FIGHTING MALARIA

GRI Standards :

416-1, 416-2: Customer Health and Safety

EXECUTIVE SUMMARY

Malaria is a complex disease and requires many different types of expertise to roll it up all over the world. Sanofi's malaria control strategy supports the WHO and the global malaria community's vision for a malaria-free world by 2030.

Despite significant multisectoral efforts, malaria remains a challenge in many endemic countries. For decades, Sanofi has played a key role in fighting malaria in low and middle-income countries with a comprehensive range of drugs and efficient disease awareness programs.

Concretely, Sanofi :

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

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1. 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 2018, from 71 to 57 cases per 1000 population at risk. This represents a 20 % reduction over the period.[1]

In 2018, an estimated 228 million cases of malaria occurred worldwide, compared with 251 million cases in 2010 and 231 million cases in 2017. The global tally of malaria deaths reached 405 000 deaths. In 2018, six countries accounted for over half of all malaria cases worldwide: Nigeria (24 %), the Democratic Republic of the Congo (11 %), United Republic of Tanzania (5 %), and Angola, Mozambique and Niger (4 % each).

National-level surveys in the WHO African Region show that only approximately 42 % 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 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.

The 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 programs, expanded access to effective interventions, especially for children and underserved populations, and 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. In 2019, the Global Fund called on the world to step up the fight against HIV, tuberculosis and malaria. The Global Fund released an Investment Case and launched the Sixth Replenishment, succeeding to raise US$14 billion to help save 16 million lives, avert 234 million infections, and help the world get back on track to end these three diseases.

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

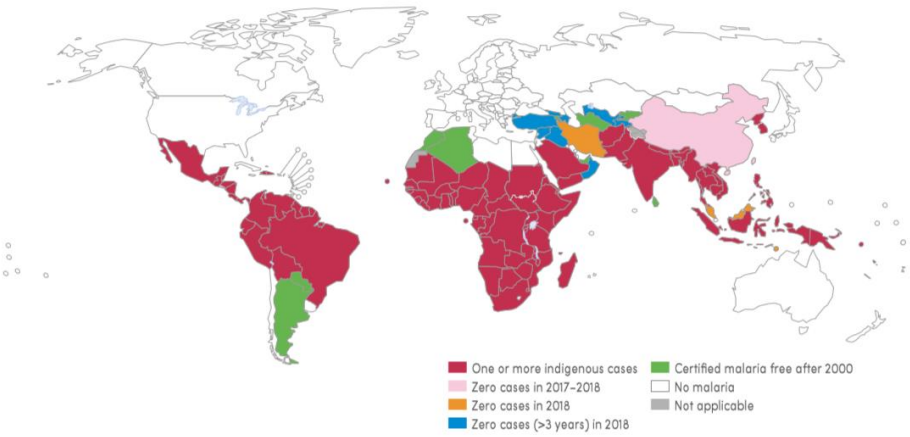
2. SANOFI GLOBAL HEALTH

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.

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

[1] World Malaria report 2019
[2] WHO Malaria draft global technical strategy post 2015: http://apps.who.int/gb/ebwha/pdf_files/WHA68/A68_28-en.pdf?ua=1

Fig 1.1: Countries with Indigenous cases in 2000 and their status by 2018



Source: FIG 1.1 WHO Malaria Report 2019

For more information about malaria, see :

- WHO, Malaria Factsheet, updated January 2020 https://www.who.int/news-room/fact-sheets/detail/malaria.
- Global Malaria Threat Mapper https://apps.who.int/malaria/maps/threats.

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, 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.

3. MALARIA INITIATIVES

Because drugs alone are 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 medical information tools to provide the most complete information possible about the prevention, diagnosis and treatment of malaria.

Targets and activities

Educational printed and digital materials 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.).

3.1. 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* (DND*i*), within the scope of their innovative public-private partnership.

ASAQ Winthrop® is an hemi-synthetic 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 with a recent renewal, 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 DND*i* 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 510 million treatments have been distributed, mainly in Sub-Saharan Africa.

3.2. Developing specific adapted formulae for children

Adapted formulae of soluble Easy dissolution of tablets of ASAQ Winthrop® tablets for children have allowed easy case management of infants and children.

On the same track, Sanofi is currently working on making accessible Primaquine dispersible 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).

3.3. 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.

Sanofi provides teachers with information about malaria in order to promote malaria prevention behaviors through the schools. In partnership with National Malaria Control Programs (NMCPs) and ministries of education, Sanofi developed a wide range of printed materials to support the teachers in delivering the key messages focused on the prevention, treatment and control of malaria. In addition, Sanofi developed games consistent with the printed materials to allow the teachers and children to play while memorizing the messages.

The overall program is called Schoolchildren against Malaria program. 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. Between 2008 and 2018, seventeen sub-Saharan African countries 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.

Recently, Sanofi took the opportunity of new technologies to developed digital solutions to complete the range of tools for children and significantly increase the population reached by prevention messages on malaria.

3.3.1. 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.

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3.3.2. Moski® Toon

Building on the success of the MOSKI KIT®, Sanofi has expanded its range of youth-oriented tools with a didactic cartoon called MOSKI® TOON. 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 Knowledge Attitudes Practices (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 available in French or English 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=i8Nq0B2CRD0 (cartoon – French version)*
  https://www.youtube.com/watch?v=6z1YxpoyGoU (cartoon – English version)
- *https://www.youtube.com/watch?v=kuUFh_dRi1s*
  https://www.youtube.com/watch?v=t831zJxNVwo
  https://www.youtube.com/watch?v=nBp9xMZV1Gc

3.3.3. Flash Malaria

The Flash Malaria videos complete Sanofi's range of Moski® edutainment tools to raise malaria awareness due to their very short duration (about 35 seconds), well adapted to social media. These eight episodes are available in French and English with subtitles and can be watched successively or on a regular basis.

The aim is to disseminate simple and short key messages related to prevention, environment and management of malaria via social media to increase the reach in malaria endemic-countries.

- *See YouTube videos* :
  - *#1: The mosquito net: https://youtu.be/fjf3rb5LF_k*
  - *#2: The wire mesh: https://youtu.be/y42lZByh1cw*
  - *#3: The environment: https://youtu.be/i78nJM7xWQY*
  - *#4: The insecticide: https://youtu.be/SWMXVDHXC08*
  - *#5: Pregnant women: https://youtu.be/vHhWbtB20ek*
  - *#6: The diagnostic: https://youtu.be/Zz2gOEPWLKc*
  - *#7: The medicines: https://youtu.be/w26Qyd5Yjro*
  - *#8: All flashes in a row: https://youtu.be/h7DrJqWOr80*

3.3.4. Moski® Memory

The latest in the range of educational tools is Moski®, which aims to raise malaria awareness among children. Moski® Memory is a Progressive Web App (PWA) to be played from any computer, tablet or mobile phone. Gamers can choose to play online or offline, in French, English, Portuguese or Swahili (*https://www.moski-memory.com*).

The objective of the game is to progress as quickly as possible in the 3 levels of play by finding the cards which allow to form "do's / don'ts" pairs. At the end of each level, an illustrated questionnaire allows to win virtual badges and move forward in the game.

Each key malaria prevention message is linked to specific drawings forming a pair and showing do's and don'ts. Through this game, players will learn and memorize key messages related to prevention, environment and management of malaria while having fun. It is hoped that players will become ambassadors of the fight against malaria to share their knowledge with their relatives and communities.

4. 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 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 educational cartoon, has been nominated for the 2018 Eyeforpharma Awards for the Most Valuable Patient Initiative category.

In 2020, Flash Malaria and Moski Memory, the newly developed flashes for social media and digital game received the award in the education category at the International Society of Neglected Tropical Diseases (ISNTD) festival.