



# 4

## Design choices

# Chapter at a glance

- The legal framework for an advance market commitment is founded on ordinary contract law. (See the draft contract term sheets in appendixes F and G.)
- Our multidisciplinary team comprising lawyers, public health specialists, economists and public policy specialists has considered the detailed design of the commitment with the aim of creating an appropriate set of incentives.
- We explain our recommendations for the arrangements for the structure of the contract, the technical specification of the vaccine and the organization of the Independent Adjudication Committee.
- Creating a market rather than a prize solves many of the challenges in designing incentives for R&D.
- The commitment is designed not only to reward the first producer to bring a product to market but also to create incentives for continuing R&D to create second-generation products that improve on the original.
- Within this broad framework are a number of detailed design choices and variants that should be considered. This will require further discussion among the stakeholders as the details of the commitment are decided.

### Legal issues: the contract structure

The advance market commitment would derive its credibility—and thus its ability to influence investment behavior—from the legal enforceability of the contracts. This is essential to provide enough assurances to developers to induce them to undertake the large investment for developing a new product.

The challenge is to design contracts sufficiently fixed to ensure that the donors cannot renege on their commitment when a vaccine is developed, but still flexible enough to accommodate contingencies not foreseen when the rules were established.

Working with experienced contract lawyers specializing in the pharmaceutical industry we have drawn up draft term sheets to illustrate the proposed contract (appendixes F and G). These are based on standard contract law, and the component parts of the proposed legal structure are common in law and business.

Some elements of the contract design and incentive structure will depend on the particular product for which the advance market commitment is implemented. But some core elements should be common to advance market commitments, whether for late-stage or early-stage products.

### Sponsors, developers and suppliers

Four parties are fundamental to the design—and eventual success—of the advance market commitment. The first is the sponsor—the entity that accepts the contractual obligations associated with funding the market demand. This may be one or more nongovernmental or government grant-making organizations, and must be a legal entity. The second is a developer—one or more pharmaceutical or biotech companies interested in pursuing the contract offered by the sponsor. The third is a designated supplier—that is, one or more developers who actually end up signing the agreement to supply the targeted product. For some products, particularly late-stage products, a single developer may also be the designated supplier. The fourth are the governments of developing countries that would benefit from the vaccines.

### Legally binding bilateral contracts

A bilateral contract is one signed by two parties: it becomes binding on the parties as soon as they exchange adequate consideration, which may be in the form of mutual promises, and it allows either party to pursue standard contract remedies, such as money dam-

ages and specific performance, if the other party fails to satisfy its contractual commitments. The bilateral structure, as distinct from a unilateral offer or a prize, creates enforceable obligations, making the funding commitment of the sponsor more credible.

The advance market commitment involves two types of legally binding agreements:

- First, an open agreement—the Framework Agreement—indicating the availability of a reward for any firms producing a product meeting pre-specified conditions. In this case, the reward is the right to sign the second contract (appendix F), which will be attached to, and incorporated into, the Framework Agreement. Firms interested in pursuing the R&D of a qualifying product, regardless of whether they are presently doing so, may sign on to this agreement, creating a binding obligation on the part of the sponsor to enter into the Guarantee Agreement with any firm that delivers a qualifying product.
- Second, a bilateral procurement agreement or Guarantee Agreement (appendix G).

The contractual commitments of the sponsor are clear from the outset to provide the promised reward: making co-payments at the guaranteed price, upon satisfaction of the eligibility criteria. Requirements on the developers under the Framework Agreement are minimal. If they succeed in developing a qualifying product, they are entitled to sign the Guarantee Agreement. Under this agreement, in return for being able to sell a number of doses of vaccine at the guaranteed price, the developer guarantees to supply the vaccine to eligible countries at a sustainable low price.

For early-stage products, it is important to have an open agreement at the outset—the Framework Agreement—so that many firms can compete to develop a product.

But for late-stage products, where the market landscape (such as first-generation suppliers and the time lag to second-generation candidates) and product profile are already known with some certainty, it is possible to proceed directly to the Guarantee Agreement, in which the sponsors underwrite a price guarantee.

### The Framework Agreement

The Framework Agreement establishes the rules for the competition among potential vaccine developers. Issued by the sponsors, it must be signed by the companies to become binding. At this stage there are only minimal obligations on the part of the signing

companies. The Framework Agreement creates the mechanism for the company to enforce the sponsors' commitment to move to a Guarantee Agreement for qualifying products.

The Framework Agreement also sets forth eligibility requirements for the vaccine (§8), creating an Independent Adjudication Committee (IAC) to adjudicate whether the requirements have been met by any candidate vaccine (§13–18) and establishing the rules for legal recourse (§27–29). Finally, the Framework Agreement specifies the incentive mechanism: that a developer of a vaccine meeting the technical specifications and usability requirements is entitled to enter the Guarantee Agreement with the sponsor (§5) (appendix F).

### The Guarantee Agreement

The Guarantee Agreement is a bilateral contract between the sponsor and any winners from the open stage (or designated suppliers). The sponsor must irrevocably guarantee that the designated supplier receives the pre-specified reward (price guarantee) for any qualified sales, subject to some also pre-specified cap on the sponsor's total commitment (§3). Qualified sales would be restricted to those that meet criteria established in the original commitment (for example, that the vaccine will be used in a Vaccine Fund–eligible country) (§6).

Guarantee Agreements could be signed with one designated supplier or with multiple suppliers, depending on the rules set out in the Framework Agreement, which would in turn depend on the objectives of the sponsors (§1). The Guarantee Agreement must also specify contract terms related to intellectual property rights, where relevant (§9) (appendix G).

### The Independent Adjudication Committee

The IAC is an impartial oversight body at the heart of the credibility of the advance market commitment. The IAC will:

- Decide if a product has met the eligibility criteria. It will have the authority to waive or modify technical specifications and usability requirements as appropriate, but only to make modifications that can lower the bar to accept vaccines that do not meet the specifications in full. The IAC will not have discretion to raise the bar once the framework offer has been made, except in the limited case of a *force majeure* event, and then only with a super-majority vote, which is subject to judicial review (§22).

- Designate approved regulatory bodies (or more likely, designate an approval mechanism—such as the WHO prequalification process) (§5).
- Be the main point of contact with developers throughout the competition.

Once a qualifying vaccine has been identified, the IAC will monitor sales, use and performance of approved vaccines and designate new vaccines as approved under the terms of the Framework Agreement (§8).

Importantly, the IAC's operational budget—to be provided by the sponsors—must be independent so that the sponsors are unable to influence the decisions of the committee after establishing the rules of the game (§18). Similarly, there will be straightforward rules allowing the IAC to recruit new members in the case of retirement or death (§13).

The composition of the IAC is critical to the success of advance market commitment. It should consist of a combination of ex-industry, global health experts, vaccine scientists and legal specialists.

In our consultations with industry, firms emphasized the need for a credible adjudication body and expressed concern about the potential for abuse. The rules must be clearly determined in advance, including dispute resolution. There was strong opinion in favor of having current or recent industry experience represented on the committee.

### Dispute resolution

It is impossible to foresee everything that may occur during the life of the advance market commitment. A number of scenarios can be imagined in advance and addressed in the contracts, but the most useful approach to the many unknown scenarios is to establish a clear and credible process for making decisions as events unfold.

While most decisions will be made by the IAC, a decision to invoke the *force majeure* clause should be subject to legal recourse through the courts if necessary (§16).

### Exit provisions

It may be sensible to include sunset provisions in the contract to allow sponsors to exit after a certain length of time. For example, if 30 years pass and no substantial progress has been made on the product of interest, a vaccine commitment may not be the most

useful approach, and the policy would be worth re-evaluating. So, a sunset clause might be included to specify that, at any time after 20 years had passed, sponsors could give notice that they would let the commitment lapse after 10 years, if no vaccine had been developed by then (§25).

Another type of exit provision—a *force majeure* clause—could allow the obligations to end if the disease environment changed enough to obviate or radically reduce the need for the vaccine. Such changes could occur, for example, if other technologies were developed to control the disease, such as vastly better insecticides against the mosquitoes that transmit malaria. To deal with such contingencies, a vaccine commitment might specify that the sponsor’s obligation would end if the independent adjudication committee determined that the burden of disease had fallen by more than 50% or 75% (§22).

To avoid the danger that a *force majeure* clause might be used by a sponsor to renege on the commitment, it would be important to:

- Establish clear standards in the Framework Agreement for invoking the *force majeure* provision.
- Vest the authority to invoke this clause with the IAC, which would be chosen for its credibility, rather than the sponsor, which might have a financial interest in the decision.
- Require a super-majority of the IAC—perhaps a three-quarters vote—to invoke such a clause.
- Make any decision to invoke the clause subject to legal challenge.

### Eligibility requirements

Eligibility requirements would define the desired product and other elements required of the developer of the desired product to qualify as a designated supplier. Defining appropriate eligibility requirements is critical to the success of the commitment.

The eligibility requirements would be set by the sponsors in advance, after discussion with key stakeholders (see appendix F). The requirements might include:

- Technical requirements on the product: indication, target population, minimum efficacy requirements, duration of protection, interference.
- Usability requirements on the product: dosage, route of immunization, presentation, storage, safety requirements.
- Specifications of regulatory approval and quality control.

Because these would become the targets of research and product development once established, the framework agreement must not allow sponsors to make the requirements more demanding after it is established. Since products may be useful without perfectly matching all eligibility criteria, the adjudication committee might be given authority to relax the requirements to accept products that nearly meet the pre-established requirement (§5).

In addition, sponsors may establish eligibility requirements on “qualified sales” of a product—for example, that products be sold to a UN agency, developing country or other approved buyer, or that products must be used in a Vaccine Fund or other eligible country. These too must be clearly established from the outset—and must not be subsequently changed to become more onerous.

In our consultations with industry, we found that firms were in favor of setting the bar on product specifications high enough that the sponsor could have reasonable assurance that the product would serve public health needs and be accepted by the relevant developing-country governments. There was also a consensus that there should be a procedure to make the specifications less onerous in case a useful product were developed that did not completely meet all specifications. Industry representatives indicated that they should have the opportunity to review and provide input on product specifications before those specifications were set.

Some firms wanted the opportunity to engage in a dialogue with the adjudication committee during the development process to determine whether the committee would be likely to grant waivers from the stated eligibility guidelines and to learn more about how those guidelines would be interpreted. (This is similar to procedures under which firms have the opportunity to consult the U.S. Food and Drug Administration so that they may structure their pivotal clinical trials and prepare drug approval applications so as to meet better the expectations of the regulatory authority that will be responsible for approving their products.)

Some public health experts were concerned that it would be difficult to establish in advance technical requirements that a vaccine would need to meet. Clearly, it is difficult to say in advance exactly what the characteristics of a successful vaccine will be. But there was a consensus that, if the requirements were framed as outputs rather than a specification of inputs, it would be possible—though complicated—to agree to product requirements in advance. For example, while it would not be desirable to specify in advance whether a malaria vaccine should be a “blood stage” vaccine, it

would make sense for the specification to include some minimum duration of protection against severe malaria.

### Co-payment and the case against quantity guarantee

We concluded that the advance market commitment should guarantee a minimum price for the vaccine but should not guarantee a minimum quantity that would be bought from each supplier at this price. In this way, the commitment is a market not a prize. There are several reasons why we concluded this was preferable.

#### The case against a quantity guarantee and for co-payment

First, a quantity guarantee would greatly complicate the drafting of the technical specifications—and perhaps make it impossible. It is possible that a product might meet all the pre-announced eligibility requirements and still be unsuitable for use in poor countries. For example, if a vaccine generated side effects that were medically harmless but culturally unacceptable, there might be an unwillingness to use the vaccine. Attempts to impose its use might even be counterproductive, reducing the acceptability of vaccination in general. It is impossible to anticipate all the possible contingencies in which the purchase of a seemingly effective vaccine would not be warranted, and consequently it is not possible to attempt to write them into the technical specifications. We concluded that the commitment should be to pay for vaccine only if there is demand for the vaccine and if a recipient country is willing to take the steps necessary to ensure that the product is delivered to those who need it. This ensures that sponsors do not find themselves legally obliged to spend \$3 billion on a vaccine that nobody wants.

A modest co-payment, either from the country or from a donor, will provide a market test of interest in the vaccine and reduce the risk of waste. As is now the case, a donor could provide the payment through development assistance.

A second benefit of not guaranteeing to buy a particular quantity is that it avoids the problem of deciding what to do if several competing products are successfully introduced. If a superior product becomes available and so qualifies for the price guaranteed under the advance market commitment, the developing countries can choose to use the product most appropriate for their

circumstances because donors are not locked in to paying for a particular quantity from a particular producer.

Our proposed approach of creating a market rather than a prize therefore greatly simplifies the problems that would otherwise occur in trying to draw up a specification that anticipates all eventualities, and in trying to create room for superior products to be developed to enter the market.

#### Keeping the co-payment low

A disadvantage of the co-payment is that it may add a small amount of uncertainty about whether a product will eventually be purchased, and so may increase the firms' perception of demand risk. This suggests that co-payments should be modest.

Furthermore, requiring a large co-payment might limit access to the product, and by reducing the prospects of adoption it would also reduce incentives for developers.

In principle, the developing country co-payment should be broadly the same amount per course of treatment as the long-term price of the vaccine under the contract. This ensures that developing countries will be asked to pay an affordable and sustainable low price from the outset, which they can be sure will continue when the commitment is exhausted.

#### The allocation of demand risk

The absence of a quantity guarantee, and the need for co-payments from developing countries, leave some demand risk in the hands of the developers. Given that our objective is to make investment in medicines for neglected diseases more attractive and less risky, we asked ourselves whether the program would be more successful if sponsors took over all the demand risk.

When we discussed this with industry, there was a good understanding of the case for a price guarantee but no quantity guarantee for early-stage products. This allocation of risk resembles the market for medicines in developed countries, in which ability to pay is relatively favorable but quantities are not guaranteed. In this environment firms must bear the risk that customers will not want their product or that they will lose market share to a better product.

The proposed pricing structure—with a high price paid for the first treatments purchased and a low price thereafter—actually transfers a substantial portion of the demand risk from the firms to the sponsors, since the net present value of the revenues to the

company is much more stable than it would be under a single price charged over a longer time period. The spreadsheet model demonstrates that, under a more pessimistic scenario in which it takes 15 years for adoption to reach steady-state levels, and adoption reached levels only 10 percentage points below the DPT3 rates, the program would still generate \$2.7 billion in revenue in net present value terms for the vaccine developer (in 2004 dollars), and would cost less than \$20 per DALY saved.

It is most efficient for risks to be borne by the party that can manage them best. It is desirable for industry to bear some of the demand risk, so that there is an incentive to focus work on producing the most effective and usable product. Under the advance market commitment we have designed, the sponsors would bear the risks associated with unpredictable donor funding and pressure for low pricing, while leaving industry to manage the risks associated with the usefulness of the product.

### The guaranteed price

Chapter 5 looks in more detail at the calculation of the appropriate guaranteed price. The goal is to set a price high enough to accelerate R&D in a vaccine for the disease, but at a level at which the purchase of the vaccine, if and when one is developed, is a cost-effective use of aid resources.

To get the full advantage of the commitment, sponsors would need to commit to an overall price well above the pennies-per-dose now paid for existing vaccines in developing countries. The benefit of low prices is that they ensure access to existing vaccines, but they are not sufficient to generate investment in new vaccines or to ensure that new vaccines are rapidly made available in developing countries. Donors increasingly understand that, for vaccines that have only a small market in affluent countries, it will be necessary for firms to recover their R&D costs through higher prices in developing countries than they charge for existing vaccines.

### Two-stage pricing

We recommend a two-stage pricing system. In the first stage, a relatively high price (the “guaranteed price”) would be guaranteed up to a fixed maximum of treatments purchased. In return for the right to sell at that higher price for the initial treatments sold, the supplier would be contractually committed to supplying further treatments at a lower price set at a level close to the cost of production (the “base price”).

### Why have two-stage pricing?

Two-stage pricing is attractive to developing countries and sponsors because it would ensure long-term sustainability of the vaccine program. This ensures that sponsors are not undertaking a long-term commitment to purchase vaccines indefinitely, but rather are making a finite commitment that pays for the risk-adjusted costs of R&D and gearing up production, albeit in a different form. Thereafter, pricing is close to marginal cost, which ensures an efficient level of use.

This price structure would also create a strong incentive for firms to accelerate development, because there would be a more substantial reward for the first developer (who could capture the bulk of the high-price market), while the prospect of capturing part of the high-price market would preserve an incentive for the development of improved vaccines later.

A two-stage pricing structure is also attractive to the vaccine developers, because the front-loading of payments would enable them to recover their investment more quickly and with greater certainty than if they charged a single lower price for more doses over a longer time. We found in our discussions with industry that the proposed two-stage price was both understood and welcome.

### How would two-stage pricing be implemented in practice?

In return for receiving the guaranteed price for the initial doses, and so recovering their investment, the designated suppliers will be contractually required to supply subsequent doses to eligible countries at the base price, until generics manufacturers take up production, if reasonable notice of demand is given. If a company is not able or chooses not to fulfill that obligation, it faces financial penalties under the contract. Alternatively, it would be required to license the technology for use for developing-country markets or to have the technology placed in the public domain to allow generics producers to meet demand instead. Once the guaranteed price commitment is satisfied, the donors are under no obligation to buy any doses at the base price, but the supplier is under an obligation to meet demand at that price.

The guaranteed (higher) price will be set in advance in the Framework Agreement, at the outset of the commitment. The Framework Agreement will specify how it is to be adjusted for inflation. The price will vary according to the disease.

The base (lower) price can either be set in advance as a dollar amount per treatment or determined by an agreed formula related to the cost of production. There are advantages and disadvantages to each approach. It would be possible to devise more complex hybrid options—for example, in which the sponsors and the producers share the benefits of reducing the cost of production through a formula.

Setting the long-term base price is a critical component of the advance market commitment. Although this is not uncomplicated, we believe that it will be possible to agree an appropriate price, or formula, that is affordable for developing countries while covering the cost of production.

### Allowing second entrants but avoiding “me too” copies

The advance market commitment is intended to create a market, not simply to reward the first supplier. We recommend that second and subsequent vaccine suppliers be allowed to compete for the market as designated suppliers, if their products are deemed (by the Independent Adjudication Committee) to be superior, at least in some relevant respect, to existing qualifying products.

### Allowing second qualifiers

The ease with which second and subsequent products can qualify needs to balance, on the one hand, the need to avoid creating incentives that lead to wasteful duplication of research that does not lead to improvements, and, on the other hand, the need to ensure that there is scope for incremental improvements as the technology improves. Our proposal—that qualifying vaccines be allowed to enter the market if they can demonstrate that they are superior—is intended to balance these considerations.

It is possible that several different products will be licensed at about the same time. In this case it would be sensible to allow them to share the market at the outset. To achieve this, the contract could allow a window—say one year—within which second

qualifying products would be eligible for the guarantee without having to demonstrate superiority.

### Sharing the guaranteed market among more than one supplier

The guaranteed price is limited to a fixed number of treatments, even if there is more than one qualifying product. In other words, if there were more than one designated supplier and countries split their demand across the suppliers, no single firm would sell the full designated number of treatments at the guaranteed price.

Once the designated number of treatments has been bought, under the contract suppliers would be required to provide vaccines at a lower price. But at that stage, no supplier would have received the full revenue of the advance market commitment.

We therefore propose that, if a designated supplier has not yet received a pre-determined minimum revenue (which would be less than the total advance market commitment), it be allowed to charge a fixed mark-up over the agreed base price, until its total revenues reach that minimum revenue.

### Should we improve the terms over time?

Some industry representatives suggested that sponsors could establish an initial contract but then improve the offer depending on market response. One suggestion was that sponsors could be encouraged to add to the market reward as a successful candidate emerges. Firms with a promising candidate would then be motivated to invest in more expensive trials to reach the growing market. Others suggested that prices or other contract terms be made more attractive to industry over time if the initial terms do not generate the expected response.

This approach has many of the attributes of an auction, which could identify low-cost producers. If the price did not rise too quickly, this would not lead to strategic delay. The Working Group felt that this approach did not have to be included in the initial contract and that it would be open to the sponsors to add it later.