

Stabilizing the antimalarial drug supply

Semisynthetic artemisinin could meet up to one-third of global need

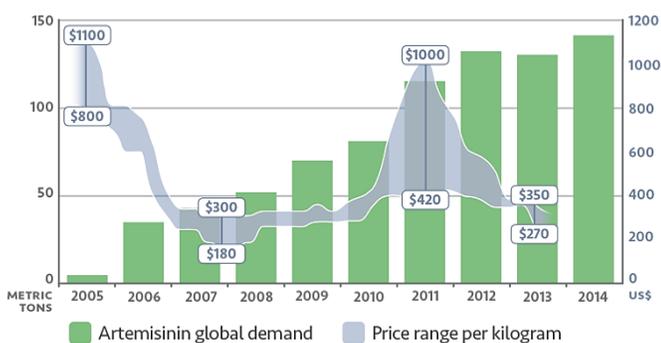
GLOBAL NEED FOR ARTEMISININ

Malaria is a significant public health and economic burden worldwide. Each year, the mosquito-borne disease sickens more than 200 million people and kills more than 620,000—most of them children under five in sub-Saharan Africa. Although malaria is often deadly in low-resource settings, it can be effectively prevented, diagnosed, and treated using a combination of available tools.

The World Health Organization (WHO) recommends artemisinin-based combination therapies (ACTs) as the first-line treatment for infection with the most deadly form of malaria, which is caused by the *Plasmodium falciparum* parasite. Globally, demand for ACT treatments from the public and private sectors has increased exponentially, jumping from 11.2 million courses in 2005 to 331 million in 2012.¹

The world's supply of artemisinin, currently derived from the sweet wormwood plant, *Artemisia annua*, is volatile. Among other factors, fluctuations in price, long growing and harvesting cycles, competing crops, political instability, and weather conditions have contributed to complicated supply planning, price volatility, and periodic shortages.

FIGURE 1. Market for artemisinin (2005–2014): Fluctuating prices complicate supply planning.²



¹ World Health Organization. World Malaria Report 2013. Available at: http://www.who.int/malaria/publications/world_malaria_report_2013/en/. Accessed February 19, 2014.

² A2S2. 2013 Artemisinin Conference. Available at: <http://www.a2s2.org/upload/5.ArtemisininConferences/1.2013Kenya/Presentations/Day1/13.A2S2MarketUpdate.pdf>. Accessed July 24, 2014; Email from Neel Lakhani, Clinton Health Access Initiative (April 2014).

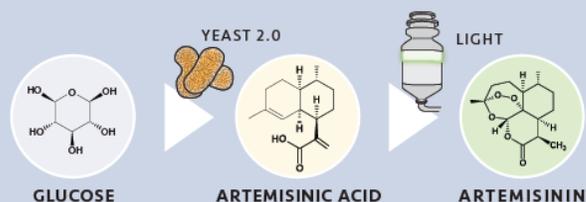
PARTNERING FOR GLOBAL IMPACT

In 2004, PATH and its collaborators launched a public-private partnership to help stabilize the artemisinin supply chain and prevent future shortages. With funding from the Bill & Melinda Gates Foundation, the group set out to develop a new pharmaceutical manufacturing process to produce commercial volumes of high-quality, non-seasonal, and affordable artemisinin to supplement the plant-based supply.

Over the next ten years, a diverse group of partners spanning the academic, biotechnology, nonprofit, and pharmaceutical sectors aligned their biochemistry knowledge, global health expertise, and manufacturing savvy to meet this goal. Together, they successfully moved the project from research to commercialization.

Several early partners held key roles. The University of California, Berkeley provided the technology on which the project was based: a process that genetically alters yeast to produce artemisinic acid—a precursor to semisynthetic artemisinin—from a simple sugar. Amyris, Inc., a biotechnology company in California, refined the process to enable large-scale production, and developed scalable processes to transfer the technology to an industrial partner.

FIGURE 2. A novel route to artemisinin.



Together, project partners developed a novel way to manufacture semisynthetic artemisinin at an industrial scale. First, genetically modified yeast converts glucose (sugar) into artemisinic acid, a precursor to artemisinin. Then, a unique process uses light to convert the acid into artemisinin.

Source: PATH

In 2007, the technology was transferred to Sanofi, a France-based global pharmaceutical company, which joined the project as the manufacturing partner. The chemistry expertise, philanthropic investment, and Sanofi's industrial experience and capacity helped bring the project from small laboratory experiments to large-scale factory production.

Other groups gave critical support by providing license rights. The National Research Council Canada Plant Biotechnology Institute, for example, granted royalty-free access to needed intellectual property.

FROM THE LAB TO THE FACTORY FLOOR AND BEYOND

In April 2013, Sanofi and PATH announced the launch of the large-scale production of semisynthetic artemisinin at Sanofi's plant in Italy. The current production capacity is 50 to 60 tons per year, corresponding to approximately one-third of the global need for artemisinin, or enough to produce 125 million antimalarial treatments per year. The current cost of semisynthetic artemisinin, from \$380 to \$420 per kilogram, is comparable to the historical average cost of high-quality, botanical production.

Semisynthetic artemisinin and Sanofi's artemisinin derivative—artesunate—received prequalification from WHO in May 2013. Prequalification ensures the quality, safety, and efficacy of semisynthetic artemisinin and confirms its comparability with plant-derived material. WHO acceptance also minimizes the regulatory burden on manufacturers who plan to use semisynthetic artemisinin in their products. Together, these advances offer a clear path to a stronger artemisinin supply chain worldwide.

Semisynthetic artemisinin creates an additional source of high-quality artemisinin to complement the plant-based supply. By doing so, it facilitates a more stable flow of artemisinin to the market, helping to ensure that the global demand for lifesaving ACT products is met.

PATH and Sanofi are continuing collaborative work on effective commercialization strategies to smooth the integration of semisynthetic artemisinin into ACTs and the global supply chain.



PATH/Laura Newman

Sanofi will distribute ACTs containing semisynthetic artemisinin through their Access to Medicines program. In 2014, Sanofi's malaria drug ASAQ is also expected to enter the market. The drug, manufactured with semisynthetic artemisinin intermediate, will pave the way for other ACT manufacturers to use semisynthetic material in other ACTs.

MORE INFORMATION

- PATH's Drug Development program: sites.path.org/drugdevelopment/
- Sanofi's Access to Medicines program: en.sanofi.com/csr/patient/priorities/access_to_care/access_to_medicines/access_to_medicines.aspx
- WHO World Malaria Report 2013: www.who.int/malaria/publications/world_malaria_report_2013/en/



www.path.org

PATH is an international organization that drives transformative innovation to save lives and improve health, especially among women and children. We accelerate innovation across five platforms—vaccines, drugs, diagnostics, devices, and system and service innovations—that harness our entrepreneurial insight, scientific and public health expertise, and passion for health equity. By mobilizing partners around the world, we take innovation to scale, working alongside countries primarily in Africa and Asia to tackle their greatest health needs. Together, we deliver measurable results that disrupt the cycle of poor health.

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