ADVANCE MARKET COMMITMENTS
Rewarding Innovation Without Picking Winners

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Babies cry when they get a jab, but parents feel good knowing that immunization prevents a lifetime of disability or even death. In the United States, Canada, and Europe, vaccine manufacturers have developed remarkably safe and effective products, pushing scientific boundaries to reduce or even eliminate the risk of such infectious diseases as polio, measles, pertussis, tetanus, pneumonia, and now human papilloma virus.

In deciding to dedicate precious research and development (R&D) resources to vaccines, those firms haven't been responding simply to a public health imperative; they also have been seeking rewards in the market. Private insurers and government health programs have been willing to pay a price for newly developed products that compensate companies for capital-intensive R&D, regulatory approval, and manufacturing capacity. As a result, vaccines are universally available to children in wealthy countries, and new ones are in the pipeline.

These same market incentives are not at work in low- and middle-income countries, where the majority of the world's children live. Traditionally, vaccines have not been affordable to governments in the developing world until long after the patents have expired and generic manufacturers have stepped in to sell a high volume of low-cost products. Moreover, private pharmaceutical firms view developing vaccines for diseases that are unique to poor regions, such as malaria and dengue, as an unattractive way to invest their scientific brainpower and capital.

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Recently, the business case for global vaccines has grown stronger, particularly with the creation in 2000 of the Global Alliance for Vaccines and Immunization (GAVI), a public-private partnership funded by the Bill & Melinda Gates Foundation, the United States, the United Kingdom, Norway, and other donors. GAVI has financed the introduction of relatively high-priced products into low-income countries. At the same time, it has sought to negotiate long-term prices that are more affordable to national governments.

However, GAVI's purchases of existing products haven't been enough to induce large pharmaceutical companies to undertake costly R&D or brick-and-mortar investments in manufacturing plants for new products, particularly vaccines that would be well suited to poor countries. So, to try to solve that problem, several philanthropic and public-sector funders started exploring ways to pay for R&D, particularly through public-private partnerships with specific pharmaceutical manufacturers.

The traditional approach would have been to fund innovators who were most likely to succeed in developing a new vaccine, essentially attempting to "pick winners" among possible innovators and pay for their research. But a technical working group convened by the Center for Global Development, a Washington, DC think tank, proposed a novel application of an idea first suggested by noted Harvard economist Michael Kremer:[1] What if GAVI instead could make a binding promise to buy a not-yet-developed vaccine at a price that would make a firm's investment pay off, if and only if the vaccine met preset standards? Rather than paying for research by pre-identified innovators, they would instead pay anyone who achieved the outcome of producing a vaccine that met the needs of public health officials and people in poor countries. Might this promise incentivize innovation by manufacturers in search of a profit while permitting funders to hold onto their money until the product they wanted was brought to market?

This insight about the potential to orient funding around desired outcomes rather than the activity required to get there led to the creation of the first advance market commitment (AMC). The AMC was created

1 Michael Kremer and Rachel Glennerster, *Strong Medicine: Creating Incentives for Pharmaceutical Research on Neglected Diseases*, (Princeton, NJ: Princeton University Press, 2004).

to spur the final stages of development and investments in scale manufacture of a pneumococcal vaccine that would protect against strains of the disease common in the developing world: a disease that kills more than half a million children each year.[2] The governments of the United Kingdom, Norway, Canada, Russia, and Italy, along with the Gates Foundation, pooled a total of $1.5 billion to back a deal: any company able to make a pneumococcal conjugate vaccine that met predetermined safety and efficacy standards would be guaranteed a relatively high price for the early doses.

The AMC sought to mimic key aspects of a market—innovators take a risk when they envision a possible payoff down the line; consumers buy a product that suits their needs if and when it is developed. As in any attractive market, the total potential revenue from the deal would be set at a level sufficient to cover the development and manufacturing costs of the product with a modest markup. That potential revenue would then permit firms to make the R&D investments. Funders would not pick the winning firm(s) in advance by funding the R&D itself or offering a purchase guarantee. They would pay only for the product and would buy it from any firm(s) producing it. If no product is developed, they would not pay a penny.

The AMC had one special feature that made it particularly useful for incentivizing innovations that would benefit low-income countries. Any supplier reaping the rewards of the AMC would have to accept a relatively low price for the product after the "payment pot" was exhausted and would have to commit to continuing to supply the product. This would help to ensure that the benefits of the AMC funding would be sustained even after the original money was gone.

The result? By 2010, pneumococcal conjugate vaccine from the first eligible manufacturer was available to countries receiving GAVI support. Subsequently, one other company's product was also deemed eligible. As of 2016, the AMC-funded vaccine was protecting children in 54 countries around the world, and about one-quarter of the original AMC payment pot still remained as an incentive for additional manufacturers to get in on the deal.

2 Advance Market Commitment Working Group, "Making Markets for Vaccines: Ideas to Action," Center for Global Development (2005).

As the vaccine case illustrated, an AMC is a way to make a future market opportunity visible to businesses that are choosing among alternative ways to use capital today, while permitting funders to pay only for results. For most not-yet-developed products, an AMC is neither necessary nor feasible because the normal workings of the marketplace suffice to stimulate innovation. But for some—particularly products where the social value exceeds the perceived willingness to pay—an AMC may be the most efficient way to create an incentive for costly R&D and manufacturing. And for funders, it may be far better than making upfront investments in R&D. Funders don't have to pick winners among companies that think they are on the path toward a viable product, and they don't have to bear the R&D risk.

In its most generic form, an AMC is an open offer committing the purchaser to pay a relatively high unit price for the first units of a product that meets the preset eligibility requirements. To simulate a natural competitive market, the sales may go to any company with an eligible product. In turn, participating companies commit to supply the product at a lower unit price (also called a "tail price") in future years after the original payment pot is exhausted.

An AMC has four core elements, each of which constitutes a design challenge.

1 **Guaranteed funding.** The AMC commits to future purchases—potentially many years hence. In the case of the pneumococcal conjugate vaccine, most of the R&D had already been done, thanks to a lucrative market for a similar product in industrialized countries. Still, the guarantee has had to be in place for several years to allow for late-stage development, regulatory approval, and the build-up of production capacity. Most products would require a similar, or longer, timeframe. Although private funders, such as foundations and some national governments, are able to make legally binding commitments, many governments (including the United States) cannot do so without special legislative action.

2 **A target product profile.** The exact, observable specifications of the product must be described *ex ante* (based on essential requirements rather than actual results). In the case of a health product, for example,

specifications may include everything from the safety and efficacy levels to the required storage conditions, means of administering the drug or vaccine, and single- or multi-dose packaging. This can be challenging for products that are many years away. Setting the bar too low may allow suboptimal products to get to market, while setting the bar too high may discourage innovation.

3 **A means of assessing eligibility.** A regulatory agency, commission, or other entity that is seen by both purchaser and supplier as legitimate, unbiased, and technically competent is essential. In the case of health products, the U.S. Food and Drug Administration or a comparable national regulatory authority can serve this purpose. For other types of products, investors in the AMC would have to create a specialized process to adjudicate whether the product meets the specifications.

4 **Established set prices at the start and end of the AMC purchasing period.** An AMC design specifies the high starting price and a ceiling for the lower tail price. This AMC element represents the biggest departure from a normal market—and potentially the most problematic, because it requires educated guesswork about production costs. To avoid a situation that would be financially nonviable for the firm(s), the tail price must at least be greater than the likely production cost once manufacturing capacity is scaled up. Although this is challenging, it also represents an opportunity to signal to firms that they need to consider the eventual production cost during R&D; there's no point in developing a product that will be unaffordable to potential purchasers. When done well, this price signal further defines the outcome that the funder values—not only the production of a viable vaccine but its on-going availability at affordable prices.

In addition to these core elements, it is useful to have a credible demand forecast for the product. Although "demand risk" is a normal part of life in the private sector, the strength of the AMC incentive is greatest when accompanied by a credible estimate of year-on-year demand so that firms can better estimate the potential ease or difficulty of recouping their investment. In the case of the pneumococcal AMC, a credible demand forecast was augmented by a volume guarantee—a commitment by GAVI to purchase a certain minimum number of units in the early years.

Beyond the application of an AMC to develop a pneumococcal vaccine, other vaccines may also be appropriate targets. Think, for instance, of an AMC to incentivize development of a vaccine to prevent Zika or Ebola, or of any vaccine that could be viable without refrigeration. A similar case might be made for some types of drugs, such as antibiotics, and health-related devices, such as improved female condoms. In fact, structuring some of the reimbursement for pharmaceutical products under Medicaid and Medicare into AMCs could help shift public spending on drugs away from "me too" products, which are just costly versions of existing generic medicines, toward products that yield far greater health benefits.

Moving out of the health sector, agricultural applications of the AMC have been explored. New, environmentally friendly fertilizers and pesticides, for example, or better seeds for crops that are staples in poor countries could be good targets for a future AMC. An AMC could potentially be a useful means of attracting innovators to work on improved safety gear for firefighters and other first responders. If police departments across multiple states pooled funds, they might be able to incentivize the development and manufacture of "personalized guns" that could be used only by a particular police officer. An AMC might be the right way to incentivize the creation of technologies for clean transportation or solutions to other parts of the clean-energy puzzle and, eventually, even innovations that address complex social challenges, such as homelessness. In all of these cases, the public sector would need to be likely to buy the products if they existed—and an AMC could help to make that future market visible to innovators and investors today.

AMCs are a clever addition to our toolbox of innovation incentives.[3] The experiences with the pneumococcal AMC, now well along in implementation, offer confidence that such a tool can be created to solve a specific problem—and can work. The trick now is to match the concept of an AMC with a particular innovation challenge and to find funders who are ready, willing, and able to send a strong signal that today's R&D effort will be duly rewarded tomorrow.

3 Center for Accelerating Innovation and Impact, "Health Markets for Global Health: A Market Shaping Primer," U.S. Agency for International Development (2014).

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