

**Ministero dell'Economia e delle Finanze**

**Advanced Market Commitments for vaccines  
A new tool in the fight against disease and poverty**

*Report to the G8 Finance Ministers*

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## EXECUTIVE SUMMARY AND CONCLUSIONS

More than 7 million people a year die from infectious diseases like pneumococcus, malaria, and HIV/AIDS, mostly in poor countries. This is an unacceptable human tragedy and a disaster from an economic point of view. Infectious diseases destroy human capital, cut back income growth, constrain development.

Immunisation is the best way to fight global diseases. It saves lives in a cost-effective way and fosters economic development through its beneficial impact on human capital. The potential impact of effective vaccines on quality of life and economic development in the developing countries as well as their contribution to achieving the Millennium Development Goals are hard to exaggerate.

However, investment by the pharmaceutical industry to develop vaccines against infectious diseases that primarily affect poor countries is very small in relative terms. From the point of view of economic analysis, this outcome is not surprising. In addition to the scientific risks inherent to the development of any new vaccine or drug, companies face additional uncertainties. Poor countries may not be able to afford to pay a price sufficient to remunerate investment costs. Moreover, there might be special difficulties in protecting intellectual property and the possibility of pressures on producers to sell the newly discovered vaccines at low prices.

Establishing Advanced Market Commitments (AMCs) is an innovative way to address these issues, correct market failures and accelerate the discovery, development and production scale-up of new vaccines by spurring investment by the biotechnology and pharmaceutical industry.

In a nutshell, the idea is straightforward. Donors commit to subsidize the purchase of a new vaccine if and when one is developed to meet the required standards and it is demanded by developing countries. This commitment creates a larger and more certain market that replicates market conditions prevailing in developed countries. By restoring appropriate incentives, AMCs can stimulate private research and investment, accelerate the discovery of new vaccines, save lives and contribute to economic development in a cost-effective way.

AMCs are a market-based form of public intervention that encourages private sector investment, competition, and continued innovation. Market forces rather than donors determine the allocation of the additional investment on vaccine development stimulated by the AMCs. AMCs would be complementary to existing publicly funded research, or immunization initiatives.

The Report – based on the analysis of six background papers collected under separate cover – is organised in three Sections.

Section I reviews the rationale of the AMC approach and shows that it is *cost effective*, it has a high social rate of return and it is *complementary to other interventions* in favour of developing countries. The *potential candidates* for the application of the AMC framework, which include some of the most important pandemics such as HIV/AIDS and malaria, are also discussed.

Section II identifies the concrete features that are necessary for an AMC framework to achieve the desired objectives. They can be summarized as follows.

- For the AMC framework to affect investment decisions, it has to be perceived as fully credible and reliable, and hence must be underpinned by *legally-binding contracts and appropriate financing arrangements*.
- The specific risks and challenges for the development of each new vaccine require the design of *a separate AMC mechanism for each target disease*, incorporating an estimate of the market size necessary to stimulate additional private investment and accelerate the development of the target vaccines.
- For AMCs to have a lasting impact on public health and development, *immunization programmes have to be sustainable*, i.e. they have to continue after the AMC subsidy terminates. This can be achieved by providing for competition (*encouraging innovation* for more efficacious products after the discovery of vaccines that meet the AMC standards) and requiring producers that benefit from the AMC subsidy to commit to supply further doses to developing countries at a price close to marginal cost, or license other firms to do so.
- The scientific and medical expertise needed for the implementation of AMCs requires the establishment of an *Independent Assessment Committee*, whose reputation and independence should make it authoritative.
- Effective AMC implementation also requires putting in place all the economic, institutional and technical arrangements *to combat corruption and ensure the actual delivery of vaccines and a strong public health and development impact*.

Section III presents a range of available options to implement an AMC framework in line with the requirements described above. They cover four areas.

i) **The size of the AMC commitment.** The selection of the diseases to be addressed by the AMC framework determines the magnitude of the necessary financial commitment. The implementation of the AMC framework could also take place in successive steps, adding further AMCs for more diseases.

ii) **Financing options.** If perceived to be reliable by industry, the AMC approach will start mobilizing private investment on target vaccines from its launch. The expenditure by donors on vaccine purchase only takes place in the future, when and if target vaccines become available and are demanded by developing countries. Three classes of financial arrangements can ensure that adequate resources are then available: full frontloaded financing, financing through periodic contributions, and financing when disbursement is required.

iii) **Legal arrangements.** The Report has explored the legal structure in detail. It can be implemented either with donors directly entering into the legal agreements or with a third party acting on their behalf.

iv) **Administration and support.** To be implemented and managed, the AMC framework only requires a very light administrative structure that does not entail the creation of any new institution. Existing institutions provide several options for supporting the AMC framework.

### *Conclusions*

In accordance with the mandate assigned to Italy last June, this Report has reviewed the AMC approach as a new mechanism to accelerate the development and delivery of vaccines against diseases that mostly affect developing countries, taking away millions of lives each year and hampering economic development.

The Report shows that the AMC framework is a market-based, result-focused initiative that is capable of mobilizing private resources before public money are spent and is very cost-effective if compared to other interventions in favour of developing countries.

With a view to assessing effective implementation, the Report identifies the specific features that are necessary for AMCs to achieve the desired objectives and presents a range of available options that could allow the G7 and other donors to implement AMCs for specific diseases that primarily affect developing countries.

The AMC initiative is feasible and stands as an innovative and cost-effective tool in the fight against global disease and poverty.

## I. INTRODUCTION AND RATIONALE

More than 7 million people a year die from infectious diseases like pneumococcus, malaria, and HIV/AIDS, mostly in poor countries. This is an unacceptable human tragedy and a disaster from an economic point of view. Infectious diseases destroy human capital, cut back growth, constrain development, as documented by numerous studies that show a direct and quantifiable impact of improved health conditions on economic growth.

Immunisation is the best way to fight global communicable diseases, a primary cause of the mortality gap between high- and low-income countries. It saves lives in a cost-effective way and fosters economic development through its beneficial effect on human capital. The potential impact of effective vaccines on quality of life and economic development in the developing countries as well as their contribution to achieving the Millennium Development Goals are hard to exaggerate.

### *Vaccine market issues and failures*

In spite of that, the future availability of public funds to purchase new vaccines against infectious diseases that primarily hit poor countries is perceived to be very uncertain. As a result, private investment to develop these life-saving vaccines is very small in relative terms.

From the point of view of economic analysis, this outcome is not surprising. Developing a new vaccine presents huge scientific challenges, can take up to twenty years and requires large investment. Vaccines mostly relevant to the developing world face additional uncertainties and risks. Poor countries may not be able to afford prices sufficient to remunerate investment costs. Their demand for vaccines is unpredictable as institutional and administrative factors may constrain actual uptake even when resources could be available.

These uncertainties and resulting market failures hamper investment and exacerbate the bias of competitive markets towards the insufficient provision of goods and services with a public good character, including research on vaccines mainly aimed at poor countries. Investment is further discouraged by special difficulties in protecting intellectual property and the possibility of pressures on producers to sell the newly discovered vaccines at low prices.

For these reasons, the developing countries' market for vaccines is perceived by industry to be small (despite its potential size), particularly risky and unpredictable, and

hence not profitable enough to warrant the volume of investment that would be desirable from a public health point of view.

*Advanced Market Commitment (AMC) can be part of a solution*

An Advanced Market Commitment for vaccines (AMC in what follows) is a commitment for an amount of funds to subsidize the purchase, at a given price, of a vaccine not yet available, if an appropriate vaccine is developed and it is demanded by developing countries.

The guarantee in advance that the funds will be available to purchase vaccines once they are available can drastically reduce the uncertainty on their effective demand. In practice it establishes a market that the biotechnology and pharmaceutical industry perceives to be too small and uncertain.

By establishing a market, AMCs create incentives for investment in vaccines for poor countries that are similar to those prevailing for medicines developed for affluent markets. Available evidence suggests that the prospect of a valuable market should increase investment in new vaccines. In this way, AMCs will mobilize additional private resources to fight poverty and global diseases even before donors disburse any money.

Because AMCs establish competitive markets for vaccines, rather than a prize for the first developer, they can be designed to encourage private sector firms not only to accelerate the development of new and effective vaccines, but also to develop second and third generation products that improve on the first, to invest in large volume production with reduced unit costs, thus providing vaccines at low prices in the long term.

Extensive consultations with vaccine manufacturers and biotechnology firms have revealed the industry's keen interest in the AMC concept. They have also led to a numbers of suggestions (e.g. on the importance of sizing AMC commitments to the target markets and of minimizing transaction costs in the contracting arrangements) that have been taken into account in the analysis of the required features of AMCs.

*AMCs are cost effective, result focused and market based*

It has long been established that immunization is a very cost-effective form of public health intervention. As shown in several studies by the World Bank and others, this is particularly true in the developing world, where infectious diseases kill millions of people each year and the direct medical benefits of immunization are even more strongly linked to improved economic performance and sustained development.

Against this background, the cost-effectiveness of AMCs results from their ability to create market incentives for private sector investment in the development and production scale-up of a vaccine to serve the developing world, accelerating the availability of life-saving vaccines in developing countries and reducing the typical 10-15 year delay in the introduction of vaccines in low-income countries after their successful use in industrialized countries. As shown by the estimates (in terms of cost per disability-adjusted life year) presented in the background paper *The rationale for AMC*, AMCs for vaccines stand as a particularly cost-effective instrument to fight disease and poverty.

There are other arguments that make AMCs an attractive tool for development policy. First, if successful, AMCs motivate additional private investment in vaccine development, so that the commitment of public resources leverages the mobilization of private resources well before any money is disbursed.

Second, AMCs focus on results; public funds are spent only if and when products that meet the required public health standard become available and are demanded by developing countries.

Third, AMCs are a market-based form of public intervention. They are not a prize for the first successful vaccine developer, but an open multi-year commitment that encourages entry, competition, and continued innovation. Market forces rather than donors determine the allocation of the additional investment on vaccine development stimulated by the AMC. AMCs are easily designed to be consistent with international rules and obligations on intellectual property.

#### *AMCs are complementary with other initiatives*

By establishing a valuable market, AMCs provide incentives for private investment in the development of vaccines against diseases that kill millions of people every year. Such a “*pull* mechanism” is not an alternative, but is highly complementary to other public and philanthropic interventions in the health sector and, more generally, in development aid.

AMCs are particularly effective when combined with *push* interventions – such as the public and philanthropic funding of research through academia, public-private partnerships and other bodies – because of the network effects of the increased number of scientific researchers working on the target diseases as well as the enhanced probability that scientific research swiftly translates into the production of effective and safe vaccines.

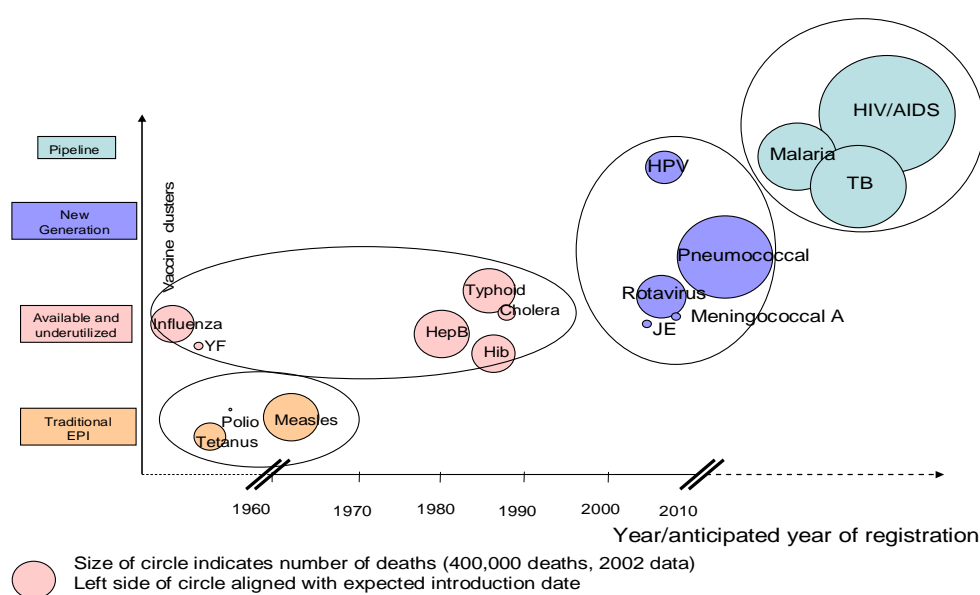
The private resources mobilized by successful AMC's would act in synergy with initiatives to expand immunization (e.g. GAVI and IFFim) and strengthen health systems.

*AMCs can be focused on vaccines that would save millions of lives*

To maximize health and development impact of AMC's, they can be targeted to a focused range of diseases that can be identified on the basis of the burden of the disease in the poorest countries, the potential effectiveness of a vaccine versus other interventions, and the capability of an AMC to motivate the appropriate industry actions.

The chart below summarizes the available information about the mortality and the state of development of vaccines against a wide range of diseases. It shows that vaccines can be divided into four groups. Vaccines in the group "traditional" (such as tetanus, polio, diphtheria) are widely available in developing countries, and those in the group "available and underutilized in developing countries" (such as hepatitis B, typhoid, cholera) are already licensed, produced and sold. Although their further diffusion in the developing world is the objective of various initiatives (including programmes sponsored by UNICEF, GAVI etc), they are not priorities for AMC's. AMC's as described here are much more relevant for the development of vaccines against diseases belonging to the other two groups: "late-stage vaccines", which have not yet been licensed but are advanced, and "early-stage vaccines", which are significantly less advanced and whose development horizon is much more uncertain.

**Figure 1. Vaccine horizon and burden of disease**



Source: WHO and World Bank analysis

This analysis (developed in more detail in background paper *Key features of the AMC framework*) leads to a focused range of potential candidate vaccines for the application of the AMC framework. They include the most important pandemics that the international community is already addressing for some aspects (e.g. the treatment of HIV/AIDS, tuberculosis and malaria through the Global Fund or immunization through GAVI) and diseases whose prevention would significantly contribute to the achievement of the MDGs. The table below summarizes the key information on these vaccines.

**Table 1. Potential candidates for AMCs.**

Vaccine	Est. annual number of deaths	At-risk populations	Vaccine Status
<b>HIV/AIDS</b>	3 million deaths	High risk groups Continent of Africa	Phase III trial ongoing in Thailand. Other candidates in Phase I or Phase II.
<b>Pneumococcus</b>	1.6 million deaths, mostly due to pneumococcal meningitis or pneumonia	Up to 50% of cases in children under 5; highest at risk are elderly and children <2	7-valent vaccine available since 2000 and used in industrialised countries, but does not contain serotypes 1 and 5 which most impact developing world. 9-valent and 11-valent candidates in late stage clinical trials; Gambia trials demonstrate 77% efficacy in preventing infections caused by 9 serotypes and 16% reduction in overall child mortality.
<b>Tuberculosis</b>	1.6 million deaths	HIV infected or others with compromised immunity	Six candidates in Phase I trials
<b>Malaria</b>	1.1 to 2.7 million deaths;	2 billion people in endemic regions; children under 5	About 90 candidates in pre-clinical or Phase I or Phase II research. Recent Phase IIb trial in Mozambique among children 1-4 years old of one candidate demonstrated 30% efficacy against clinical disease and 60% efficacy against severe disease for six months (still under evaluation in study population).
<b>Rotavirus</b>	440,000 to 500,000 deaths	Children under five; between 6 months and 2 years most vulnerable	One vaccine licensed and under review in several middle-income countries. Clinical trials in developing country settings. Late phase clinical trials for one other candidate and submittal to FDA.
<b>Human Papillomavirus</b>	250,000 - 270,000 deaths	Women, primarily in developing countries	Phase III trials have been successfully completed for a 4-valent product with late stage development for a 2-valent candidate. Licensing expected in 2006-2008.

## II. NECESSARY FEATURES FOR AMCs TO BE EFFECTIVE

This section presents the features that an AMC mechanism must possess to be effective in accelerating the development of new vaccines by biotechnology and pharmaceutical firms and, then, in ensuring that AMCs translate into the delivery of vaccines and a significant public health impact.

The various features discussed in this Section reflect the consensus results of the background work on AMCs (including work done before the preparation of this Report), which has involved extensive consultations with all the stakeholders. They can be grouped under five headings:

1. Reliability in the eyes of the industry;
2. Appropriate incentive structure;
3. Appropriate size of the market;
4. Fair and efficient management;
5. Arrangements to ensure effective execution and public health impact.

### **1. Reliability in the eyes of the industry**

The very purpose of AMCs is to modify the behaviour of the industry by establishing a market that is to all intents missing, as it is not perceived to be sufficiently reliable and profitable. For the industry to take such a market into account when making R&D and investment decisions, the AMC mechanism has to be fully reliable – i.e. underpinned by legally-binding contracts and appropriate financing arrangements (for details, see Section III).

### **2. Appropriate incentive structure**

AMCs should have the maximum public health impact possible. Accordingly, the design of AMCs should be tailored to establish appropriate incentives for stimulating investment in the research and development of the relevant vaccines (including continuing research into new and improved vaccines after the discovery of the first generation of effective products). The design should also ensure that immunization programmes are sustainable in the long-term, when the financial support from AMCs is no longer available. This section translates these general principles into specific requirements for the design of AMCs.

## 2.1 *The definition of the AMC terms*

The basic principle underlying the AMC framework is to spur private investment in vaccines for the developing world through the creation of markets by a credible commitment to subsidize their purchase once they are developed. In addition, AMC should promote competition and ensure multiple suppliers.

To achieve the desired result, however, the specific characteristics of an AMC in terms of medical efficacy, market size, price per dose, and other provisions must reflect the specific market risks and scientific challenges faced by the industry in the discovery and development of the target vaccines. Indeed, as argued in the background paper *Key features of the AMC framework*, the maximum degree of effectiveness of the AMC approach is obtained by defining, within a common framework, the specific terms of each AMC mechanism for each disease.

For example there are different risks and challenges associated with earlier- and later-stage vaccines. Earlier-stage products face huge scientific and technical challenges, compounded by large demand uncertainties. Consequently, AMC terms would have to be designed to attract biotechnology and pharmaceutical firms' investment in the relevant scientific research and then in the development of candidate vaccines into viable products, as well as in sufficient production capacity. Later-stage products, on the other hand, are scientifically and technically more advanced, but still face substantive demand uncertainty – much higher than for products directed at the developed countries' market. AMC terms would therefore have to attract firms to invest in the last steps of development and licensure, and in the production capacity needed to meet demand by developing countries as well as to stimulate R&D on improved products.

As with earlier- and later-stage products, each vaccine faces specific scientific challenges and market risks that must be considered explicitly in the design of an AMC mechanism.

## 2.2 *Long-term sustainability of the vaccine programmes*

To ensure public health impact, immunization programmes must be sustainable in the long run, i.e. they can continue after the vaccine doses subsidized by the AMC are used up. To achieve this, firms that participate in the AMC must commit to supply subsequent doses at a lower price, or to license other producers to do so.

As discussed in the background paper *Key features of the AMC framework*, a two-stage pricing structure both ensures that donors are not committed to purchase vaccines

indefinitely to guarantee long-run sustainability and allows vaccine developers to recover their investment more quickly than if they charged a single lower price for more doses. Contacts with pharmaceutical companies and other stakeholders have shown that two-stage pricing is understood, acceptable and can be effectively implemented.

The financial and scientific terms of AMC agreements have to reflect this concern and identify an appropriate two-stage pricing structure (which requires either fixing the lower price *ex ante*, or agreeing in advance on a process to determine it when more information is available on production costs) that strikes the right balance between the public health goal of sustainable supply and the need to establish a sufficient return on the investment of successful vaccine developers.

### *2.3 AMCs and innovation*

The purpose of AMCs is to prevent deaths and disability by accelerating the development of and access to effective new vaccines. This means not only encouraging the discovery and development of a first-generation product (as well as investing in the necessary production capacity), but also the development of subsequent improved vaccines, which have a superior efficacy and/or are easier to distribute and use.

In order to achieve this objective, the AMC terms can be designed to maintain incentives in continued research on new and improved vaccines even after the first vaccine meets the scientific requirements specified in the AMC.

It is possible to maintain incentives for vaccine innovation by increasing the size of a specific AMC at a later stage or by designing the AMC terms appropriately.

### **3. Appropriate size of the market**

For an AMC to be effective in terms of behaviour change on the part of the biotechnology and pharmaceutical industry, the commitment for each disease must create a market of sufficient size. If the commitment is too small the AMC approach will have little effect, as it would not motivate increased investment by the industry.

Determining the appropriate size of an AMC is a difficult exercise because R&D on vaccines is an uncertain investment, particularly when scientific challenges are still very hard, and donors imperfectly observe the costs and risks faced by the industry.

The estimates of the appropriate size of an AMC presented below have been developed through a modelling exercise and cross-checked using different approaches. The methodology employed, discussed in detail in the background paper *The appropriate*

*size of AMCs*, mimics industry's own approach for assessing investments on the basis of expected demand, likelihood of success and probable costs. For later-stage products, such as the vaccines against rotavirus and pneumococcus, the estimates based on firm-level costs provide a greater degree of certainty. For vaccines at an early stage of development, notably against HIV/AIDS and tuberculosis, estimates are necessarily more tentative and contingent on complementary support for scientific research that strengthens the effectiveness of AMCs.

The Table below presents the estimates of the size of the commitment which, for each of the vaccines that stand as potential candidates for an AMC, is estimated to be necessary to achieve the desired policy goals.

**Table 2. AMC: commitment size and expected effects**

Vaccine	Nominal value (\$ billion)	Years to estimated availability	Net Present Value (\$ billion)	Nominal yearly contributions by all donors (\$ million)	An AMC would...
<b>Rotavirus</b>	0.8-1.0	2	0.7-0.8	250-320	<ul style="list-style-type: none"> <li>• influence decisions to expand capacity to meet a larger share of developing country demand;</li> <li>• accelerate access to vaccine.</li> </ul>
<b>Human Papillomavirus</b>	0.8-1.0	2	0.7-0.8	250-300	<ul style="list-style-type: none"> <li>• create incentives to invest in the incremental studies and production capacity to serve developing world.</li> </ul>
<b>Pneumococcus</b>	1.0-1.5	4	0.8-1.1	180-270	<ul style="list-style-type: none"> <li>• create incentives to invest in the incremental studies and production capacity to serve developing world.</li> </ul>
<b>Malaria</b>	4.5-5.0	11	2.4-2.6	300-330	<ul style="list-style-type: none"> <li>• attract additional investment in establishing proof of concept and developing and producing viable products;</li> <li>• influence decisions to expand capacity and accelerate access to vaccine;</li> <li>• encourage investment for second generation products.</li> </ul>
<b>HIV/AIDS</b>	5.5-6.0	15	2.3-2.5	240-260	<ul style="list-style-type: none"> <li>• attract additional investment in establishing proof of concept and developing and producing viable products;</li> <li>• influence decisions to expand capacity and accelerate access to vaccine;</li> <li>• encourage investment for second generation products.</li> </ul>
<b>Tuberculosis</b>	5.5-6.0	15	2.3-2.5	240-260	<ul style="list-style-type: none"> <li>• attract additional investment in establishing proof of concept and developing and producing viable products;</li> <li>• influence decisions to expand capacity and accelerate access to vaccine</li> <li>• encourage investment for second generation products.</li> </ul>

In the Table above, the size of the AMC commitment is expressed in three different ways, which are equivalent from a financial point of view. Column 2 presents the commitment in nominal terms, conventionally assessed in its entirety at the time when vaccines become available, even though actual disbursement would take place over a number of years. Vaccine availability is taken to be 3 years in the future for Rotavirus and HPV, 5 for Pneumococcal, 11 for Malaria, and 15 years for HIV/AIDS and Tuberculosis.

Column 4 expresses the same estimates in terms of 2005 Net Present Value, on the basis of the hypothesis of a 6% interest rate and the assumption that the funds are available at the time of vaccine availability.

Column 5 translates the same estimates in terms of the constant nominal yearly contributions, to be divided by donors, that would generate the value of column 2 at the time when the vaccine is assumed to be available. For illustration purposes, contributions are taken to be constant through time and cover the period from the launch of the AMC to the assumed time of vaccine availability.

In the background paper *The appropriate size of AMCs*, the estimates presented in Table 2 have been cross-checked with the ones presented in several other studies and obtained through different methodologies. It is reassuring to note that the results are all roughly comparable (when expressed in common units).

As discussed in the background paper *The rationale for AMCs* and recalled in Section I of the Report, spending under AMCs of this size would be very cost effective. Cost effectiveness is also ensured by the fact that AMCs are result-based: there is no expenditure unless a suitable vaccine is produced.

Within the ranges presented in Table 2, there is no single “correct” market size: larger commitments provide greater incentives for more research that would in turn increase the likelihood of a new vaccine being developed sooner – a benefit which is estimated to be worth the additional cost.

As a final point, it should be mentioned that it could be possible to increase the size of an AMC commitment at a later stage if the initial commitment turned out to be insufficient to stimulate adequate industry response. An increase at a later stage could also be an option to strengthen incentives to innovate and develop improved products after the development of the first-generation vaccines that meet the AMC requirements. Monitoring the industry’s response to AMC and evaluating the public health need for improved second- and third generation products is one of the tasks of the Independent Assessment Committee (IAC), discussed below.

#### **4. Fair and efficient management of the AMCs: the role of the Independent Assessment Committee (IAC)**

The definition of the conditions of the contracts underpinning each AMC requires specific scientific and medical expertise. Moreover, the products that the donors would commit to buy through AMCs do not yet exist. The concrete implementation of the AMC framework thus requires establishing fair target standards for the target vaccines and procedures to assess whether the candidate products meet them as well as addressing other issues that may arise.

Fair and efficient management of AMCs cannot rely on the mechanical application of the legal contracts, but has to be complemented with a process agreed upon by all stakeholders. The IAC is the cornerstone of this process (see the background paper *The scope and functions of IAC*). Its tasks include specifying the required vaccine standards for public health performance and the verification procedures for each vaccine to be specified in the contract; accepting/endorsing the decisions of competent regulatory authorities on safety and efficacy; reviewing the additional information that might be required to prove efficacy in developing countries; monitoring the effectiveness of AMCs in obtaining the desired results etc. These tasks would be performed relying as much as possible on available information and processes to avoid duplications and inefficiencies.

Another noteworthy task of the IAC will be suggesting donors the split of each AMC commitment between unitary price and number of doses. The suggestion will aim at balancing two objectives: accelerating the development of the first product (obtained by setting a higher price, which, for a given commitment, corresponds to a lower number of doses, and, for a given uptake, to a shorter-lived AMC) and fostering competition for the development of superior second-generation products (obtained, other things being equal, through a lower price and a longer-lived AMC).

The IAC will have to be authoritative and independent so that its decisions are recognized as fair and justified by all the parties involved: governments, manufacturers and the public health community.

The composition of the IAC and the selection process for its members will have to be fair and transparent to ensure credibility of the IAC. Issues, such as the risk of conflicts of interest, will have to be addressed in detail. Experience from international health and non-health entities (e.g. WHO, EU, FDA) shows that these issues are manageable.

## **5. Arrangements to ensure effective execution and public health impact**

The ultimate goal of establishing AMCs is save human lives and also foster long-term economic development. Incentives for greater investment in the development and production of vaccines are necessary but intermediate steps to achieve the actual and sustained delivery of vaccines through health systems. Public health impact is only realized if the vaccines reach the target population in synergy with the country's own development strategy.

To obtain the maximum effect from AMCs, they have to be complemented by additional efforts to improve all the administrative procedures and institutional arrangements for the delivery of vaccines. As discussed in the background paper *Ensuring effective execution and public health impact* (which also discusses in detail these issues with reference to the vaccines against HIV/AIDS, pneumococcus and malaria) several interlinked aspects have to be considered. They may be grouped in three main areas.

First, vaccines supported by AMCs must reach the intended recipients through effective public financial management and procurement systems that ensure transparency and avoid corruption. Appropriate safeguards will have to be established, defining the implementation details in collaboration with existing entities operating at country level, such as UNICEF, GAVI and WHO.

Secondly, recipient countries need the capacity to administer AMC-supported vaccines through effective health systems, public-awareness campaigns and immunization programmes. Complementary capacity-building interventions may be required, such as the GAVI initiative "Advanced Development and Introduction Plans", which aims at reducing the time lag in the adoption of new vaccines by developing countries.

Thirdly, the vaccines programmes supported by AMCs must be an integral part of the long-term health and development strategy of recipient countries. This requires both the long-term sustainability of the immunization programmes in economic terms (possibly with the help of bilateral or multilateral funding if the post-AMC price of vaccines is still too high for the poorest countries) and their consistency with the other health and economic policies.

### **III. IMPLEMENTATION OPTIONS**

This section presents a range of options to implement the AMC framework through the establishment of a series of AMCs, each targeted to a single disease. All the options meet the requirements outlined in Section II and thus allow an efficient and effective implementation of the AMC, ensuring the maximum impact on health and development from the use of donors' resources.

The work done so far clearly indicates that all the alternatives presented below are concretely feasible. Further analysis is however needed to reach a precise definition of all the operational details.

#### **1. The size of the AMC commitment**

Section II.2.1 has shown that maximum effectiveness is obtained by establishing an overarching AMC framework, under which one or more AMC mechanisms can be tailored to the development of a vaccine against a specific disease. Section II.2.2 has indicated the diseases that stand as prime candidates for the application of an AMC. Against this background, the choice of the magnitude of the financial commitment is determined by the selection of the diseases that are to be addressed through the AMC framework.

The selection of the target diseases need not be final – and this should be also made clear to the public to avoid misunderstandings. Implementation of the AMC framework can take place in successive phases, starting with a limited number of diseases that put the AMC concept to the acid test of practical implementation and pave the way to extending the initiative to other diseases.

#### **2. Financing options**

By the very nature of the AMC framework, it is not known when, and possibly even if, the commitment to buy vaccines that meet the standards specified in the AMC will become effective. One of the attractive features of the AMC approach is that, if it succeeds in its aim of motivating industry, it will mobilize R&D and investment in the target vaccines well before any money is disbursed. The bulk of the expenditure through AMCs will take place only in the future. Thus financial resources need not be fully available at the time the AMC is launched, even though appropriate arrangements must ensure that the resources are available once vaccines meet the specified standards.

Financial arrangements can be grouped into three broad categories, each of which can be implemented with different instruments and techniques:

- i) Full financing at the time of the launch of the AMC;
- ii) Building up the necessary resources through periodic contributions;
- iii) Contingent financial commitments that automatically enter into force when disbursement is required.

The three classes of financing options are not mutually exclusive and arrangements can be envisaged to accommodate donors' preferences for different mechanisms.

### *2.1 Full frontloaded financing*

Under this option, all the necessary resources to finance the AMCs are made available at the time of the launch, with a safeguard clause providing for an alternative use of the resources if, for any reason, the AMC mechanism does not eventually translate into the purchase of new vaccines.

This approach to financing can be implemented through different operational techniques, whose details are known from experience in similar situations. For example, a Trust Fund could be established with the interest on deposited funds accruing to the Trust Fund. Another possibility could be the deposit of promissory notes, letters of credit or other instruments that provide for the payment over a certain time span.

Although institutional and budgetary features vary from country to country, arrangements under this option would most likely involve budgetary appropriation of all the resources immediately following the launch of the AMC. Donors might view this in conflict with both the reality of the national budget process, the need to continue funding direct public research, and the effort made in other initiatives (e.g. the IFFim) to frontload expenditure for a given time profile of appropriation. In some countries, there might even be legal impediments to the cash contributions where funds are not needed for disbursement.

### *2.2 Financing through periodic contributions*

Under this option, the necessary resources to finance the AMCs are made available through yearly contributions, before vaccines are purchased under the AMC. Again, a safeguard clause would provide for an alternative use of the resources if the AMCs mechanism does not eventually translate into the purchase of new vaccines.

This approach to financing can be implemented through well-known operational techniques, duly amended to address the possibility that, because of the quick development of an effective vaccine, the disbursement is triggered by the AMC mechanism before the required resources have been built up. For example, a Trust Fund could be established and financed by depositing yearly instalments. This could be complemented with the institution of a contingent facility for bridge financing to be activated in the case of a temporary gap between the resources readily available in the Trust Fund and the obligations ensuing from the AMC.

Although institutional and budgetary features vary from country to country, arrangements under this option would most likely involve yearly budgetary appropriations of the contributions, which, for some countries, could be provided for by legislation covering the entire stream of payments, without necessarily scoring all the expenditure immediately in the budget. Some donors might view the gradual building of resources in a Trust Fund in conflict with both the reality of the national budget process and the objective of frontloading expenditure. Other donors, on the contrary, may find this option attractive because it would smooth disbursements (and possibly budgetary scoring) to finance the AMCs and it fits the economic reality and the institutional mechanism of their national budget process better than other options.

### *2.3 Financing when disbursement is required*

Under this option, at the time of the launch of the AMC donors would pledge to make available the resources needed to finance the commitment at the time they are called for by the terms of the AMCs. Only the limited funds to pay for a lean and cost-conscious administration of the AMCs (see Section III.4 below) would have to be disbursed immediately. Donors' pledges would be underpinned by national financial commitments and possibly legislation, which, according to the institutional arrangements prevailing in each country, would buttress the political commitment. For some donors, a possible source of financing might be revenues from innovative sources of financing for development, such as global airline ticket taxes.

The detailed features of the arrangements under this option would have to be defined so that the specific format of each donor's commitment is consistent with the relevant institutional and budgetary features, which vary from country to country. The analogy that springs to mind, of course, is the financial arrangement underpinning the cancellation of HIPC countries' debt with the IFIs.

The strength of the commitments accompanying donors' pledge should ensure that AMC's are perceived as fully reliable by the industry. From the point of view of the donors, this option aligns the timing of disbursement with the purchase of the vaccines. The form of the commitments that underpin the pledge to support the initiative would also take into account the implications in terms of fiscal scoring.

#### *2.4 ODA scoring issues*

When considering financing options, attention can also be paid to their implications for the scoring of donors' support to AMC's in terms of Official Development Assistance (ODA).

Although DAC also records donors' aid commitments, ODA is measured in terms of disbursement. According to current rules, disbursement is defined with reference to the time when resources are placed at the disposal of a recipient country or agency, even if recipients, at their discretion, decide to make use of the resources at a later stage. By contrast, the deposit of Instruments of Commitment and guarantees, as well as pledges withheld by governments, are not scored as ODA at the time of the commitment.

Currently, discussions are taking place within DAC on the application of criteria for ODA scoring in relation to innovative financing mechanisms for development, such as the one underpinning the IFFim. The result could have implications for the ODA scoring of donors' support to the AMC framework.

### **3. Legal Agreements**

Building on previous work, a pilot legal structure has been explored in detail in the background paper *Legal arrangements*.

This legal structure is organized in two stages. At the launch of the AMC, the donors issue the (first-stage) framework agreement, which establishes the IAC, sets the eligibility requirements for target vaccines in terms of public health performance, commits the donors to enter the second-stage contract when signing companies develop a suitable vaccine, and provides the signing companies with the option to trigger the drawing of the second-stage contract. No financial transaction with suppliers is expected to take place at this stage.

When the IAC determines that a target vaccine meets the requirements, its manufacturer(s) have the right to enter the second-stage contract. This gives the vaccine manufacturer(s) the right to supply the vaccine on AMC terms to recipients making the

baseline co-payment (subject to the commitment on post-AMC price and supply requirements to ensure long-run sustainability), while donors commit to pay the pre-specified price for any qualified sales up to the total amount of the AMC.

This legal framework is based on the hypothesis that donors directly enter into both the framework agreement and the second-stage contract, rather than mandating a third party to do that on their behalf, with underpinning financing arrangements to make this possible. Some industry representatives have expressed their preference for a third-party arrangement in order to minimize transaction costs.

The work done, however, shows that a viable legal framework to implement the AMC approach can be devised to accommodate delegation arrangements between donors and entities acting on their behalf.

#### **4. Administration and support**

To be implemented and managed, the AMC approach only requires a very light administrative structure that does not entail the creation of any new institution. Indeed what is needed is a slim secretariat supporting the work of the IAC, coordinating donors, industry and the public health community, monitoring and reporting as well as managing contractual and financial requirements. The procurement of the newly discovered vaccines, both at AMC and post-AMC prices, would be carried out through suitable existing organizations.

To minimize costs and avoid unnecessary bureaucracy and duplications, the administration and support functions will be assumed by an existing entity or entities and thus be embedded within existing structures. At the appropriate stage, an assessment of the existing institutions and the costs of their provision of the necessary administrative support will be carried out to determine the most efficient fit.