Incentives for development of new drugs and vaccines for low-income countries

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What is the problem?

- About 10M people are dying every year from easily curable diseases.
- Why?
  - Shortage of human resources
    - Doctors per 1000 people
      - U.S. 2.3
      - Mexico 1.5
      - Brazil 1.13
      - India 0.6
      - Namibia 0.3
      - Cambodia 0.16
      - Zambia 0.12
      - Uganda 0.08
What is the situation?

- Percentage of child-births that have no trained attendant
  - Brazil 3%
  - South Africa 8%
  - Mexico 17%
  - India 53%
  - Zambia 57%
  - Cambodia 68%
Health Care State in the Low Income Countries: Shortage of Drugs and Vaccines

- There are 12 global pharmaceuticals only 4 are involved in research and developed of neglected diseases.
- Many diseases can be effectively treated, managed, or prevented with pharmaceuticals and vaccines.
- The WHO figure of 30 percent of the world's population lacking access understates the reality;
Health Care State in the Low Income Countries: Shortages of drugs and Vaccines

- Similarly, immunization coverage globally has remained static for more than a decade at about 75 percent of children fully immunized.
- With about 27 million children born every year with no access to immunization services.
- Some effective vaccines, such as hepatitis B (HepB), are still not in routine use in many countries.
Are we doing any good?

- Kim argues by the end of 2007 3 million people in Africa are on antiretroviral drugs, a notable accomplishment even if it occurred two years late.
Are we doing any good?

Children Surviving

Child mortality rates around the world have declined by more than a quarter in the last two decades.

Under-5 mortality rate
(per 1,000 live births)

200
150
100
50

Least developed countries
Developing countries
World
Industrialized countries

Source: Unicef

THE NEW YORK TIMES
Let us look at the situation

- There are enough funds
- Health of the population is improving
- Yet, more than 10M people, per year, are dying of easily curable diseases
- If there is enough funds why are so many people die?
  - Even when there are enough drugs they are not distributed efficiently.
  - High and low levels of corruption
  - Shortages of drugs and vaccines for neglected diseases.
What can be done?

- Better supply chain management
  - For example:
    - Procurement
    - Demand forecast
    - Visibility
    - Corruption reduction
    - Reduce uncertainties in the system

- Develop and produce the necessary drugs and vaccines.
New drugs and vaccines

Drugs and Vaccine

Manufacturers are not interested to develop and produce drugs and vaccines for the developing world.

- Most vaccines that are used were developed long ago for use in the developed world. (Polio, HIV).

- There is need for new vaccine for use mostly in the developing countries (Malaria...)
Development of new drugs and vaccines

Why are new vaccines and drugs not developed?
- There is no market.
  - People and governments can’t afford paying the full price of drugs and vaccines.
  - The size of the market might be too small.

Uncertainties
- Low success rate
- Uncertainty in the underline demand
- Uncertainty in the actual orders
Development Subsidies

- Provide the drug-companies with a subsidy to develop, produce and deliver drugs and vaccines
  - What is the most efficient way to provide a vaccine or drug subsidy?
- Grants for developments
  - The manufacturer gets a grant to develop a new drug or vaccine. (push)
    - Who gets the grants?
    - What is the size of the grants?
    - Risky for the donors
    - Not efficient?
Development Subsidies

Why are pharmaceuticals willing to invest in R&D in the developed world?

- There is a chance to cover the investment
  - High price of the drug or the vaccine
  - Large markets.
    - Orphan drugs

- Is it possible to mimic the market conditions in the developing world?
A Different Type of Subsidy
Advanced Market Commitment (AMC)

• An AMC creates the **market conditions similar to those in the developed countries** to stimulate private investment in vaccine R&D and manufacturing capacity for future vaccines.

• An AMC requires donors to make **legally binding financial commitments** to support a market of a pre-agreed value. Notice the this reduces the funds-uncertainty.

• The AMC minimizes donors risk.

• **Companies** participating in an AMC **commit to supply** certain quantities of a successful vaccine.
What is an AMC (cont.)

• As demand from GAVI eligible countries materializes, the companies can receive a relatively higher price for the first few doses of vaccine (AMC price).

• Once the AMC is exhausted, companies are required to ensure the supply of the vaccine at a long term price below a pre-set cap (tail price cap).
Pneumococcal AMC

Overarching goal: reduce morbidity and mortality from pneumococcal disease.

- Accelerate development of vaccines that meet developing country needs.
- Bring forward the availability of effective pneumo vaccines - scale up of production capacity.
- Accelerate vaccine uptake - predictable vaccine pricing for countries and manufacturers.
- The AMC concept

- Financial commitment: US$ 1.5 billion from Italy, UK, Canada, Norway, Russia, Bill & Melinda Gates Foundation.
- In addition, GAVI endorsed a budget of up to US$ 1.3 billion (2010-2015)
Pneumococcal AMC

• Why make a commitment of US$1.5B?
  • It is the average revenue of a vaccine in the US.
  • The main idea is to mimic the market in the US,
How does it work? Supply Commitments

• Suppliers make a 10-year commitment to supply a share of the total demand forecast of 200 million doses annually.

• The AMC provides a directly proportional share of the US$1.5 billion.

Example:
• Firm A makes an offer to supply 100M doses (50% of 200M)
• Firm A is entitled to US$ 750M (50% of the total US$ 1.5B AMC)
How does it work? Prices & Funding

AMC Price

AMC Envelope

FIRM A US$ 750 M

Country Co-pay

GAVI

AMC Period

Tail Period

10 yrs

9/2/2010

OM-Winter Conference
The entire $1.5 billion aggregate AMC contribution is on offer at the launch of the pneumo-AMC. UNICEF will issue calls for offers based on the long term demand forecast.

Offers cannot be higher than the forecasted demand for the start date proposed by the supplier.

Offers must have a start date no more than 5 years into the future.
Stakeholders and activities overview

World Bank
Financial Management for Donor Funds

Donors
Financial Support

UNICEF
Procurement Agency

Manufacturers
Develop and produce vaccines

WHO
Technical support
Defines TPPs Pre-qualification

GAVI
Financial, Administrative, Programmatic support

Countries
Decide to adopt vaccine and co-finance

Donors Offer 2009

UNICEF Call for Supply Offers

AMC Manufacturers Registration

Manufacturer supply offer

Application for pre-qualification

WHO prequalifies pneumococcal vaccine

IAC assesses if the vaccine meets the Target Product Profile

GAVI Strategic Demand forecast updated biannually

Application for vaccines

Entry into a Supply Agreement
What does this mean for GAVI countries?

• The Same
  • Countries express their preference on pneumo vaccines
  • GAVI co-financing and default policies will apply to the AMC without modifications
  • Vaccines are procured through UNICEF
What does this mean for GAVI countries?

- But different:
  - Vaccines will be available in the right quantities to cover demand
  - Availability of support funding is known years in advance
  - The price of these vaccines for developing countries is known years before procurement starts
Advanced Market Commitment (AMC)

Notice that:

- The donors don’t assume the risk. If the vaccine does not sell then the donors don’t pay.
- It is not clear that the manufacturers will get the 1.5B. The market size may be very small.
- But this is exactly what happens in markets in the developed world.
Advanced Market Commitment (AMC)

Questions
- What should be the total price-commitment be?
- What should the price per unit be?
- If there are several manufacturers, how do we allocate the subsidy?
- Should the countries also make a commitment?
Advanced Market Commitment (AMC)

- What is the actual size of the market?
- Is the price commitment mechanism really mimics the markets of the developed world?
Advanced Market Commitment (AMC): Total price-commitment

- The average net present value of sales (2004) was $2.8B.
- No need for marketing. Thus needs to raise only $2.5B
- But the development of a vaccine for malaria is complex. Thus choosing the net present value of the 80th percentile is more appropriate. Total adjusted revenue is $3B
Advanced Market Commitment (AMC): Total price-commitment

- Thus, the price commitment should be $3B
- What should the price per unit be?
  - Fixed
  - Higher at the beginning and decreasing with time.
    - Higher incentive for the leader.
    - Still providing some incentives for the followers
Advanced Market Commitment (AMC)

- Are we mimicking the markets in the developed world?
  - Nature of competition
  - Adoption rates
  - Efforts by the countries affect the usage
  - Patients don’t like to be vaccinated
  - Flow of drugs can’t be controlled
  - Manufacturers don’t have a good estimate of the market size
# Advanced Market Commitment (AMC)

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<tr>
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<th>Strength</th>
<th>Limitation</th>
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<tbody>
<tr>
<td><strong>Donors</strong></td>
<td>1. Increases incentives for drug development and supply.</td>
<td>1. Does not induce drug firms to disclose costs of R&amp;D and manufacturing.</td>
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<td>2. Limits payment amount to commitment.</td>
<td>2. Cannot be used to signal true demand to drug firms.</td>
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<td>3. Permits procurement from alternate sources.</td>
<td>3. Offers no assurance of supply from drug companies.</td>
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<td><strong>Low Income Countries</strong></td>
<td>1. Offers a well defined subsidy.</td>
<td>1. Offers no assurance of supply from drug companies.</td>
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<td></td>
<td>2. Ensures stable and reliable supply of funds.</td>
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<td>3. Increases access to drugs.</td>
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<td><strong>Drug Developers</strong></td>
<td>1. Increases purchasing power of low income countries.</td>
<td>1. Does not assure accurate information about demand.</td>
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<td>2. Reduces uncertainty in availability of funding during each procurement cycle.</td>
<td>2. Does not protect market from new entrants who have not borne the drug development costs.</td>
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<td>3. Does not induce the firm to disclose its costs.</td>
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<td>4. Allows the firm to use the donor fund to cross subsidize high income markets.</td>
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Advanced Market Commitment (AMC): Revealing the market size

- Donors and countries have an incentive to inflate the demand.
Advanced Market Commitment (AMC): Revealing the market size

“There can be no guarantee that Novartis will be able to achieve any particular level of Coartem production in the future. Any such results can be affected by, among other things, uncertainties regarding the timeliness of the orders to be placed for Coartem by the ordering countries, uncertainties regarding the ability to obtain the necessary raw materials, uncertainties relating to the performance of our suppliers, uncertainties relating to regulatory actions or government regulation.
Advanced Market Commitment (AMC): Revealing the market size

- Is it possible to develop a mechanism to force the donors (countries) to reveal their true belief on market demand?
Advanced Market Commitment (ACM): The Model

- We consider the issue of building production capacity
- Single donor
  - The donor knows the true demand distribution
  - The donor provides a price-commitment
- Single Manufacturer
  - Assumes two possible demand distribution: High and Low. The demand distribution differ only in their means
  - Demand distribution are Normal.
  - The donor has an incentive to inflate the demand
Advanced Market Commitment (ACM): The Model

- The donor has an incentive to inflate the demand.
  - Why?
Advanced Market Commitment (ACM): Notation

- The donor announces that he will pay $w per unit.
- The total price-commitment is $K.
- The manufacture has a capacity cost of $b per unit of capacity.
- The manufacturer builds $B$ units of capacity.
- Variable production cost, $c$
Advanced Market Commitment (ACM): The solution

- If the demand is low (say low mean, ) the donor will purchase a small quantity \( q \) and the revenue \( wq \) may not cover the investment in capacity and the variable cost. That is:

\[
\text{w}_{LE}[S|\mu_L,B_L] < bB_L + cE[S|\mu_L,B_L]
\]

- The donor has an incentive to convince the manufacturer that the mean demand is High and that:

\[
\text{w}_{HE}[S|\mu_H,B_H] > bB_H + cE[S|\mu_H,B_H]
\]
Let us assume, for the time being, that the demand is low and it is common knowledge. In this case the manufacturer must ensure (participating constraints) that:

\[(w_L - c)E[S | \mu_L, B_L] > bB_L\]

or

\[w_L > c + \frac{bB_L}{E[S | \mu_L, B_L]}\]
Advanced Market Commitment (ACM): The solution

- The donor commitment to spend $K$ must satisfy:

$$w_L \ast B_L < K$$
Advanced Market Commitment (ACM): The solution

If the demand is high and it is common knowledge we get:

$$(w_H - c)E[S | \mu_H, B_H] > bB_H$$

or

$$w_H > c + \frac{bB_H}{E[S | \mu_H, B_H]}$$
Advanced Market Commitment (ACM): The solution

- The donor commitment to spend $K$ must satisfy:

$$w_H B_H < K$$
Advanced Market Commitment (ACM): The solution

- We assume that:
  \[ w_L = c + \frac{bB_L}{E[S \mid \mu_L, B_L]} \]

- And
  \[ w_H = c + \frac{bB_H}{E[S \mid \mu_H, B_H]} \]

- Lemma 1: \( w_H < w_L \)
Advanced Market Commitment (ACM): The solution

Lemma 2: \( w_H \mu_H > w_L \mu_L \)
Advanced Market Commitment (ACM): The solution

- Separating equilibrium
  - The manufacturer would like to offer the donor a contract so that the donor will have an incentive to reveal his true type.
  - Suppose the demand is low. But the donor decides to announce that it is high and pay \( w_H \) (recall that \( w_H < w_L \)).
  - The donor expected cost is: \( w_H \mu_L \)
  - The manufacturer wants to avoid this situation and be paid: \( w_L \mu_L \)
Advanced Market Commitment (ACM): The solution

The manufacturer offers the following contract:
- A fixed cost $G$ and a variable cost per unit $\tilde{w}$ for a total of: $G + \tilde{w} \mu E(d)$ where $G = w_L \mu_L$ and $\tilde{w}$ is determined by solving $w_H \mu_H = w_L \mu_L + \tilde{w} \mu_H$

Or
- Paying $w_L$ per unit

Lemma 3: The above contract is a separating contract
Advanced Market Commitment (ACM): The solution

- In order to reveal the true demand the donors must make a quantity commitment.
Advanced Market Commitment (ACM)

- More difficulties with the concept.
  - Assuming that the donors will pay for actual sales.
  - Suppose the demand realization is small.
  - Pharmaceuticals may convince the participating companies to inflate the demand and to purchase more vaccines than they actually need.
  - Pharmaceuticals will be able to provide the countries with a kick-back
Advanced Market Commitment (ACM)

- The ACM contract provides an incentive for grand corruption.
Advanced Market Commitment (ACM)

- Can the Grand corruption be avoided?
  - Making a quantity commitment and reducing the purchasing cost per unit will reduce the Grand corruption.
  - The quantity commitment may be done after the drug (vaccine) is approved but before the production capacity is built.