

Economic Perspectives on the Advance Market Commitment for Pneumococcal Vaccines

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Abstract: With little prospect of earning an attractive return, biopharmaceutical companies have long been reluctant to invest in new vaccines aimed at the developing world. One means of stimulating such investment is the use of an advance market commitment, an innovative financing program guaranteeing a viable long-term market for the vaccine. Under this arrangement, international donors agree to pay a premium for initial doses sold to developing countries. In exchange, companies agree to continue supplying the vaccine over the longer term at more sustainable prices. This article provides a preliminary economic analysis of the pilot program for pneumococcal vaccines. We discuss the economic principles underlying the program design, trace its evolution as concerns were addressed, and suggest some guidelines for its evaluation.

The GAVI Alliance -- a partnership formed in 2000 among governments, non-governmental organizations, foundations, and vaccine manufacturers -- supports immunization programs in more than seventy eligible countries (defined as having per capita national income below \$1,500). As procurement agents for GAVI, the World Health Organization and UNICEF purchase vaccines for developing countries with funding from industrialized countries. They pay a fraction of industrialized-country prices, often not much more than production costs.

These organizations have greatly enhanced developing countries' access to traditional vaccines. Yet they have been less successful in inducing manufacturers to build sufficient capacity to roll new vaccines out in poor countries as quickly as in industrialized countries.

The organizations have also had less success in providing companies with incentives to develop new vaccines for diseases such as malaria and yellow fever posing the greatest burden in poor countries. If prices do not provide a margin over the cost per unit of production, firms cannot recoup any of their investments in capacity or research and development, which could amount to hundreds of millions of dollars.

The advance market commitment was designed to address this underinvestment problem.¹ In such a program, donors enter into a long-term agreement to pay a premium above incremental

production cost (the manufacturer's cost of producing one more unit of the product). This premium provides the manufacturer an economic return making the investment needed to produce the product more attractive.

In this paper we provide a preliminary economic analysis of the pilot advance market commitment announced in 2007 for pneumococcal vaccines. We use both conceptual and empirical methods.

In the conceptual analysis, we construct an economic model in which the pneumococcal vaccine is supplied by profit-maximizing firms. The details are relegated to an online Appendix.² We use this model to simulate vaccine supply under alternative designs for the financing program.

In the empirical analysis, we provide a preliminary assessment of the pilot advance market commitment. We compare the rollout in GAVI-eligible countries of the pneumococcal vaccines supported by the pilot program to the rollout of earlier-generation pneumococcal vaccines, which received much less donor support.

Before proceeding with the analysis, we provide some background on the history of the pilot program and the experience from its first year of operation.

The Pneumococcal Advance Market Commitment

Milestones In 2003 the Center for Global Development convened a working group to explore the merits of advance market commitments and to consider design details.³ Initial interest had focused on creating incentives for research and development for malaria vaccines. For several reasons the focus shifted to pneumococcal vaccines already in late-stage development. Pneumococcal disease is the leading vaccine-preventable killer of young children worldwide, according to recent estimates leading to over 800,000 deaths annually of children under age five, with over 80% of the deaths occurring in GAVI-eligible countries.^{4,5}

A pneumococcal vaccine protecting children against seven strains of the disease had already been launched in the developed world. This vaccine, PCV-7, also called Prevnar, was originally manufactured by Wyeth.

The working group believed that it would be possible to accelerate production of second-generation vaccines for the developing world. Two such vaccines -- GlaxoSmithKline's vaccine covering 10 strains of the disease (PCV-10, also called Synflorix) and Wyeth's vaccine covering 13 strains (PCV-13, also called Prevnar-13) -- were known to be in late-stage development. Each covered additional strains which, though relatively rare in industrialized countries, are responsible for

12-25% of invasive pneumococcal disease in poor countries. Given the advanced development of these second-generation vaccines, the working group concluded that they would be an ideal pilot to demonstrate quickly the practical feasibility of advance market commitments.³

In February 2007, the Gates Foundation and the governments of Italy, UK, Canada, Russia, and Norway pledged \$1.5 billion for a pilot pneumococcal commitment program (all monetary figures herein are in nominal US dollars). In March 2009, GlaxoSmithKline received European regulatory approval for PCV-10. Soon after, the company opened a \$411 million plant in Singapore with a 300 million annual dose capacity.⁶ That same month Wyeth applied for a license for its PCV-13.⁷

In October 2009, GlaxoSmithKline, Pfizer (which by then had acquired Wyeth), the Serum Institute of India, and Panacea Biotech filed expressions of interest with the advance market commitment. Based on its strategic demand forecasts, GAVI set a goal of allocating 200 million doses of pneumococcal vaccines annually by 2015.⁸

In March 2010, GlaxoSmithKline and Pfizer each entered into commitments to supply 30 million doses of their second-generation pneumococcal vaccines annually through the advance market commitment.⁸ Since each supplier's commitment is 15% of GAVI's 200 million-dose target, GlaxoSmithKline and Pfizer were

each allocated 15% (\$225 million) of the \$1.5 billion fund.

In addition, the companies agreed to provide a combined 7 million, 24 million and 20 million doses in 2010, 2011 and 2012 to GAVI-eligible countries in the transition period before their formal supply commitments began.

Funding Structure Exhibit 1 shows the funding structure that ultimately emerged. For concreteness, the exhibit takes the example of GlaxoSmithKline's annual 30-million-dose supply commitment and assumes that demand materializes for the manufacturer's entire commitment each year.

For the first 20% of its supply (the 30 million doses sold in each of 2013 and 2104), GlaxoSmithKline receives a guaranteed price of \$7 per dose. The price is divided up as follows.

First, countries' copayments and GAVI's contribution combined amount to \$3.50 per dose. Copayments vary by countries' per capita income, ranging from 20 cents per dose for the lowest-income countries to a rising payment schedule for the highest-income countries that has them cover the full \$3.50 after five years.⁹ The exhibit graphs the average country copayment in purple and GAVI's contribution in blue.

Second, the commitment fund "tops up" this \$3.50 with another \$3.50 upfront payment (the green bars in the exhibit).

This additional subsidy is available for just the first 20% of units supplied. In the example, GlaxoSmithKline exhausts its allocated subsidy by the end of 2013. In 2014, it enters the "tail period," receiving a total of \$3.50 per dose for the remaining portion of its ten-year commitment.

The \$3.50 "tail price" is envisaged as approximating incremental production costs while the \$7 "topped up" price for the initial 20% of the commitment provides extra revenue for the supplier to recoup some of the fixed costs of research, development, and manufacturing-capacity construction.

The final agreements obligate manufacturers to supply whatever amount is demanded up to the supply commitment (thirty million doses annually in GlaxoSmithKline example). By contrast, GAVI has the option, but not the obligation, to purchase any amount up to the limit of the supply commitment. Suppliers, therefore, bear substantial risk if forecasted demand does not materialize.

This risk is tied to the inherent difficulties in forecasting take-up of vaccines by GAVI-eligible countries as well as the uncertainty over whether GAVI will have sufficient donor funds to sustain its contribution. To offset this risk, GAVI's procurement agent, UNICEF, agreed to purchase a minimum of 20% in year one, 15% in year two, and 10% in year three of

the supplier's annual committed supply regardless of whether demand materializes in those years.⁸

With only 30% of the \$1.5 billion fund allocated so far, 70% remains in reserve for future tenders (future supply requisitions under the program from companies registered with UNICEF). Officials stated that the purpose of leaving a reserve was to encourage the entry of new suppliers, increasing competition for pneumococcal vaccines, leading to lower prices over the long term. Uncertainty regarding donor funding of GAVI commitments, however, also likely played a role.⁸

We have been unable to ascertain whether firms, GAVI, or both balked at committing to more than 30% of the total 200 million target, so cannot deduce from this unfilled commitment that that the program provides inadequate supplier incentives. Recent discussions with industry officials suggest a willingness to commit to further quantities.

Rollout in GAVI Countries Exhibit 2 provides data on the approved shipments and introductions of second-generation pneumococcal vaccines to GAVI countries. As of September 2010, 19 countries were approved for the introduction of PCV-10 or 13 through the commitment. Nicaragua was the first to introduce the second-generation vaccines in December 2010. Kenya, Yemen, Sierra Leone, Guyana, Mali, Honduras, and the Democratic

Republic of Congo followed in order in the first half of 2011. The remaining approved countries are scheduled to introduce the vaccines by the end of 2011.

Design Principles

We next turn to an economic analysis of various program design features (total fund size, tail price, subsidy caps, etc.), investigating how important each feature is to the overall performance of the commitment program. We employ an economic model calibrated to the market for pneumococcal vaccines in GAVI-eligible countries. Our goal is not to provide an exact calibration but to use round numbers to illustrate and provide intuition regarding the underlying principles and tradeoffs of the commitment program.¹⁰

Model A detailed presentation of the economic model is provided in the online Appendix. The notes to Exhibit 3 list the specific numerical values assumed in the analysis. Most values were set to reflect the actual terms of the program, but two deserve explicit discussion.

Let b denote the monetary value that donors place on the health benefits from a dose of the vaccine administered in GAVI-eligible countries. Based on a study of the cost-effectiveness of the pneumococcal vaccine in African trials, we set $b = \$8.50$.^{11,12,13}

Let k denote a supplier's upfront cost of installing a unit of capacity. In addition to factory construction costs (about \$1.40 per dose for GlaxoSmithKline's aforementioned Singapore facility), k can also reflect more subtle bargaining costs, which can be understood as follows. If take-up under the program ends up being low, leaving excess capacity, the supplier is in a worse position in negotiations with higher income countries because the supplier's threat of restricting output becomes less credible. The loss of revenue from these higher income markets could dwarf construction costs. We set $k = \$4$ but perform a sensitivity analysis around this number.

Benchmark Analysis For the benchmark analysis, suppose a single firm participates in the advance market commitment, supplying the quantity that maximizes its profit stream (revenue minus cost, discounted to reflect the interest rate). The results are shown in the first row of Exhibit 3. Under the maintained assumptions, the firm ends up supplying the entire 200 million dose target annually, generating a discounted stream of social benefits (net of program costs) of \$9.1 billion.

This benchmark result differs from the experience to date with the pneumococcal vaccine pilot program. Participating firms so far have committed to supply only 30% of the target 200 million doses annually. As discussed above, we cannot rule out

that more supply would have been forthcoming if GAVI had requested more: GAVI may have considered this smaller commitment level to be suitable for current country demand or may have faced constraints on its fundraising.

From a purely experimental perspective, however, it would have been useful to observe firms' reaction to an unlimited initial tender to test the limits of how much capacity an advance market commitment could generate. Upcoming supply requisitions may provide more evidence on this issue.

Subsidy Cap Next we turn to an analysis of a feature of the advance market commitment that was not part of the original design but was added later on the recommendation of the Economics Expert Group (economists and experts from other fields tasked with studying the economic issues with the program's implementation).¹⁴ The recommendation was to cap the proportion of the \$1.5 billion fund allocated to a firm at the proportion of the target 200 million doses it commits to supply annually.

There was no such cap in the original design. A single firm could tap the entire fund whether or not it met the full target; increasing production only affected the rate at which the fund was paid out.

Exhibit 3 shows that the lack of a cap in the original design may weaken supply incentives. The benchmark case in the

first row of the exhibit shows that removing the cap shrinks annual supply from 200 to 55 million doses and social benefit from \$9.1 to \$1.7 billion. Reducing supply allows the firm to save on construction and other upfront costs but still appropriate the entire \$1.5 billion fund if no cap prevents it. The lower supply requires the firm to wait longer to appropriate the entire fund, but waiting entails only a modest loss of revenue from discounting.

Competition The advance market commitment functions better with more competition among suppliers. This principle is demonstrated in the numerical examples in row 2 of the exhibit, which adds a second and then third supplier. The increase in competition does not change the outcome with the commitment as implemented with the subsidy cap: this version of the program already resulted in the 200 million dose target being met even with a single supplier.

However, the advance market commitment without a subsidy cap benefits considerably from the addition of competition. The supply predicted by the model increases to 95% of the target with two competing firms and reaches the full target with three competing firms. Net social benefit increases from \$1.7 to \$8.5 to \$9.1 billion as competitors are added. In essence, competition fills in for the missing subsidy cap as firms race

to capture more of the subsidy for themselves by expanding supply.

An optimistic view of these results is that advance market commitments can be expected to be quite efficient regardless of design details the more competitive is vaccine supply. Yet policymakers agonized over design details because of a concern that sufficient competition might not materialize. Few manufacturers had suitable products in late-stage development, and it was feared that fewer -- perhaps just one -- had low enough costs to be a viable supplier in the pilot program.

Private Cost Information A difficulty in designing an advance market commitment for late-stage products such as pneumococcal vaccines is that suppliers may have better estimates of costs than do program designers. The difficulty is particularly acute with pneumococcal vaccines because the complex technologies required to combine protection against multiple disease strains into a single dose entail a wide range of cost uncertainty.

Designing an advance market commitment when suppliers have private cost information involves a delicate balance.¹⁵ More generous program terms increase the probability that firms participate and supply a substantial amount but also increase the overall cost of the program. Even the best designed program

has a chance of being rejected by all suppliers (if costs turn out to be high). If accepted, the program would end up conferring at least some extra profit to the supplier. Neither outcome is proof of a design flaw but is a natural consequence of the designer's incomplete information about suppliers' costs.

To gauge the role of cost uncertainty in the model, we return to the numerical example with a single supplier, but instead of assuming unit costs are $c = \$3.50$, we suppose the specific value is known only to the supplier; the commitment designer only knows c is equally likely to be any value between \$3.00 and \$4.00. This numerical example is shown in row 3 of Exhibit 3.

Consider first the commitment program with a subsidy cap. The supplier commits to the full target of 200 million doses annually for most cost realizations in the model. Only for the highest costs ($c = \$3.80$ or higher) does a problem arise, with the supplier rejecting the commitment and supplying nothing. Nevertheless, supply (at 164 million doses annually) and net social benefit (at \$7.5 billion) are still fairly high on average across cost realizations.

Instead of setting the tail price at the average value of unit cost ($t = \$3.50$), setting a higher tail price raises net social benefits. The exhibit shows the results from increasing t to \$3.75. This higher tail price induces the firm to supply

the whole 200 million annual dose target for all realizations of cost c between \$3 and \$4. Though program costs are higher, the health benefits from having the vaccine supplied even when costs are high raise net social benefits to \$8.7 billion. The version of the commitment without a supply cap likewise performs better with a higher tail price, with net social benefits increasing from \$2.8 to \$4.5 billion under this program design.

Importance of the Tail Price Attention has understandably been focused on the considerable size of the \$1.5 billion program fund. However, the tail price can have much more of an impact on suppliers' participation in the program. This has been demonstrated in the numerical examples presented so far, but can be seen more directly in Exhibit 1. The area of the green bars representing the portion of a supplier's revenue coming from the commitment fund is a small fraction (15%) of revenue from all sources. Spread out over all ten years of the supply commitment, the commitment program subsidy would only amount to 70 cents per dose. Because of this, a \$1 reduction in the tail price would be more harmful to a supplier than the elimination of the entire program subsidy.¹⁶

Demand Uncertainty Requiring countries to pay a copayment serves several purposes. Among these is to ensure that new vaccines "meet the market test," meaning that they have

attributes (disease strains covered, packaging, etc.) that are attractive to end users. This is the "market" part of the term "advance market commitment." A drawback of a copayment is that it risks reducing take-up by price-sensitive countries because of limited national health budgets. GAVI mitigates this drawback to some extent by tailoring copayments to countries' per capita income. Nevertheless, there may be other barriers to country take-up including a reluctance to introduce new vaccines if the health benefits and risks are not thoroughly understood or if complementary investments in clinical infrastructure (e.g., cold storage) for the vaccine are required.

These barriers contribute to uncertainty regarding the quantity of vaccine countries demand under the program. Our conversations with officials in industry and non-governmental organizations pointed to demand uncertainty as one of the chief concerns about program participation.

The point can be demonstrated in the numerical example in Exhibit 3. Demand uncertainty is modeled as an equal probability that demand for the full 200 million units materializes or no demand materializes. As row 4 of the exhibit shows, the supplier now finds the supply commitment to be unprofitable, and so the program generates no supply. (The version of the advanced market commitment without a subsidy cap

does result in some vaccine supply, but only 37 million doses annually, providing net social benefits of \$400 million.)

To compensate for this demand uncertainty, the total fund amount, tail price, or some other terms could be made more generous. An economic argument can be made for yet another alternative: a guarantee to purchase some of the committed supply regardless of what level of demand materializes.

Economic logic suggests that the party with most control over an uncertain situation should insure the other party against risk, because the insurer will exercise its control to mitigate the risk. Given that the quality of these late-stage vaccines is well established now, there is little the supplier can do to affect demand; country demand hinges largely on donor and GAVI investments in facilitating rollout. This provides a rationale for some form of a purchase commitment in the program to insure suppliers against demand fluctuations.¹⁷

The pneumococcal pilot program included purchase guarantees of 20% the first year, 15% the second, and 10% the third, even if sufficient demand does not materialize. In the model, these modest guarantees are just at the right level to overcome the demand risk and induce the supplier to commit to the entire 200 million dose target.

Perhaps the most significant source of uncertainty lies with GAVI's ability to meet its financial obligations under the

program. To see the magnitude of the issue, assume supply commitments for the entire 200 million dose target eventually materialize for all ten years. Calculations based on Exhibit 1 show that GAVI would end up spending \$6.3 billion to meet its obligations under the program (proportional to the area of the blue bars), four times more than the \$1.5 committed subsidy fund (proportional to the green bars). The problem is inherent in advance market commitments for any complex vaccine involving high production costs. High tail prices are required to cover these production costs, which end up dwarfing other program expenses over the long run. Setting aside funds to cover not just the subsidy but also tail prices would increase suppliers' confidence in the availability of financing in future programs.

Sensitivity Analyses The last rows of Exhibit 3 show that the main conclusions from the model hold if different numerical values are used. Typically, the advanced market commitment as implemented (with a cap on the subsidy) results in the full 200 million dose annual target being supplied. However, cost terms can be ratcheted up to the point where the commitment delivers no supply (for example when k is increased to \$10, though this is an extreme increase, seven times higher than the cost of GlaxoSmithKline's Singapore plant per dose). Changing the health benefit per dose b does not affect supply but has a

substantial effect on the social value of that supply. Reducing b to a level near costs causes the program's social benefit to disappear, but this benefit can grow without bound with higher values of b .

Vaccines in Early-Stage Development: The Problem of Incentivizing Research and Development Most of the analysis so far has focused on advance market commitments for products in late-stage development because this is the nature of the pneumococcal vaccine targeted by the pilot program.

Advance market commitments were originally conceived for a different purpose: to provide incentives for research on new products. The problem of private cost information is less severe for products in the early stages of research and development because biopharmaceutical firms themselves face considerable uncertainty regarding costs for products that are a long way from production. The advance market commitment will still need to provide a margin over production costs to induce firms to undertake research, with higher margins generally inducing more research effort.¹⁸

Evaluating the Performance of the Advance Market Commitment

The commitment program has not been operating sufficiently long to allow a comprehensive assessment. Here we provide our preliminary impressions and offer suggestions for subsequent

assessments when more data become available.¹⁹

Judging whether the program was a success requires choosing a standard for comparison appropriate for the question being asked. Did the advance market commitment result in faster and broader rollout than if no initiative were undertaken? What if traditional procurement methods and resources were employed? What if advance market commitment level resources were expended but using typical procurement methods?

Exhibits 4 and 5 provide one useful comparison, that between the rollout of PCV-10 and 13 under the advance market commitment and the earlier rollout of PCV-7. The earlier rollout provides an example of a similarly complex vaccine introduced without the benefit of a well-endowed initiative. Exhibit 4 shows a nine-year lag between the introduction of PCV-7 in industrialized countries relative to its introduction in a GAVI-eligible country and a widening gulf between the number of GAVI countries adopting compared to others.

Exhibit 5 presents a contrasting picture for the introduction of PCV-10 and 13 under the program. The lag between rollout in GAVI relative to other countries was virtually eliminated and the gap in cumulative introductions reduced. (The same picture emerges were we to graph quantity of vaccine shipped rather than cumulative country introductions.) We cannot conclude that the advance market commitment alone

accelerated the introduction of pneumococcal vaccine to GAVI-eligible countries; other programs were initiated around the same time with the same goal. The exhibit suggests that the portfolio of initiatives had a dramatic effect on the rollout of pneumococcal vaccines to GAVI-eligible countries relative to the absence of such initiatives.

More difficult is to determine whether the advance market commitment had more effect than if the same resources were spent via more traditional procurement channels. No previous experience is closely comparable to the pneumococcal pilot program. Some authors have suggested comparing the pneumococcal pilot to the introduction of Hib or rotavirus vaccines.^{19,20} Although this comparison provides useful insights, the introduction of a Hib vaccine may have been slowed by inadequate initial funding²¹ and the rotavirus vaccine by a shift in funding priority toward pneumococcus and by initial concerns with the vaccine's safety in developing countries.²²

Conclusions

We analyzed an economic model of the supply of pneumococcal vaccines under an advance market commitment. In many numerical examples we found large potential gains from incentivizing greater vaccine supply with more generous program terms.

Compared to the experience with first-generation

pneumococcal vaccines such as PCV-7, which lacked a concentrated initiative behind its rollout in developing countries, the rollout of second-generation vaccines has been rapid. We cannot say whether this can be attributed to the specific structure of advanced market commitment or simply the level of resources that has been marshaled.

The broader question addressed by the pilot advance market commitment for pneumococcal vaccines was not whether suppliers would respond to an increase in market resources -- basic economic principles instruct us to expect that -- but whether donors would have the appetite for a new way of procuring vaccines involving a new set of challenges. So far it appears the donors do.

Notes

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11. The cited study is Sinha A, Levine O, Knoll MD, Muhib F, Lieu TA. Cost-effectiveness of pneumococcal conjugate vaccination in the prevention of child mortality: an international economic analysis. *Lancet*. 2007;369(9559):389-96. The authors found that accounting for mortality benefits and some reduction in hospitalizations, vaccination with PCV-9 would have a cost-effectiveness ratio of \$80/DALY (disability-adjusted life year, a standard measure of health benefits) across GAVI

countries. The assumed cost per dose was around \$5.62 (adding the \$5 price and the sixty-two-cent midpoint of the range of administration costs considered by the study).

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13. We further scaled it up by 1.2 to account for greater coverage of PCV-13 relative to PCV-9 in GAVI countries. Based on our computations from Figure 3(a) of GAVI Alliance, PneumoADIP. GSP summary report for SAGE meeting Nov. 6-8 2007 [Internet]. Geneva: GAVI Alliance; 2007 Oct 19 [cited 2011 May 13]. Available from: [http://www.preventpneumo.org/pdf/GSP Summary for SAGE Nov6-8 2007_Oct 19-07.pdf](http://www.preventpneumo.org/pdf/GSP_Summary_for_SAGE_Nov6-8_2007_Oct_19-07.pdf)

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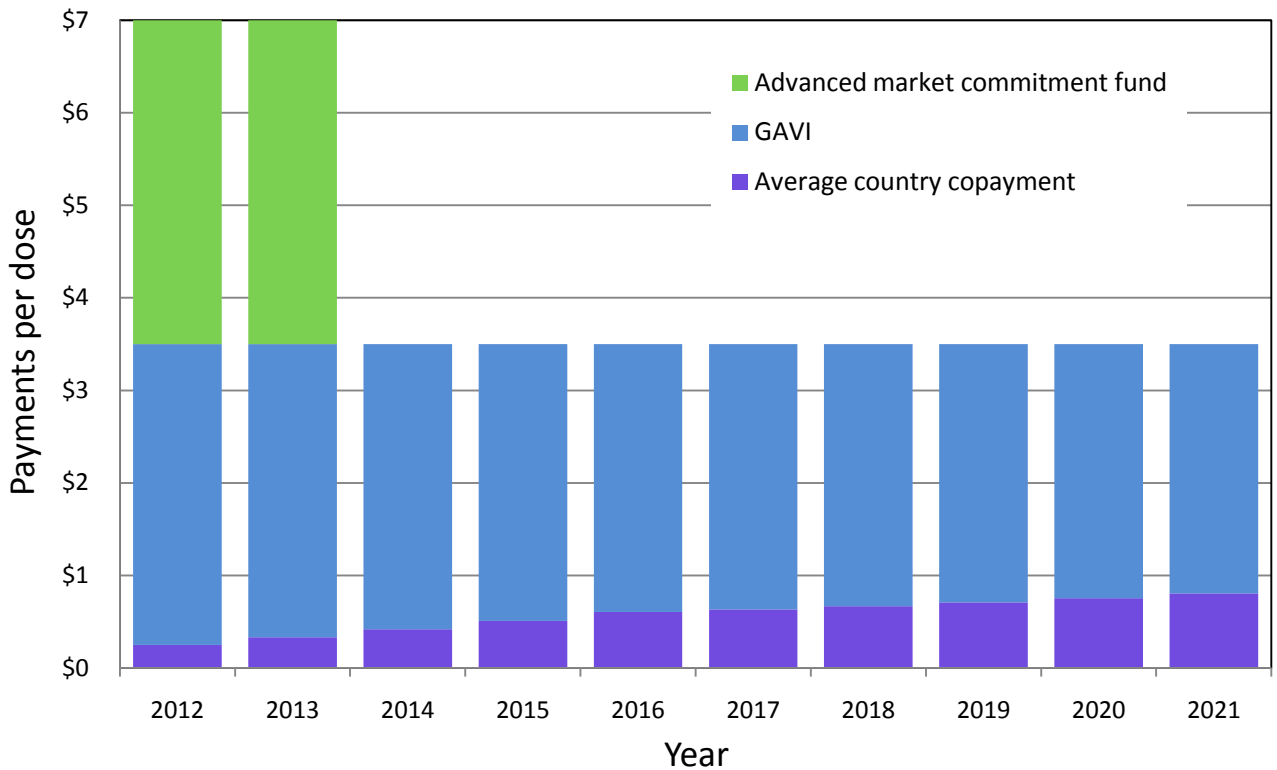
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EXHIBIT 1

Program Financing Structure Using the Example of GlaxoSmithKline's Supply Commitment



Sources: Advanced market commitment and GAVI contributions from GAVI Alliance Secretariat (2010) *Advance Market Commitment for Pneumococcal Vaccines: Annual Report 12 June 2009 – 31 March 2010*, pp. 9-10. Country copayment policy from GAVI Alliance Secretariat (2010) "GAVI Alliance Revised Co-financing Policy," December 2010, downloaded April 29, 2011 from http://www.gavialliance.org/resources/Co_financing_Policy_final.pdf. Classification of countries into three GAVI categories from GAVI Alliance Board Meeting Doc #11.d, "Co-Financing Policy Revision," Annex 2, downloaded April 29, 2011 from http://www.gavialliance.org/resources/DOC__11d_Co_financing_Policy_Revisions.pdf.

Notes: Average country copayment is a weighted average of the GAVI copayment levels for the three classes of countries: low-income countries, which pay 20 cents per dose, intermediate-income countries, which pay 20 cents per dose plus a 15% increase each year, and graduating countries, which pay a linearly increasing amount over time, covering the whole \$3.50 tail price after five years. Weights are based on the number of under-14 youths in each group of countries. Prices in nominal US dollars. GlaxoSmithKline's supply commitment involves 30 million doses annually over the ten years.

EXHIBIT 2**Scheduled Shipments and Introductions of Second-Generation Pneumococcal Vaccines to GAVI**

Countries	Vaccine	Status of Introduction	First shipment	Number of doses approved	
				For shipment in 2010	For shipment in 2011
Kenya	PCV-10	Introduced	Sep. 2010	1,200,000	5,874,700
Sierra Leone	PCV-13	Introduced	Oct. 2010	388,800	388,200
Nicaragua	PCV-13	Introduced	Nov. 2010	149,400	538,200
Yemen	PCV-13	Introduced	Nov. 2010	970,650	2,395,800
Guyana	PCV-13	Introduced	Dec. 2010	19,800	33,300
Honduras	PCV-13	Introduced	Dec. 2010	199,800	651,500
Dem. Rep. Congo	PCV-13	Introduced	Feb. 2011		5,409,300
Mali	PCV-13	Introduced	Mar. 2011		2,062,800
Gambia	PCV-13	Switch from donation	Feb. 2011		174,700
Rwanda	PCV-13	Switch from donation	May 2011		1,002,600
Cameroon	PCV-13	Expected Jun. 2011	Apr. 2011		1,542,300
Central African Rep.	PCV-13	Expected Jun. 2011	Apr. 2011		302,400
Congo Rep.	PCV-13	Expected Jan. 2012	Oct. 2011		309,600
Benin	PCV-13	Expected Jul. 2011	TBC		TBC
Burundi	PCV-13	Expected Jul. 2011	TBC		TBC
Ethiopia	PCV-10	Expected Sep. 2011	TBC		TBC
Malawi	PCV-13	Expected Oct. 2011	TBC		TBC
Madagascar	TBC	TBC	TBC		TBC
Pakistan	TBC	TBC	TBC		TBC

Source: UNICEF. "GAVI/VF Shipments" (various years). Available at http://www.unicef.org/supply/index_gavi.html, accessed April 29, 2011. Supplemented by personal communication with GAVI staff. **Notes:** TBC stands for "to be confirmed."

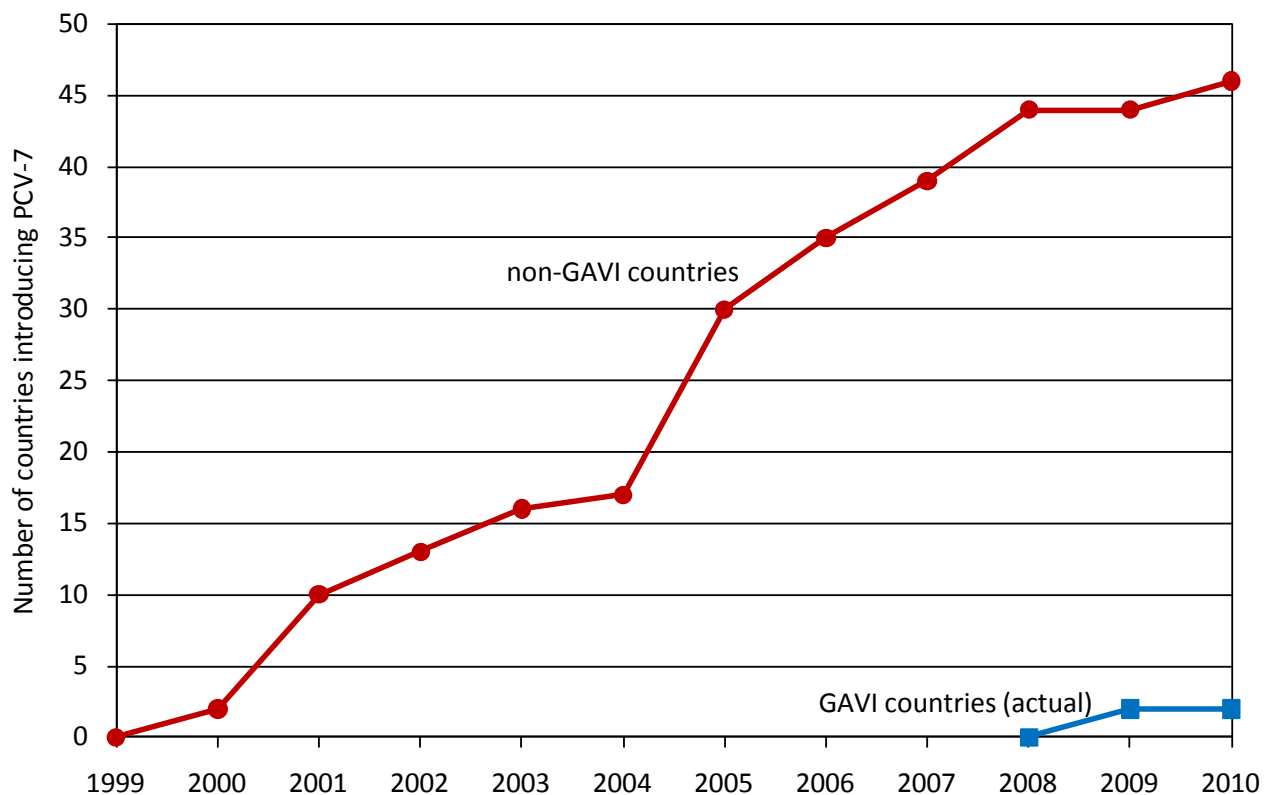
EXHIBIT 3
Numerical Examples from the Model under Various Scenarios

Scenario	Commitment as implemented (cap on subsidy)		Commitment as initially proposed (no cap on subsidy)	
	Quantity (million doses)	Net social benefit (billion \$)	Quantity (million doses)	Net social benefit (billion \$)
1. Benchmark	200	9.1	55	1.7
2. Competition				
Two suppliers	200	9.1	187	8.5
Three suppliers	200	9.1	200	9.1
3. Cost uncertainty				
Maintaining benchmark tail price	164	7.5	85	2.8
Increasing tail price to $t = \$3.75$	200	8.7	114	4.5
4. Demand uncertainty	0	0	37	0.4
5. Sensitivity analyses				
<i>k</i> increased to \$10	0	0	32	0.8
<i>k</i> reduced to \$2	200	9.1	81	3.1
<i>b</i> increased to \$20	200	33.4	55	8.4
<i>b</i> reduced to \$5	200	1.7	55	-0.4

Source: Authors calculations based on theoretical economic model. **Notes:** Quantity is annual market quantity supplied. Social benefit is the discounted stream of social benefits net of program expenses. The benchmark model involves the same terms as actually employed in the advanced market commitment: a subsidy fund $A = \$1.5$ billion, tail price $t = \$3.50$, up-front subsidy $s = \$3.50$ per unit, maximum vaccine demand of 200 million doses annually, and program length $T = 10$ years. In the version of the program analyzed with no cap on subsidy, T is taken to be the length of the tail period (the period after exhaustion of the subsidy fund during which the firm has to supply at price t). The other parameters in the benchmark model parameters are set as follows: social benefit per dose $b = \$8.50$, unit production cost $c = \$3.50$ (same as the tail price), up-front fixed cost $k = \$4$, interest rate $r = 5\%$, and manufacturing facility lifespan $L = 15$ years. The scenario with cost uncertainty involves equal probabilities that c takes on values in 10 cent increments between \$3 and \$4, inclusive. The scenario with demand uncertainty involves an equal chance of demand materializing or not. Entries in scenarios involving uncertainty scenario are expected values.

EXHIBIT 4

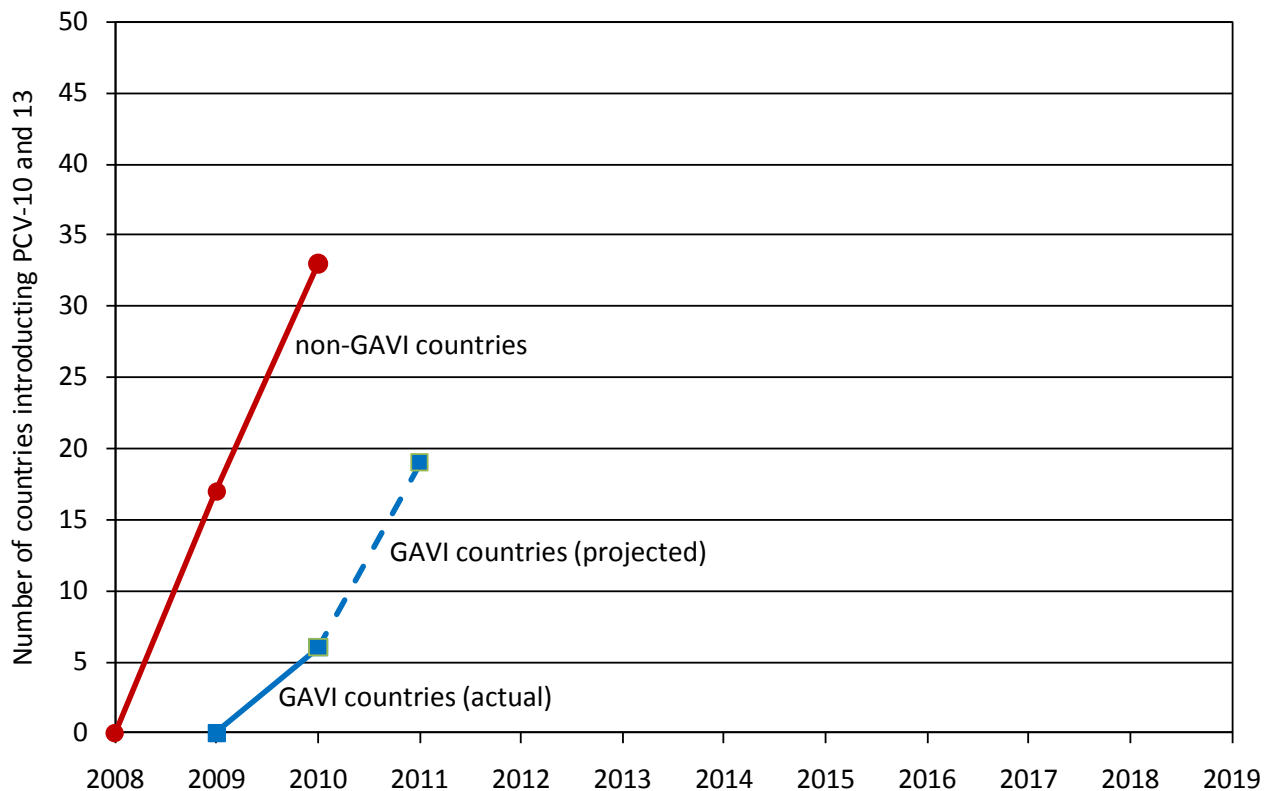
Rollout of First- Generation Pneumococcal Vaccines in GAVI Countries



Sources: Data on non-GAVI countries are from IMS MIDAS (sales 2000-2010). Data on GAVI countries are from UNICEF. GAVI/VF Shipments (various years) [Internet]. New York (NY): UNICEF; [cited 2011 Apr 29]. Available from: http://www.unicef.org/supply/index_gavi.html. **Notes:** Years on the horizontal axis have been lined up so the origin represents the year before initial adoption in both Exhibits 4 and 5. IMS data do not cover all channels for all countries, but they cover the same channels for PCV-10 and PCV-13 as for PCV-7, so results are comparable across vaccine types.

EXHIBIT 5

Rollout of Second-Generation Pneumococcal Vaccines in GAVI Countries



Sources: Data on non-GAVI countries are from IMS MIDAS (sales 2000-2010). Data on GAVI countries are from Exhibit 2.

Notes: Dotted line is a projection based on GAVI approvals. Years on the horizontal axis have been lined up so the origin represents the year before initial adoption in both Exhibits 4 and 5. IMS data do not cover all channels for all countries, but they cover the same channels for PCV-10 and PCV-13 as for PCV-7, so results are comparable across vaccine types.