# Interventions for an Artemisinin-Based Malaria Medicine Supply Chain

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### 1. Problem Description

Artemisinin combination therapy (ACT), the most effective malaria treatment today, is manufactured from an agriculturally derived starting material *Artemisia annua*. Artemisinin, the main ingredient in malaria medicines, is extracted from Artemisia leaves and used in the production of medicine for treating malaria.

The artemisinin market has witnessed high volatility in the supply and price of artemisinin extract. Recently, a semi-synthetic source of artemisinin has been developed that may help stabilize the price of artemisinin. While commercial-scale manufacturing of semi-synthetic artemisinin from this project is just beginning (Paddon and Keasling 2014), it is unlikely to resolve all the problems in the short- to medium-term because the initial capacity will only be a small fraction of the total artemisinin supply. Some argue that a larger supply of semi-synthetic artemisinin could disrupt an already volatile market as agricultural production may decrease more than the increase in semi-synthetic (Peplow 2013).

While such ups and downs are observed in many markets with demand and supply uncertainty, the malaria-medicine market serves a larger social and public health goal where increases in consumption create a benefit externality. Because fluctuations in the artemisinin price and the uncertainty in supply and demand of artemisinin impact both the price and availability of ACTs for end patients, organizations such as the Bill and Melinda Gates Foundation, UNITAID, Clinton Health Access Initiative, Global Fund to fight AIDS, TB and Malaria, and the UK Department for International Development have started focusing on this issue. In particular, these organizations explore if certain investments/interventions can improve outcomes in terms of availability and price. Our work responds to the needs of multilateral

agencies and philanthropic organizations that are considering and pursuing interventions that affect the availability and price of ACTs and its main ingredient artemisinin. These organizations would like to know where to invest their time and effort in order to create the highest positive impact in treating malaria.

In this paper, we develop a model of the supply chain that captures the effects of such factors as available farm space, farmer's self-interest, volatility in crop yield, volatility in demand, and the introduction of semi-synthetic artemisinin on such measures as the level and volatility of medicine price and supply. We calibrate the parameters and functions of our model using data from the field and we investigate the impact of various interventions. Some of these interventions are under consideration by the global agencies and others are new areas of focus that are exposed through our analysis.

## 2. Methodology and Key Assumptions

There are two levels in our artemisinin supply chain model. Level 2 corresponds to farmers (hereinafter referred to as suppliers) and level 1 corresponds to the ACT manufacturers. While farmers and extractors are separate entities, the relevant decisions are adequately captured by treating artemisinin suppliers as a single unit.

Suppliers decide whether to produce artemisinin or the best alternative to artemisinin by comparing utilities of these two alternatives. A supplier's utility from artemisinin is positively influenced by the expected value of the artemisinin spot price and, due to supplier risk aversion, is negatively influenced by its variance. The volatility of the spot price is influenced by the degree of volatility in the harvest yield and in the size of the market. Price is assured for units under forward contract. The forward contract price is aligned with the expected spot price. Artemisinin not under contract is sold in the open market, and as such, the spot price reflects the

market clearing price. Accordingly, there is a negative relationship between the fraction of growing capacity dedicated to artemisinin and the expected spot price.

Our model contains 11 parameters and four functions. The functions are (1) a cdf of a supply random variable, (2) a cdf of a market size random variable, (3) a cdf of a willingness-to-pay random variable, and (4) a cdf of the utility of the best alternative to artemisinin. We characterize the space dedicated to producing artemisinin under equilibrium, and show that a unique equilibrium exists under mild conditions. We examine five measures of performance—expected total supply, expected fraction of total need satisfied, supplier surplus, mean spot price, and variance in spot price. We develop comparative-statics results and we numerically investigate the sensitivity of performance to changes in parameters.

**3. Summary of Major Results and Implications**

Our main conclusions are that initiatives aimed at improving average yield, creating a support-price for agricultural artemisinin, and a larger but carefully managed supply of semi-synthetic artemisinin have the greatest potential for improving supply and reducing price volatility of artemisinin-based malaria medicine.

**4. References**

Paddon C. J., J. D. Keasling. 2014. Semi-synthetic artemisinin: A model for the use of synthetic biology in pharmaceutical development. *Nature Reviews Microbiology* **12** 355–367.

Peplow, M. 2013. Malaria drug made in yeast causes market ferment. *Nature* **494**(7436) 160-161.