-private partnership. ASAQ Winthrop® is an hemisynthetic quality assured artemisinin combination therapy (ACT) particularly adapted to the needs of African patients, especially children, who are most vulnerable to malaria. Dosing is simple: one or two tablets once a day, depending on weight and age. This ease of use contributes to better patient compliance and helps reduce the risk of drug resistance.

This drug is manufactured in Morocco, and is registered in most sub-Saharan African countries. Being pre-qualified by the WHO for 10 years, ASAQ Winthrop® is accessible to major international programs, such as the Global Fund, UNICEF, and the President's Malaria Initiative.

To ensure its accessibility, ASAQ Winthrop® is sold according to adapted policies consistent with applicable laws to public organizations (such as governments, NGOs, and international funders). The price, which was set by Sanofi and DNDi when ASAQ Winthrop® was first launched, at less than one dollar to treat an adult and 50 cents to treat a child, has become the standard reference price for new anti-malarial drugs.

To date, more than 490 million treatments have been distributed, mainly in Sub-Saharan Africa.

2. Developing specific adapted formulae for children

Adapted formulae of soluble Easy dissolution of tablets of ASAQ Winthrop® tablets for children has allowed easy case management of infants and children, Sanofi provided more than 200 million treatments for infants and children under five.

On the same track, Sanofi is currently working on making accessible Primaquine watersoluble tablets for children. This molecule which is widely used for *Plasmodium vivax* malaria radical cure is also recommended as transmission blocking agent in *Plasmodium falciparum* malaria elimination. In order to ensure accurate dosage per weight and ease of use, it is critical to make available adapted dosages and formulae for this essential drug.

Sanofi Global Health Programs involved in this development the center of Luleburgaz (Turkey) as well as the industrial site currently manufacturing Primaquine tablet 15mg in Cali (Colombia).

3. R&D alliances to meet future needs

Combating drug resistance: An agreement with MMV and WWARN

Given the risk of emerging drug resistance, research aimed at developing new treatments remains a priority. Although mortality rates due to malaria have fallen by more than 25% since 2000, these gains are now threatened in Southeast Asia by emerging resistance to artemisinin, a critical component in currently recommended treatments. It is crucial that all stakeholders join forces to monitor and fight the spread of resistance to life-saving drugs, and invest in the search for new medicines.

In 2011 Sanofi entered into an agreement with Medicines for Malaria Venture (MMV) to conduct research on novel malaria treatments. Both parties work to identify, characterize, and optimize new candidate compounds to treat malaria, and carry out early development programs where appropriate. This research project agreement, mainly dedicated to the smart orthology approach to malaria, has led to the identification of drug candidates from a set of Sanofi compounds selected for their potential action against malaria parasites. Each stage of the project is evaluated by the Sanofi-MMV Joint Steering Committee. Sanofi and MMV are developing a fixed-dose combination of antimalarials independent of artemisinin, currently in the Phase II stage of clinical development.

4. Addressing supply chain challenges through partnerships

In most of developing countries, public health challenges are immense, and mismanagement of the procurement, storage, distribution, and quality assurance of medicines, as well as poor communication between stakeholders, can have a dramatic impact on countries where health and transport infrastructure are often inadequate.

“Having the right drugs available, at the right time, in the right place, in sufficient quantity, and of adequate quality” could be the motto of the training program organized by the Sanofi Global Health Programs, covering the entire medicines supply chain.

The training program is developed around eight modules. These alternate teaching, evaluation, implementation, experience-sharing and group work. The program covers every step of the supply chain, from the identification and quantification of the need to the audit of medication management through procurement, quality assurance and distribution logistics. To date, the national professional staff of seven countries (Côte d’Ivoire, DRC, Ghana, Liberia, Niger, Niger, and Togo) receives this training. Through this initiative, which complements many existing information-education-communication tools, the Sanofi Global Health Programs make expertise available to its partners. Since 2016, Sanofi has been working with other pharmaceutical industries grouped in an accessibility platform to expand this initiative to more countries through partnerships to actively contribute to improving the last mile delivery challenges encountered in the developing world.

In the field, a lack of data about consumption and inventories at the local level, coupled with long supply lead times, results in frequent stock-outs in various countries. The Rapid Supply Mechanism (RSM), as part of Global Fund (GF) tenders, addresses shortages of critical medicines (which could lead to treatment disruption) by positioning inventory in the supply chain, to enable fast response times when needed. As one of the selected vendors, since 2014 Sanofi has committed to keeping a rotating stock of ASAQ in the form of finished goods ready for immediate delivery. Oftentimes, availability and readiness, the very first challenges in the supply chain, are key to ensuring accessibility of medicines. Sanofi is committed to addressing these challenges by using best forecasting practices and appropriate buffer stocks when needed.

The Malaria community is facing an emergency situation in Great Mekong Subregion (GMS) where the parasite is quickly developing resistance to current antimalarial drugs. The situation is particularly serious in very remote cross-border regions where hard-to-reach populations are exposed to almost untreatable malaria. To help delivering diagnostic and treatments there, Sanofi is working with state-of-the-art drone technology companies to develop innovative solutions. Under the name ‘Faster2Care’, this proof-of-concept project intends to demonstrate drones might represent the best, safest and cheapest way to ensure underserved population have permanent access to appropriate case management tools.

5. Promoting Behavior Communication for Change through children

Children are the primary victims of malaria, and they are also the adults of tomorrow. Educating them is an essential part of the fight against malaria. A total of over 340 000 schoolchildren, mostly between 10 and 12 years of age, have taken part in these initiatives. Over time these children are expected to convey their acquired knowledge about malaria to their peers and families. It is difficult to estimate the total number of people reached indirectly through such an initiative, since knowledge dissemination can take many different forms. Since 2012, in Côte d’Ivoire, a popular TV show for children called *Petit à petit* has broadcast the national Schoolchildren against Malaria inter-school theater contest, with an estimated audience of around eight million viewers each year.

Schoolchildren Against Malaria

The Schoolchildren against Malaria program is a behavior change communication project that focuses on the prevention, treatment and control of malaria. Through this initiative, set up in partnership with NMCPs and ministries of education, Sanofi provides teachers with information about malaria in order to promote malaria prevention behaviors through the schools.

This program aims to use schoolchildren as change agents to lead to individual behavior change and engage the community in the fight against malaria. The Schoolchildren against Malaria program was first developed through collaboration between Sanofi and the NMCP in Côte d’Ivoire. Since 2008, seventeen sub-Saharan African countries have adopted the program: Burkina Faso, Burundi, Cameroon, Côte d’Ivoire, Democratic Republic of the Congo, Gabon, Ghana, Guinea, Kenya, Madagascar, Mozambique, Niger, Nigeria, Senegal, Tanzania, Togo and Uganda.

A comprehensive range of learning tools

Moski Kit

With the MOSKI KIT, Sanofi offers children the opportunity to learn essential information about malaria, its dangers, and its prevention in a fun and interesting way. Presented in a school carrying case, the MOSKI KIT contains several complementary tools to teach key messages and remember key points. The MOSKI KIT has already been used successfully in Benin, Burkina Faso, Cameroon, Côte d'Ivoire, the Democratic Republic of the Congo, Gabon, Ghana, Guinea, Kenya, Mozambique, Niger, Nigeria, Senegal, Tanzania, Togo and Uganda. In March 2016, the MOSKI KIT was awarded the Most Valuable Patient Initiative or Service Award at the eyeforpharma Barcelona Awards.

Knowledge, Attitude and Practices Survey is currently underway in Senegal. The results will be available soon.



Moski Toon

Building on the success of the MOSKI KIT, Sanofi has expanded its range of youth-oriented tools with a didactic cartoon. This new awareness tool focusses on a boy who teaches his young cousin about the various methods for prevention and management of malaria. Its impact on children's malaria knowledge attitudes and practices has been evaluated through a dedicated KAP study in December 2016, on 410 children from 7 to 12 years old, in a mix of urban and rural households in Cote d'Ivoire and Kenya with IPSOS. This cartoon allowed children to acquire a better level of knowledge on the disease. It also encouraged them to change their behaviors regarding malaria, and to convince their relatives to do the same.

See YouTube videos:

- https://www.youtube.com/watch?v=kuUFh_dRi1s
- <https://www.youtube.com/watch?v=2ySd3WWAi5k>
- <https://www.youtube.com/watch?v=ibN48ko5oJE>
- <https://www.youtube.com/watch?v=i8Nq0B2CRD0> (cartoon – French version)
- <https://www.youtube.com/watch?v=6z1YxpoyGoU> (cartoon – English version)

IV. AWARDS

In 2015, the Chinese scientist Youyou Tu was awarded the Nobel Prize in Physiology or Medicine for the discovery of artemisinin and her role in creating a drug that helped slash malaria mortality rates in Africa and Asia, saving millions of lives. In April 2015, at the White House, Sanofi received the prestigious Patent for Humanity award from the United States Patent and Trademark Office (USPTO) in recognition of its patent on semi-synthetic artemisinin. This approach seeks to guarantee a constant supply of raw materials for the reliable production of quality medicines at a stable price. The award attests to Sanofi's commitment to public-private partnerships.

In 2016, Sanofi received an Honorable Mention from the 2016 Patents for Humanity Awards of the US Patent and Trademark Office for researching new malaria drug candidates with shorter, simpler treatment regimen that can potentially counter growing antibiotic resistance.

The educational value of the MOSKI KIT has made it a reference tool specifically for children in the fight against malaria. and was recognized with the first prize in the Most Valuable Patient Initiative or Service Award at the 2016 Eyeforpharma Barcelona Awards: <https://social.eyeforpharma.com/content/sanofis-moski-kit-wins-most-valuable-patient-initiative-or-service-eyeforpharma-barcelona>.

In 2017, Moski Toon, the newly developed educational cartoon, has been nominated for the 2018 Eyeforpharma Awards for the Most Valuable Patient Initiative category: <http://www.eyeforpharma.com/awards/finalists-2018.php>