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**Assessment of
Advance Market
Commitments
(AMCs) for vaccines**

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Client:
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Summary and conclusions

Abstract

The Advance Market Commitment (AMC) is a proposed financial mechanism to create a “market” for vaccines against diseases that are a priority for developing-countries. The governments of Italy, Canada and United Kingdom currently are behind a proposal to conduct a pilot AMC for pneumococcal disease, with another for malaria expected to follow. Norway is being asked to make a financial contribution. Based on ECON’s brief review of the issues, a pilot AMC seems worthwhile. However, ECON would signal a few issues regarding AMC size, continued funding for other aid channels (particularly those likely to be critical for AMC success), consideration of independent monitoring, and the possible need to signal which diseases will have AMCs in the future.

Background

Lack of buying power in developing countries results in low economic incentives to invest in the development and production of vaccines to serve developing-country markets. This means little research is focussed on some of the most important diseases affecting developing countries. The Advance Market Commitment (AMC) is a proposed financial mechanism to create a “market” for vaccines against important developing-country diseases. It would do this by engaging donors in legally binding commitments to cover a pre-determined price per dose of future vaccines. The AMC would pay a vaccine developer the pre-agreed price per dose if the vaccine met certain pre-determined effectiveness criteria and was demanded by developing countries – while paying nothing if no vaccine met such criteria or if no developing countries demanded an approved vaccine.

The governments of Italy, Canada and United Kingdom currently are behind a proposal to conduct a pilot AMC for the development of a vaccine against pneumococcal disease. Another pilot for malaria is expected to follow. Norway is being asked to make financial contributions to these initiatives.

Problem statement

The Norwegian Ministry of Foreign Affairs asked ECON to perform a rapid assessment of AMCs with a focus on 12 specific questions relating to what AMCs can accomplish, their design and their financing. The terms of reference are provided in Annex 1.

Conclusions and recommendations

It appears that there has been wide consultation on the AMC pilot and general support for the concept among stakeholders. Based on this and our own brief review of the issues, a pilot AMC seems worthwhile. However, we would signal a few issues regarding AMC size, continued funding for other aid channels (particularly those likely to be critical for AMC success), the need for independent monitoring, and the possible need to signal which diseases will have AMCs in the future. Recommendations on these are followed by a brief summary of findings under each of the specific questions raised by the MFA.

Recommendations

Size of pilot AMC

From a practical point of view, erring on the high side, as opposed to the low side, in funding a pilot AMC is likely to help demonstrate more quickly and decisively whether the AMC concept could ever be a success – which is ultimately the goal of a pilot. If price per dose, along with overall AMC size, are clearly on the high side and firms are still not motivated, this would be a good indication that AMCs are unlikely ever to succeed. On the other hand, if the price used in the pilot is close to the borderline of what could be expected to stimulate one or more firms, it would be more difficult to say whether failure was due to a too-low price or to something more fundamental in the AMC concept.

Other aid channels

Special notice should be paid to continued funding for primary research, strengthening vaccine delivery systems and improving demand forecasting, since these activities are likely to be critical for the success of an AMC.

Independent monitoring

The AMC secretariat, housed by GAVI, is to regularly report on progress toward AMC objectives by tracking and reporting on “firms engaged, level of investment, status of product development and installed capacity, and country demand”. GAVI is also to report on the public health impact of the AMC. While GAVI and the AMC secretariat would be in a good position to perform these monitoring roles, it may be desirable to institute an additional, independent monitoring and evaluation procedure in order to avoid possible conflict of interest. Such a supplementary M&E role could be performed, e.g., under the auspices of the Donor Committee.

Monitoring the possible effect of AMCs on donor flows to other aid channels should also be considered, especially for the activities (noted above) that are likely to be critical to AMC success.

Signals regarding which diseases will have AMCs

If and when the AMC concept becomes more established and developers begin anticipating AMCs for other diseases, there could be a risk that some developers hold off on the final, more expensive phases of vaccine development that they might otherwise have pursued without subsidies. In order to minimise such gaming activity, the expert vetting process for AMCs eventually may need to be in a position to declare whether or not AMCs are likely to be developed for particular diseases.

Brief summary of findings for specific questions raised by the MFA

The following section briefly summarises the main findings for the specific questions raised by the MFA in the terms of reference (the full ToR may be found in Annex 1). We have divided these questions into three thematic chapters within the report: What AMCs can do, Design issues, and Financing issues.

What AMCs can do

The ability of AMCs to compensate for market failure

The fundamental market failure related to vaccines stems from the fact that scientific knowledge is a public good. Without government intervention in the market, rewards perceived by a private firm for developing a new vaccine would be too low – even in developed countries. To address this problem in developed countries, governments allow intellectual property to be protected through patents. However, this works by raising prices, which unfortunately puts them out of reach of many developing countries. AMCs are designed to help address the affordability problem by covering the difference between a price that is high enough to provide developers a reasonable return on investment and a price low enough to promote widespread uptake of the eventual vaccine by governments of poor countries.

Uncertainties relating to donor pledges are also generally perceived by private firms as too great to justify development of new vaccines aimed primarily at developing countries. Related to this, there is the “time inconsistency” of donor incentives: Once a vaccine has been developed, policy makers in donor and recipient countries have strong political incentives to force manufacturers to lower their prices in order to distribute benefits as widely as possible. Since potential manufacturers know that donors’ incentives will change this way over time, they usually forego the risks of such an investment. The AMC is designed to address this problem by legally binding donors to subsidise a number of doses large enough to allow manufacturers a reasonable return on investment.

The extent to which an AMC can address either of these market failures will depend critically on the ability of donors to convince potential investors that the AMC will result in a market for developing-country vaccines that is reliable enough to make the required investments.

The use of the World Bank to “bundle” multiple donor commitments is likely to increase industry’s confidence in eventual donor payments. However, important aspects of developing-country markets that AMCs do not address include in-country delivery systems, planning systems and forecasting, all of which will play key roles in eventual vaccine demand. Since the AMC pays the vaccine producer only for what developing countries demand, these factors will also have an important influence on whether developers decide to proceed with investments.

What AMCs can do that other aid channels cannot

AMCs have the following main potential advantages over other aid channels: They can stimulate innovation even before any money is paid out. They can decrease donor risks because they do not require a payout if an adequate vaccine is not developed (and after that, payment is made only in proportion to actual demand by developing countries). And they can stimulate a large number of players, rather than essentially serve as a bet on one or several potential developers that may or may not produce a successful product.

AMCs are not likely to substitute for very many aid channels, but could complement such channels as public funding of basic research, strengthening of developing country delivery channels, Product Development Partnerships (PDPs), and the International Finance Facility for Immunisation (Iffim). Continued funding of such complementary

channels in parallel with an AMC may enhance the effectiveness of each. As noted above, special attention should be paid to continued funding for primary research, strengthening delivery systems and improving demand forecasting, since these activities may even be crucial for AMC success.

Possible effects of AMCs on other aid channels

Some proponents of AMCs point out that there is no direct budgetary pressure to reduce spending in other areas when a donor makes a financial commitment to an AMC. This is because the donor must pay only after the vaccine has been developed and demanded. However, two of the three financing options for AMCs (see below) would require donors to contribute money up front or over time to an AMC fund. Under such scenarios, a donor could, in theory be faced with the need to cut an equivalent sum elsewhere in the budget.

There may also be pressures for donors to cut back on other forms of aid if it is felt that such channels are essentially duplicating rather than enhancing AMC work. However, it is difficult to see this representing a significant threat to other vaccine-related funding until one or several successful pilot AMCs have taken place and donors are able to judge the effectiveness of AMCs compared to that of other aid channels.

In the case of the pilot for a pneumococcal vaccine, most of the work remaining to be done is not the sort normally funded by aid but by private companies, i.e., there is no real threat to public funding for research on a pneumococcal vaccine because the product pipeline is beyond that phase.

The Ministry of Foreign Affairs noted that it was particularly interested in the possible affect of AMCs on Product Development Partnerships (PDPs): There does not appear to be any specific threat to PDPs other than the general threat already mentioned regarding temptations to diminish all “push” funding. Moreover, PDPs do not seem to be fundamentally at more risk than other aid channels in this regard. According to one PDP interviewee, an AMC may even be able to help PDPs working on the same disease to attract additional funding, since creation of an AMC would send a signal that work on that disease has become a priority. Overall, most PDPs involved with diseases relevant to the proposed pilot AMCs appear to view AMCs as a positive development.

Design issues

Ensuring that AMCs focus on the “right” diseases and vaccines

There are a number of institutional arrangements being adopted for the pilot AMCs that, if also used by future AMCs, should increase the likelihood that AMCs focus on the “right” diseases in terms of developing-country needs, and furthermore select the “right” vaccines to deal with those diseases.

In selecting the diseases for the pilot AMCs, the G8 created an Independent Expert Committee, the members of which covered a broad range of expertise and were chosen based on suggestions from various governments, international agencies and public-private partnerships. There was also an independent Advisory Group, similarly chosen, that advised on key aspects of AMC design and was responsible for vetting data for Expert Committee papers and reports.

In order to help ensure that AMCs encourage and approve the “right” vaccines for the selected diseases, an Independent Assessment Committee (IAC) will be formed for the pilot. The IAC is to comprise 7-10 members with no vested interest in the specific products under consideration. The IAC will oversee the establishment of the Target Product Profiles (TPPs), against which candidate vaccines for AMC funding will be judged. In practice, the IAC is expected to ask WHO to form an expert group to draft the TPPs, and once a candidate vaccine has been developed, it will first go through an established WHO pre-qualification process similar to that required of any vaccine distributed by GAVI.

Finally, there will be a Donor Committee to “refine and agree on procedures, responsibilities and review mechanisms”.

Ensuring “correct” pricing within AMCs

In order to help learn more about price levels likely to stimulate the right response from developers, the World Bank commissioned a consultant to develop a model to replicate the pharmaceutical industry’s valuation methodology. The model highlighted three areas of data critical to firms’ likely responses to an AMC: demand forecasts, status of development and probabilities of success/failure (including for likely rivals), and estimated cost of goods. However, the earlier a product is in the development pipeline, the more difficult it is to estimate any of these factors – and consequently (in ECON’s opinion), the higher the AMC price per dose may need to be in order to compensate companies for perceived risks.

There are risks for donors in setting a price too low and too high. However, the risks in setting it too high (i.e., development of only one vaccine as opposed to several competing ones) seem less serious than those of setting it too low (development of no vaccine), particularly in the case of a pilot.

Risks that AMCs will subsidise pharmaceutical giants

It is usually difficult for smaller firms to bring new products through the later, relatively expensive phases of vaccine development. Thus, strictly speaking, the large pharmaceutical firms are probably the ones most likely to get direct AMC funds. However, the existence of the AMC may create incentives for small firms to invest in new technologies in the hope of selling or licensing it to larger companies. In this way, AMC money may trickle down to smaller firms before it is even distributed to the large ones.

In the case of some later-stage vaccines, for which large pharmaceutical firms may have already developed products but never took them to market because additional costs did not justify expected economic returns, an AMC could end up motivating firms to take such projects off the shelf. To the extent that such cases are known (and it does not appear that many are known), The Independent Assessment Committee for the AMC could limit the price per dose to cover only the development costs needed to get an existing vaccine through the last hurdles to market, since previous investments on research could be considered sunk costs. However, it is unclear that GAVI or others will have sufficient knowledge of such cases at the time when the IAC is setting the AMC’s overall size and price per dose.

Risks that AMCs will support monopolisation

According to the World Bank's model for simulating the way the pharmaceutical industry is likely to evaluate an AMC (noted above), the greater the time gap between products in the vaccine development pipeline, the more challenging it is likely to be to find an AMC market size and price scenario that could support 2-3 manufacturers rather than just one. In such cases, as already noted, the trade-off may be between one monopoly supplier and no supplier at all.

Even if there is a monopoly supplier, however, there would seem to be factors mitigating against monopoly pricing. Most importantly, the price-per dose is set in advance by the Independent Assessment Committee. Moreover, the manufacturer would seem to have an incentive not to have the co-payment price (paid by the developing country) set so high that it risked lowering developing-country demand and hence receipt of the per-dose subsidy.

What happens if the AMC does not lead to a vaccine being developed

If an AMC is not able to stimulate development of a vaccine within an expected time period, it is proposed that the IAC would make a judgement on whether the price per dose should be increased and/or the TPP made less stringent. In order to help it make such decisions, the IAC would call upon WHO to convene a group to consider changes to the TPP and/or call upon the AMC secretariat (presumably the GAVI Board) to convene a group to consider changes to price. The literature notes that raising prices would be more likely than lowering TPPs, however, since a lowered TPP could be disruptive for manufacturers that had invested in research and development to meet the original higher standards. In any case, donors and other stakeholders have yet to agree on the events that would trigger any reassessment.

According to the World Bank and GAVI, given the advanced stage of vaccine development for pneumococcal disease, it is at least "unlikely that the TPP or AMC prices set in the framework will need to be revised" for the first pilot.

Proposed governing structure, including relationship to GAVI's institutional mechanisms

After consultations with various existing institutions, the Technical Working Group for the pilot AMC decided to locate the AMC secretariat within GAVI and have the World Bank administer its funds. Both organisations appear well placed to carry out their proposed functions, which seem to mesh with existing structures and processes.

Once a candidate vaccine becomes available, the IAC will rely on WHO to perform a pre-qualification recommendation similar to procedures WHO already uses for other vaccines distributed through GAVI. Developing countries will also apply for the AMC-supported vaccines through the established GAVI process of national applications and requests. After that, GAVI's regular implementing partners (WHO and UNICEF) will deliver the vaccines using regular GAVI channels. GAVI is also expected to carry out much of the complimentary investments for strengthening health systems and vaccine management in-country, as well as demand forecasting – activities it already carries out to support the uptake of other vaccines. (As noted elsewhere, it will be important to continue supporting GAVI in these activities.)

The World Bank will be responsible for the financial functions of the AMC, notably bundling the commitments of the various donors into one financial instrument and ensuring that the AMC makes required payments on time. Although the bundling role will be somewhat new for the World Bank, it is probably better placed than other public institutions to perform the role, not least because of its experience as trustee and administrator for several billion dollars in various donor trust funds.

Financing issues

Financing alternatives for individual donors

There are three basic ways that individual donors could contribute to an AMC: 1) Full up-front payment; 2) annual payments timed to build up the full amount by the time funds are expected to be needed; and 3) payments only when actually required to compensate developers.

The main advantage of full up-front payment is likely to be maximum credibility to potential developers. However, if all commitments were bundled into a single financial instrument, the perceived reliability of the World Bank may go some way in compensating for possible doubts about specific donors' pledges. The main disadvantage of this option is that it has the highest opportunity cost, since the full amount of the money would not be available for other activities for the full duration of the AMC.

Advantages of the periodic-contribution option include lowering opportunity costs, especially if contributions start small and increase over time ("back-loading"). This option also appears most amenable to most donors' budgeting systems, following generally well-established precedents for full authorisation followed by annual appropriations.

The third option, payment on demand, would minimise opportunity costs and may be particularly advantageous in the case of early-stage vaccines, for which the date of future payment is distant and hence relatively uncertain. However, this uncertainty about when payment will be made may pose problems for some national budgeting systems. This option may also provide the least assurance to industry – while the need for such assurance may be greatest for the early-stage vaccines.

Implications of Norwegian budgetary regulations

Because all three financing alternatives imply funds will not be paid out to developing countries during the same budgetary year that the commitment is made, special consent from *Stortinget* apparently would be needed for each option. In order for *Stortinget* to give such consent, a specific amount and year for disbursement must be specified. In our opinion, this would favour contributions up front or periodically into a fund (options 1 or 2). Such an arrangement bears similarity to the current setup for funding from Norway to the World Bank: There is a decision to pay out money over periods of three years to an account in Norges Bank, from which the World Bank can then draw the funds. (This arrangement also required special consent from *Stortinget* to establish.)

DAC ODA scoring

The main potential difficulty in counting donor payments to an AMC fund as Official Development Assistance (ODA) is the conditionality clause that each AMC is likely to

contain. This clause, which relates to use of funds in case no vaccine is developed, effectively introduces an element of uncertainty regarding whether or not the deposited funds will be used for development purposes. From discussions with the OECD Development Assistance Committee (DAC), it appears that the earliest time at which ODA scoring may take place under any of the three financing options is after a vaccine has been developed, approved and demanded. However, donations to cover the administrative costs of the AMC probably could be counted as ODA at time of payment.

Bundling of financial commitments

One of the World Bank's key roles will be to bundle the various donor commitments into a single financial asset so that developers will not have to judge the reliability of individual donor pledges. According to the World Bank and GAVI, however, the precise details of the financing arrangements cannot be specified at this point, since much will depend on the nature of donors' individual pledges. Nevertheless, the World Bank and GAVI note that possible elements of a solution might include a third-party guarantee by a commercial entity (effectively re-insurance), and the use of cash from eventual up-front and annual payments by some donors to help underwrite the risks associated with future payments by others.

In principle, if the World Bank were to provide the bundling directly, it should be less expensive than if a commercial provider were to do so, since the World Bank is not a for-profit institution. In any case, donors reportedly still have yet to officially ask the World Bank to take on this role, which would need to be approved by the Bank's Board.

The need for start-up funds

According to GAVI, start-up costs for the pneumococcal AMC are likely to be around US\$2.5 million, compared to the estimated AMC total size of US\$1.5 billion. These start-up costs would cover work to develop the TPP, hold initial IAC meetings, structure the financing, hire two new staff at GAVI, and cover the legal costs (likely to be significant) involved in developing the agreement.

1 Introduction

The Norwegian Ministry of Foreign Affairs asked ECON to perform a rapid assessment of Advance Market Commitments (AMCs) for vaccines as put forward by the governments of Italy, UK and Canada. As requested by the Ministry, this assessment focuses on the following issues, which we have presented under three headings:

What AMCs can do

- The ability of AMCs to compensate for market failure;
- What AMCs can do that other aid channels cannot;
- Possible effects of AMCs on other aid channels, especially Product Development Partnerships (PDPs);

Design issues

- Ensuring that AMCs focus on the “right” vaccines;
- Ensuring “correct” pricing within AMCs;
- Risks that AMCs will subsidise pharmaceutical giants;
- Risks that AMCs will support monopolisation;
- What happens if the AMC does not lead to a vaccine being developed;
- Governing structure of pneumococcal AMC, including relation to GAVI.

Financing issues

- Financing alternatives;
- Bundling the financial commitments;
- The need for start-up funds to get AMCs “up and running”.

Each issue is introduced with the issue statement from the terms of reference. The full terms of reference (in Norwegian) may be found in Annex 1.

1.1 Background

Variations on the concept currently called “Advance Market Commitments” (AMC) have been around for about a decade, although many of the main points of the proposal currently on the international agenda were developed in a September 2005 paper by the Washington D.C.-based Center for Global Development (CGD), called *Making Markets Work: Ideas to Action* (principle authors: Ruth Levine of CGD and Michael Kremer of Harvard University) (Dobbs 2005). This report came out of a working group established by the CGD in 2003 to “bring together economists, public health professionals, lawyers, experts in public policy and pharmaceutical and biotech experts, with the mandate to develop a practical approach to the vaccine challenge” (Levine et al 2005, p. vii).

Early work by the CGD apparently led the G8 to take interest in the AMC concept (Dobbs 2005). In February 2005, the Italian finance minister, with the support of the UK finance minister, presented the AMC concept to G8 colleagues, and in June 2005 the G8 gave Italy the mandate to develop a concrete AMC proposal. A working group was formed, consisting of representatives of the Italian Treasury Department and the World Bank, with contributions from the Global Alliance for Vaccination and Immunisation (GAVI), the pharmaceutical industry and several vaccine-related public-private partnerships.

Italy presented a paper (the “Tremonti report”) to G8 ministers on 2 December 2005. This report recommended conducting one or two pilot AMCs and suggested six disease candidates (Monticelli 9/2006).

During 2006 an ad hoc Advisory Group of Experts examined the six diseases in the Tremonti report and recommended that the first pilot AMC be targeted at pneumococcus and the second at malaria. At the G8 summit held in July 2006 in St. Petersburg, Russia, several G8 governments stated their commitment to launch an AMC pilot for pneumococcus by the end of 2006 (Monticelli 10/2006).

A technical Working Group on AMCs for vaccines held its first meeting on 7 September 2006, jointly convened by the Finance Ministers of Italy, the UK and Canada and attended by representatives of 15 countries,¹ as well as the pharmaceutical industry and institutions such as the European Commission, WHO, the World Bank, GAVI, and the Bill & Melinda Gates Foundation. The Rome meeting reviewed the work undertaken so far on the technical, legal, institutional and financial aspects of the proposed AMC pilot. A decision was taken to meet again in November 2006 to “agree the details necessary for donors to make concrete financing commitments and to launch a pilot” (Monticelli 11/2006).

The technical Working Group held its second meeting on 9 November 2006 in London, hosted by the UK Treasury and attended by representatives of the same governments and institutions that attended the first meeting. The group “considered the technical work on the pilot AMC to be significantly advanced and agreed that the critical challenge now is to secure the donor financial commitment to launching a pilot early in 2007” (London 2006a).

How an AMC would work

- Donors commit (and sign a legally-binding contract) to fund the AMC for the target vaccine.
- Target vaccine specifications (effectiveness, public health impact) AMC market size, and AMC price per dose are established.
- An Independent Assessment Committee (IAC) determines if a vaccine meets the target specifications.
- When a vaccine meets the specifications and countries are interested in introducing the vaccine, donors pay the subsidy and recipient countries provide a small co-payment.
- When the AMC funding is depleted, a manufacturer is obligated to continue to provide an established amount at a relatively low, pre-agreed price.

Source: GAVI Alliance 2006

¹ Australia, Brazil, Canada, China, France, Italy, Japan, Netherlands, Norway, Russia, Spain, Sweden, Switzerland, United Kingdom, United States.

2 What AMCs can do

2.1 The ability of AMCs to compensate for market failure

The ability of AMCs to compensate for “market failure” in the development of new medicines/vaccines (AMCs evne til å kompensere for ”markedssvikt” ift utvikling av nye medisiner/vaksiner)

A number of papers on AMCs, such as the Tremonti report (2005), emphasise that AMCs could help address “market failures” that cause an underinvestment in R&D for diseases that primarily affect the world’s poor.

Developing countries’ lack of buying power means that private firms have little economic incentive to develop vaccines for which there is no parallel market in rich countries. Poor countries represent about 90% of the world’s population, while R&D to address diseases that primarily affect such countries attracts only about 10% of the total global investment in disease-related R&D (Levine et al 2005, p. 3). As a result, most vaccines currently available to developing countries were originally developed with rich-country markets in mind, while few are focussed on the diseases that have the most impact on such countries, such as malaria or rotavirus (diarrhoeal disease). Moreover, the vaccines for “rich-country” diseases that do become available to developing countries usually do so only after considerable delay, typically around 15 years, i.e., after the manufacturer has had time to recoup investment costs in developed-country markets.

The fundamental market failure for vaccines for both developed and developing countries stems from the fact that scientific knowledge is a public good. Public goods are those that can be enjoyed by people simultaneously, while it is difficult and sometimes impossible for the provider to prevent this. Public goods carry a free-rider incentive and risk being under-provided without official or collective action. A private company will be reluctant to invest in vaccine R&D if the cost of doing so is higher than the reward it can expect to receive for it. Without government intervention in the market, rewards perceived by a private firm for developing a new vaccine would be too low even in the developed world. To help get around this problem, governments allow intellectual property to be protected through patents. The legal prohibition against unlicensed firms producing the vaccine means that the patent owners or licensees can charge prices high enough to provide an attractive rate of return. The knowledge that they can do this gives firms the security they need to invest in vaccine R&D in the first place.

Unfortunately, solutions to the global public goods problem that rest on protection of intellectual property alone will only help rich countries. This is because such solutions work by creating higher prices. This puts them out of the reach of many developing countries.

The way that governments have gotten round the affordability problem so far has been either to force firms to sell at lower prices to developing countries, or by donor governments subsidising the price at which the developing governments buy. Since

governments are the major purchasers of drugs for developing countries, they can effectively enforce lower prices. However, they cannot force a firm to produce. If the private firm owning the drug perceives the enforced price as too low, it will not have enough incentive to invest in the manufacturing capacity needed to supply those markets. The result will still be no vaccines for these countries.

In practice, many vaccines originally developed for rich-country markets are now distributed to developing countries thanks to donor price subsidies, e.g., via GAVI and its partners. However, sufficient drug availability typically remains a problem, because private firms may not perceive donor commitments as reliable enough to justify the extra investment needed to expand production to cover developing-country markets. This in turn keeps costs – and consequently the necessary subsidies – high, limiting the number of doses that can be distributed in practice.

Lowering the price of vaccines through a combination of pressure and traditional subsidies works (at least to some extent) for making available those vaccines that have already been developed for rich countries. However, uncertainties relating to donor pledges are generally perceived by private firms as too great to justify development of new vaccines aimed primarily at developing countries. Related to this, there is the “time inconsistency” problem of donor incentives: It means that, once a vaccine has been developed, policy makers in donor and recipient countries have strong political incentives to pressure manufacturers to accept a low price in order to distribute the benefits as widely as possible. Since potential manufacturers know that donors’ incentives will change over time, they simply may decide to forego the risks of such an investment. This can be considered another market failure.

Proponents of Advance Market Commitments claim that AMC’s could help address the affordability problem in developing countries by covering the difference between a price that is high enough to provide developers a reasonable return on investment, and a price low enough to promote widespread uptake of the eventual vaccine by governments of poor countries. They also hope it will address the “time-inconsistency” of donor incentives by legally binding donors to subsidise the price for a given number of doses that hopefully will be large enough to allow manufacturers a reasonable return on investment.

In theory, there would seem to be no major reason why AMC’s could not address these market failures. In practice, success will depend on how attractive the AMC is regarded by potential vaccine developers, both in terms of price and reliability. If the price that developers can expect to receive is not large enough to motivate them, they will not invest. (Aspects of price are dealt with below.) Similarly, they will not invest if the market is perceived as insufficiently reliable.

Lack of market reliability can stem from lack of faith in donors’ ability to deliver the promised subsidies, either because they may change their minds, or because their ability to deliver funds at some distant date in the future is questioned. Current proposed design features of AMC’s are aimed at addressing these problems by making agreements legally binding and by drawing on the credibility of the World Bank, which could help coordinate pledges from multiple donors into a unified financial instrument (see below).

Some market reliability problems that AMCs will not be able to address on their own are poor planning and delivery systems for vaccines in developing countries, along with poor demand forecasting. This is why AMC proponents emphasise that efforts to strengthen planning, health systems and demand forecasting in developing countries must continue (see below).

While discussions with industry by AMC proponents seem to indicate that potential developers will be assured by these measures, it is impossible to say for certain yet whether such assurance actually will be enough to motivate the development of new vaccines. In large part this is because AMCs do not yet have a track record. The only way to know for sure may be to test the concept with a pilot, as proposed. If the private sector sees that AMCs can deliver a reliable market, industry is more likely to trust them in future and increasingly make them part of its strategy – much as it currently counts on intellectual property protection rules in developed country markets. This also implies that future AMCs may not require as much money to motivate firms, since they will not need to compensate for so many uncertainties.

2.2 What AMCs can do that other aid channels cannot

What one can accomplish with AMCs that cannot be accomplished with other channels for health assistance (Hva man oppnår med AMCs som ikke oppnås ad andre kanaler for helsebistand)

The main potential advantages of an AMC over other aid channels – existing or proposed – are that AMCs could

- stimulate innovation even before any money is paid out;
- decrease donor risks because they do not require a payout if an adequate vaccine is not developed – and after that, payment is made only in proportion to actual demand by developing countries;
- stimulate a large number of players, rather than essentially serve as a bet on one or several potential developers that would use donor funds but may or may not produce a successful product.

This section reviews the main advantages and complementarities of AMCs vis-à-vis other important aid channels.

Purchase Guarantee

A purchase guarantee (sometimes called an Advance *Purchase* Commitment) is a potential aid channel that is probably the most similar to an AMC. The main difference is that the purchase guarantee would pay out when a drug met the pre-set technical specifications, whereas the AMC also would require developing countries to buy it. This additional requirement may put more pressure on vaccine developers to come up with a good product, since it must survive a “market test”. It consequently would reduce the risk that donors would pay for a drug that developing countries did not want.

Guaranteed patent buyout

A prize or guaranteed patent buyout for the first developer of a vaccine for a particular disease would not provide possibilities for multiple entries to the market. And if only

one can win, too many companies may find it too risky to participate in the first place. AMCs are supposed to be designed with the intention of eventually funding 2-3 different products. (Its supporters often stress that it is “not a prize but a market”: Levine et al 2005). However, it is not certain yet whether even this will be enough to stimulate some companies to participate, especially in cases where a potential vaccine is in the very early development phases (e.g., see Applied Strategies 2006 for a simulated market evaluation from a drug company perspective).

Vaccine purchase funds

There are purchase funds set up by donors to help developing countries buy vaccines, e.g., those administered through GAVI. However, as long as donors do not have a legally binding commitment to deliver the funds or to keep payments to developers at a level that allows the latter to receive an adequate return on investment, they may not provide sufficient incentives for developers to scale-up production of an existing vaccine, let alone develop a new one (Tremonti 2005b, p. 7). On the other hand, AMCs are not likely to provide any major advantage over vaccine purchase funds for vaccines that have already been developed and for which sufficient production capacity exists. Moreover, vaccine purchase funds may be used to help developing countries with their co-payment during the period when the AMC is active, and/or afterwards when the “tail price” comes into force.

Strengthening developing country delivery systems and demand forecasts

Price is not the only demand-side problem. An important problem that AMCs do *not* directly address is that demand for vaccines in developing countries is not as reliable as in developed countries, and historically demand estimates “have been quite inaccurate. This contributes to industry’s unwillingness to invest” (Tremonti 2005b, p. 20). Important contributors to this demand problem are inadequacies in developing-country planning and delivery systems (Tremonti 2005a, p. iv).

Under an AMC, donors do not pay suppliers for vaccines unless developing countries demand them. This provision potentially is a double-edged sword for vaccine developers, since problems in developing country delivery systems may keep effective demand low. Thus proponents of AMCs stress that the scheme must be accompanied by continued efforts to improve demand forecasting, planning and delivery systems in the developing countries that are expected to order them. Many of these activities are already carried out through GAVI to help the uptake of other vaccines and could be leveraged for AMC-supported vaccines.

Public funding of basic research

AMCs cannot replace traditional public funding of basic research on diseases. Such public funding is considered to be an essential component of basic research even for vaccines aimed at developed-country markets, where it is subsequently leveraged by private research. What has been missing along the product development pipeline for developing-country vaccines is a similar level of private investment to complement the public research in this area. What AMCs could do is provide the “pull” for private companies to build on the existing public investment, rendering the latter more productive in the long run because it may lead to more end products.

Product Development Partnerships

Public-private partnerships to develop neglected diseases (sometimes called Product Development Partnerships or PDPs) cover different parts of the product development pipeline, but tend to focus on the latter parts that are mainly covered by private companies in the case of developed-country vaccines. However, there is always a risk that a particular funded partnership will not produce successful results. In contrast, an AMC is not a bet on a particular consortium but a potential enticement for a wide range of players, including PDPs.

International Finance Facility

Another financing innovation for neglected diseases is the International Finance Facility for Immunisation (IFFIm). Donor grants to IFFIm provide an asset base on which AAA-rated bonds are issued in the capital markets. The IFFIm, launched in 2006 and currently financed by the governments of the UK, France, Italy, Sweden, Spain and Norway, is expected to make an additional US\$4 billion available to GAVI over the next 10 years. The IFFIm provides a new source of funding that can be used for a number of different purposes. However, since IFFIm's purpose is to frontload funding for near-term disbursements, and AMCs will generally backload disbursements, AMCs may not be an effective use of IFFIm funds.

IFFIm should help make donor funding more reliable, but it may not address the “time-inconsistency” problem: As an editorial by Gordon Brown and Bill Gates inadvertently points out, the increased predictability of the funding is to be used as a bargaining chip, “allow[ing] for the negotiation of cheaper prices for these lifesaving drugs” (Independent 7/9/2006).

Summary

In general, AMCs could be seen as a substitute for APCs, guaranteed patent-buyouts and even certain vaccine purchase funds (but not those for vaccines that already have been developed), while they should be seen as a complement to PDPs, Iffim, public funding of basic research, and strengthening of developing country delivery channels. Continued funding of the latter group of aid channels in parallel with an AMC may enhance the effectiveness of both. Special notice should be paid to continued funding of primary research, strengthened delivery systems and improved demand forecasting, since these are even likely to be crucial for an AMC's eventual success.

2.3 Possible effects of AMCs on other aid channels

Possible effects of AMCs on other channels, particularly Product Development Partnerships. (Mulige effekter av AMCs på andre kanaler, spesielt produkt-relaterte offentlig- private samarbeidsprosjekter (Product Development Partnerships – PDP))

Many stakeholders have welcomed the AMC initiative “as long as it was clear that resources for AMCs would not be at the expense to current commitments to research support and other programmes” (Dfid 2006, p.2). One source even reported a “backlash” against AMCs by persons who “wanted to defend the importance of ‘push’ funding by governments and PPPs, and call attention to the potential crowding out problems if massive funding went into APC/AMC proposals” (Love 2006).

Proponents of AMC's usually are careful to stress that AMC's compliment and do not substitute for other measures. Some also point out that there is "no direct budgetary pressure to reduce other spending when a commitment is made", since it is only after the vaccine is developed and demanded that donors must pay (Levine et al 2005, p. 67). On the other hand, according to the first two financing methods (see section 4.1), donors contribute money up front or over time to the AMC fund, thus possibly requiring an equivalent amount of money to be cut elsewhere in the budget.

Even if no money must be spent until the vaccine is developed and demanded, there may well be pressures or temptations for donors to cut back on other forms of aid if it is felt that such channels are essentially duplicating rather than enhancing AMC work. However, it is difficult to see this representing a significant threat to other vaccine-related funding until one or more successful pilot AMC's have taken place and we know more about what AMC's really can and cannot do. In any case, there would seem little reason to forecast cutbacks aimed directly at diseases not covered by the two pilot AMC's.

In the case of the pilot for a pneumococcal vaccine, most of the work remaining to be done is not the sort normally funded by aid but by private companies, i.e., there is no real threat to public funding for research on a pneumococcal vaccine because the product pipeline is well beyond that phase. Funding for strengthened developing country delivery systems should not be under much (additional) threat due to AMC's either, since such efforts must continue for the uptake of all vaccines, even those that already have been developed.

In theory, the threat to Malaria funding could be greater, since development of a Malaria vaccine is not yet as advanced as it is for a pneumococcal vaccine. Donors thus may need to be more wary about cutbacks to other malaria-related funding, including for other methods of fighting the disease, e.g., treatment and prevention.

In general, as future AMC's tackle diseases for which a vaccine is further from development, changes to other types of funding could be more likely. However, this may not always mean cuts. For example, "fundors of research could explicitly take the existence of an AMC into consideration when negotiating upfront support or milestone payments" (Levine et al 2005, p. 7). Donors could also end up concentrating public funding on diseases covered by AMC's in order to enhance the synergies between AMC's and other aid channels. This could mean cutting aid to channels that did not contribute such synergies or were focussed on diseases not (yet) covered by an AMC. Similarly, the private sector may be drawn away from work on developing-country diseases for which there was no AMC. However, these would not necessarily be negative developments if they served to reinforce coordinated policy priorities.

AMCs and PDPs

A few observers have expressed concern that AMC's could pose a threat to PDPs, since at least pilot AMC's will "focus on the plans of the PDP, which is to take a product to licensure" (Dfid 2006, p. 6). However, most PDPs involved with the diseases relevant to the proposed pilot AMC's appear to view AMC's as a positive development, e.g., see joint media advisory issued by PneumoADIP and the Malaria Vaccine Initiative (PneumoADIP & MVI 2006).

According to a representative of MVI we spoke to, most PDPs that MVI has worked with view AMC's as a good thing. The main potential negative seems to be the general

risk that AMCs could lead short-sighted donors to diminish funding to all “push” activities, which could include PDPs. However, MVI apparently does not see PDPs fundamentally at more risk than other channels in this regard, and the representative we talked to even questions whether such risk is very substantial. He points out that similar fears were raised about the creation of GAVI leading to cuts in bilateral funding for immunisation, which he says did not happen. He notes that an AMC potentially could even help relevant PDPs attract additional funding, since the creation of an AMC is likely to send a signal to the market that work on a particular disease has become a priority. In theory at least, it should be possible to combine the “push” funding of PDPs with the “pull” funding of AMCs as a way to further enhance the effectiveness of both.

3 AMC design issues

3.1 Ensuring that AMCs focus on the “right” vaccines

How to ensure that one aims for the “right” medicines with respect to developing countries’ needs? (Hvordan sikre seg at man går for de “riktige” preparatene ift u-lands behov?)

This section reviews institutional arrangements that may help AMCs focus on the “right” diseases and choose the “right” vaccines to deal with those diseases in terms of developing-country needs. While it focuses on arrangements being developed for the pilot AMCs, it is assumed that future AMCs will follow similar procedures.

The original set of disease candidates for a pilot AMC came from a paper by Italian Minister of Finance and Economy, Giulio Tremonti, who was assigned the task of identifying such candidates by the G8 (Tremonti 2005b). The Tremonti paper notes that factors determining which diseases might most effectively be supported by an AMC notably include “a) the seriousness of the disease in the poorest developing countries (mortality), b) the potential effectiveness of a vaccine versus other existing interventions, and c) the potential value of an AMC to motivate the appropriate industry actions given the scientific and market risks”. According to this paper, diseases that may particularly benefit from an AMC include rotavirus, pneumococcal pneumonia, HPV, malaria, tuberculosis and HIV/AIDS (Tremonti 2005b, pp. 15-16). The authors of the Tremonti paper reportedly based their selection on analysis performed by WHO, World Bank and GAVI. The resulting list of candidates is similar to that provided in the influential 2005 paper by the Centre for Global Development (Levine et al 2005). There does not appear to have been any major criticism of the candidate diseases that were listed in the Tremonti report.

The next step was to create an Independent Expert Committee to provide “an evidence based recommendation to governments on the vaccine(s) most suitable for the AMC pilot”. The Expert Committee reviewed the six candidates identified in the Tremonti report to find the candidate most likely to “provide a measurable and timely indication of AMCs’ impact on industry decisions”. Members of the Expert Committee were “experts without conflict of interest [...] in the areas of public health, epidemiology, industry economics, vaccine development and law,” chosen “based on suggestions from numerous bodies including governments, UN agencies, public-private partnerships and foundations” (WB & GAVI. 9/2006, p. 3). The work of the Expert Committee led to a recommendation that the first pilot AMC should be for pneumococcal disease, and the second for malaria. A pneumococcal vaccine has been called by some experts the “low hanging fruit of pandemic preparedness” (WB & GAVI 10/2006, pp. 2-3).

An Advisory Group was consulted “throughout the development of the pilot proposal to advise on key aspects of design”. This included vetting data for the Expert Committee papers on candidate diseases. The Advisory Group was made up of “health policy makers, public health experts, researchers, industry and biotech leaders, immunization managers, developing country experts, the partnerships of the six diseases of focus, and international organisations” (Rome 2006d).

In order to help ensure that AMCs encourage and approve the “right” vaccines for the selected diseases, an Independent Assessment Committee (IAC) will be formed. The IAC will be comprised of 7-10 members “with no vested interest in the specific products under consideration” (WB & GAVI 9/2006, p. 8). GAVI and World Bank “in consultation with stakeholders, will be responsible for outlining and implementing the process to identify the IAC members” (WB & GAVI 10/2006, p. 11).

The IAC will oversee the establishment of the Target Product Profiles (TPPs) against which candidates for AMC funding will be judged. In practice, the IAC is expected to ask WHO to form an expert group to draft the TPPs (WB & GAVI 9/2006, p. 8). Once a candidate vaccine has been developed, it will first go through an established WHO pre-qualification process to assess its eligibility to receive AMC funding (WB & GAVI 10/2006, p. 39-44). Apart from use of TPPs, this process is expected to be similar to that of any vaccine distributed by GAVI.

A Donor Committee is to be formed to “facilitate donor engagement [...] refine and agree on procedures, responsibilities and review mechanisms” (London 2006b, WB & GAVI 10/2006, p. 39). Since different donors may have different disease priorities, a potential advantage of having an institution such as GAVI serve as AMC secretariat may be that it can put into a clearer immunisation policy context the possible conflicting priorities of different donors (Dfid 2006, p. 8).

3.2 Ensuring “correct” pricing within AMCs

How to ensure “correct pricing” of as-yet undeveloped medicines? (Hvordan være sikre på “riktig prising” av ennå ikke utviklede preparater?)

Three prices must be determined under an AMC: the price per dose paid to developers, the co-payment portion of that price paid by developing countries, and the “tail” price at which the developers must sell the vaccine to developing countries after the AMC has been depleted. The latter two prices are to be determined after the vaccine has been developed, i.e., after most cost factors have become known (the second by the IAC and the last apparently by the producer). This section focuses on the first price, which must be determined in advance for as-yet undeveloped vaccines.

Both the overall size of the AMC fund and price per dose will be important factors for motivating firms. They will be chosen based on the “risks and challenges and desired outcomes” (Tremonti 2005b, p. 15). In practice, the overall size of the AMC will be determined first. It will then be the job of the IAC to suggest the division of the AMC into price per dose and consequently the number of doses (p. 11).

At a minimum, the price per dose must be “less than the social value of preventing the disease and better value for money than alternative uses for the funds” (Tremonti 2005b, p. 14). After that, the price (like AMC size) must be set to achieve the AMC’s policy goals, which may be somewhat different in the case of different diseases, e.g., whether a vaccine is in early or late stages of development, the number of potential products in the pipeline, and the spacing of those products along the pipeline.

According to AMC planners, a higher price per dose is expected to accelerate development of the most advanced vaccine in the pipeline, but lead to a lower number of doses supported by the AMC. This may allow the first to market to obtain the lion’s share of AMC money, consequently leaving the AMC less able to support – or

stimulate development of – second or third-generation vaccines (Tremonti 2005b, p. 11).

The Tremonti report and others postulate that a lower price per dose may stimulate more firms to compete for AMC funds if it is clear to developers that this will lead to a longer-lived AMC and hence a greater chance of supporting second and third-generation products.² However, this would seem to depend crucially on the spacing of potential products in the development pipeline. Moreover, a price that is “too” low obviously will not stimulate any potential developers. AMC planners expect that firms will carefully take AMC size and price per dose into consideration when deciding whether or not to compete for AMC funds.

In order to help learn more about price levels likely to stimulate the right response from developers, the World Bank commissioned a consultant, Applied Strategies, to develop a model that “replicates the industry’s valuation methodology”. The model “highlighted three areas of data that are critical to firms’ likely responses to an AMC: demand forecasts, status of development and probabilities of success/failure [including likely rivals], and estimated cost of goods” (Tremonti 2005b, p. 20). However, all of these factors become more difficult to estimate the earlier that a vaccine is in the development pipeline. For some later-stage vaccines, such as those for pneumococcus, cost of goods, for example, might be based on existing production costs for the developed-country version of the vaccine.

There are thus risks involved in setting a price too low and too high. However, the risks in setting it too high (development of only one vaccine) seem less serious than those of setting it too low (development of no vaccine), particularly for a pilot. Among the “key points” noted by panellists at the UK consultation meetings was that, “where the payoff (in DALY terms) is great, it is better to err on the side of being too generous than being too stingy” (Dfid 2006, p. 20).

From a practical point of view, erring on the high side may also help demonstrate more quickly whether the AMC concept could ever be a success – which is ultimately the goal of a pilot. If price per dose, along with overall AMC size, are clearly on the high side and firms are still not motivated, this would be a good indication that AMCs are unlikely to ever succeed. On the other hand, if the price used in the pilot is close to the borderline of what could be expected to stimulate one or more firms, it would be more difficult to say whether failure was due to a too-low price or to something more fundamental in the AMC concept.

The Tremonti report notes that, since industry periodically re-evaluates its risks and costs before making an investment at each stage along the product pipeline, the AMC may also need to periodically review AMC terms. However, it cautions that, “once price expectations have been set, they may be difficult to change,” e.g., because it may interfere with developing country planning (Tremonti 2005b, p. 15). This would also seem to argue for erring on the high side, at least in the case of the pilots.

In general, the earlier a product is in the development pipeline, the greater the cost uncertainty faced by firms; consequently, the higher the AMC price may need to be in

² The Tremonti report notes that vaccine manufacturers “have consistently stated their preference for an AMC that encourages competition rather than a ‘winner (first to market) takes all’ approach” (Tremonti 2005b, p. 15).

order to compensate companies for perceived risks, which include not only cost of goods, but demand risks and the risks of success or failure. On the other hand, if pilot AMCs are able to show convincingly that AMCs can work, future AMC prices may not need to compensate for as many uncertainties.

3.3 Risks that AMCs will subsidise pharmaceutical giants

*The related risks of unintended official subsidising of pharmaceutical giants
(Den tilhørende risikoen for uheldig offentlig subsidiering av farmasigiganter)*

In general, it is difficult for smaller firms to bring new products through the later, relatively expensive phases of vaccine development. Thus, strictly speaking, the large pharmaceutical firms are probably the ones most likely to get direct AMC funds. However, the existence of the AMC may stimulate activity by smaller firms further up the pipeline. For instance, the Tremonti report notes that an AMC will “create incentives for small firms to invest in new technologies, in the hope of selling or licensing their technology to larger companies that will produce the vaccine” because they will know that such products would have market value. And “developing country firms are also likely to benefit from contracts to manage or participate in large-scale trials in developing countries (Tremonti 2005b, pp. 1, 8). The UK consultation paper similarly notes that it “has been difficult for small-scale innovative biotechnology companies to commit resources to the field of vaccine research – the AMC may be able to unlock the potential of this sector” (Dfid 2006, p. 5). Thus, “AMC money” may trickle down to smaller firms before it is even distributed to the large ones.

For some later-stage vaccines, where large pharmaceutical firms may have already developed vaccines but never took them to market because the additional costs did not justify expected economic returns, an AMC could end up motivating firms to take such projects off the shelf. This in fact has been one of the stated aims of the AMC concept. Although this could be considered subsidising, it presumably would not be paying the pharmaceutical giants for doing something that they would have otherwise done without such subsidies. GAVI notes that it will monitor what companies are doing to address diseases targeted by AMCs. To the extent that such cases are known, this could help the IAC limit the AMC price per dose to cover only the development costs needed to get an existing vaccine off the shelf and through the last hurdles to market, since previous investments on research could be considered sunk costs. However, it is unclear that GAVI or others will have sufficient knowledge of such cases at the time when the AMC’s overall size and price per dose are being set.

As the AMC concept becomes more established and AMCs are anticipated for other diseases, there could be a risk that developers (and particularly giant pharmaceutical firms) hold off on the final, more expensive phases of development for a vaccine that they might otherwise have developed without subsidies. In order to minimise such gaming activity, the expert vetting process for AMCs may need to be able to assess such cases and declare early and decisively whether or not an AMC is likely to be developed for particular diseases.

3.4 Risks that AMCs will support monopolisation

*The risks for de facto support to monopolisation of the international pharmaceutical industry
(Risikoen for de facto støtte til monopolisering i internasjonal farmasøytisk industri)*

As noted above under Pricing (3.2), the intention is to design an AMC to be large enough to sustain 2-3 firms in order to foster competition (Rome 2006e). However, there could be a tradeoff between accelerating development of the first vaccine through a higher price 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)” (Tremonti 2005a, p. 11).

The strategy taken by a particular AMC would depend on a number of factors, notably including the number of products in the pipeline that are relatively close to development. However, the World Bank/Applied Strategies valuation model shows that “the greater the time gap between successive products in the pipeline, the more challenging it is to find an AMC market size and price scenario that could support 2-3 manufacturers” (Tremonti 2005b, p. 23). In such cases, the tradeoff seems to move to one between monopoly supplier and no supplier at all.

Even if there ends up being a monopoly supplier, there may be factors that may mitigate against monopoly pricing. Once a supplier accepted the terms of the AMC, it would be subject to the price per dose determined by the AMC, and after that to a “tail” price, which, according to current plans, will be up to the supplier to determine and agree to in advance. In theory, a supplier would not know at the time it began receiving AMC funds whether it would end up being a monopoly supplier of vaccines against a particular disease. This could keep it from setting the post-AMC “tail” price too high. On the other hand, since there appears to be no prohibition against lowering the “tail” price later, a supplier receiving AMC funds may have an incentive to hedge its bets by committing to a relatively high “tail” price at the outset, knowing that it could cut this price later if others entered the market. This may be an argument for linking the “tail” price to the co-payment, which is the portion of the price paid by developing countries during the AMC. If the co-payment and “tail” prices were linked, a supplier would not want to set the co-payment (and ultimately the “tail” price) so high that it risked lowering developing-country demand and hence receipt of the per-dose subsidy. (The current intent is to link the co-payment to the “tail” price, probably in a ratio.) There are reportedly discussions about providing additional subsidies to help developing countries afford the co-payment. Eventual design of such subsidies should take into account the need to avoid undermining incentives against monopoly pricing.

3.5 What happens if AMC does not lead to a vaccine being developed

What happens if there is no success in developing an “ordered” vaccine/medicine? (Hva skjer dersom man ikke lykkes i utvikingen av “bestilte” vaksiner/medisiner?)

A paper by GAVI, World Bank and WHO notes that, “although the TPP-setting process relies on experts in the vaccines field, the TPPs may still prove to be unattainable in practice, particularly for difficult-to-predict early-stage vaccines” (GAVI et al 2006, p. 7). In such cases, it is proposed that the IAC would make a judgement on whether the price should be increased and/or the TPP made less stringent. In order to help it make such decisions, the IAC would call upon WHO to convene a group to consider changes to the TPP and/or call upon the AMC secretariat (presumably the GAVI Board) to convene a group to consider changes to price (Rome 2006b and WB & GAVI 10/2006,

p. 43). However, “donors, industry and other stakeholders” still need to agree on what “significant events could trigger a reassessment” (WB & GAVI 10/2006, p. 39).

It appears more likely that prices would be raised rather than TPPs lowered, since a lowered TPP “could still be disruptive for manufacturers that had invested in research and development to meet the original higher level. Therefore, modification of TPPs should be a rare event” (GAVI et al 2006, p. 7).

The Tremonti report points out that donors have “little to lose” if a vaccine is not developed, since commitments will not be disbursed (Tremonti 2005b, p. 1). However, this will depend on the financing method chosen by individual donors. The cost would be minimal for those governments that had chosen not to set aside any funds but to pay only when funds were required, i.e., after a vaccine had been developed, approved and demanded. For donors that had chosen to build up their commitment over time, there would be some opportunity costs, though these could be offset to some extent by investing the funds – to the degree this becomes possible under bundling arrangements, which have yet to be decided (see below).

As mentioned already, demand-side risks also include uncertainties related to demand forecasts and planning and distribution systems in developing countries. Complementary investments in these areas are thus likely to help lower the overall risk of AMC failure and avoid necessary TPP and price revisions.

According to the World Bank and GAVI, given the advanced stage of vaccine development for pneumococcal disease, it is at least “unlikely that the TPP or AMC prices set in the framework will need to be revised” for the first pilot (WB & GAVI 10/2006, p. 42).

3.6 Proposed governing structure

An assessment of the proposed institutional mechanisms for a pneumococcus AMC, including the relation to the GAVI Alliance’s institutional mechanisms. (En vurdering av foreslåtte styringsmekanismer for pneumokokk AMC, inkludert relasjon til GAVI-alliansens styringsmekanismer)

After consultations with various existing institutions, including the Bill & Melinda Gates Foundation, the Global Fund, UNICEF and WHO, the Technical Working Group for the pilot AMC decided to locate the AMC secretariat within GAVI and have the World Bank administer the AMC’s funds. Both organisations appear well placed to carry out their proposed functions, which seem to mesh with existing structures and processes.

GAVI and the World Bank, in consultation with other stakeholders, are to first identify members of an Independent Assessment Committee (IAC). The IAC will rely on WHO to create a group of technical experts to develop a Target Product Profile (TPP) that will be used as the terms of reference in judging whether an eventual candidate vaccine meets the AMC criteria for funding. In practice, there is likely to be one IAC with a separate group of technical experts for each additional eventual disease-specific AMC.

GAVI, acting as the AMC secretariat, plans to hire two dedicated persons to provide administrative and programme support to the IAC.³

Once a candidate vaccine becomes available, the IAC will rely on WHO to perform a pre-qualification recommendation similar to procedures WHO already uses for other vaccines distributed through GAVI. This includes review by the SAGE expert group that advises the WHO Secretary General on immunisation issues (WB & GAVI 10/2006, p. 36). The main difference from ordinary GAVI procedures would be that WHO would perform the review against the TPP. The SAGE would pass its recommendation to the IAC, which would have final approval.

Developing countries will apply for the AMC-supported vaccines through the established GAVI process of national applications and requests. After that, GAVI's regular implementing partners, WHO and UNICEF, will deliver the vaccines using regular GAVI channels (WB & GAVI 10/2006, pp. 8-9).

GAVI will also be responsible for much of the complementary investments for strengthening health systems and vaccine management in-country, as well as demand forecasting (WB & GAVI 10/2006, p. 40). These are activities it currently carries out to support the uptake of other vaccines, so can be leveraged in large part by AMC-supported vaccines.

The AMC secretariat, housed by GAVI, will regularly report on progress toward AMC objectives by tracking and reporting on “firms engaged, level of investment, status of product development and installed capacity, and country demand”. And GAVI will report on the public health impact of the AMC (London 2006b). While GAVI and the AMC secretariat would be in a good position to perform these monitoring roles, it may be desirable to institute an additional, independent monitoring and evaluation procedure to avoid possible conflict of interest. Such a supplementary M&E role could be performed, e.g., under the auspices of the Donor Committee.

A Donor Committee is to be formed to “facilitate donor engagement” and input during the development stage of the AMC and to oversee progress once the AMC has been launched (London 2006b). However, it is not clear yet how the donor committee will fit into the eventual governing structure. Major donors, along with other key stakeholders, presumably will also have influence on the AMC secretariat via representation on the GAVI Alliance Board.

The World Bank will be responsible for the financial functions of the AMC, notably bundling the commitments of the various donors into one financial instrument and ensuring the AMC honours its required payments. Although the bundling role will be new for the World Bank, it is probably better placed than other public institutions to perform the role of AMC funds administrator. As one presentation points out, the World

³ While a good case could be made for GAVI hosting subsequent vaccine-related AMCs, it would seem less logical for a common GAVI-based secretariat to host non-vaccine AMCs. Moreover, it appears that so far relatively little attention has been given to the institutional arrangement or placement of the second pilot, expected to be for malaria. GAVI apparently expects it to be housed under the same secretariat as the pneumococcal AMC, i.e., within GAVI. A GAVI representative expected that a malaria AMC would necessarily involve coordination with the Global Fund – the main institution coordinating international efforts against malaria – but noted that there had been no real discussions yet between GAVI and the Global Fund in this regard.

Bank is already “trustee and administrator for \$9 billion in trust funds from donor sources, has extensive fiduciary experience and capacity to manage multi-donor guarantees and arrangements, manage and disburse funds as required and to negotiate and sign complex contracts” (Rome 2006a). Participation by the World Bank should also help reassure potential vaccine developers about the reliability of AMC funds, in turn increasing the power of the AMC to motivate vaccine development.

4 Financing issues

This chapter contains four sections: The first reviews the three major timing options that individual donors could use to fund their commitments to an AMC. The second examines the implications of Norwegian budgetary regulations. The third looks at the implications of each method for the scoring of Official Development Assistance (ODA) under the rules of the OECD Development Assistance Committee (DAC). The fourth section reviews plans to “bundle” the commitments of individual donors into a single financial instrument, and the fifth deals with the need for “start-up” funds.

4.1 Financing alternatives for individual donors

A pro-contra evaluation of the three financing alternatives for AMCs. (En pro-contra vurdering av de tre finansieringsalternativene for AMCs.)

Most background papers on AMCs note that, in theory, there are three main ways that individual donors could contribute to an AMC:

- Full up-front payment by donor at the beginning of the commitment period, with the money held in some sort of trust fund until it is needed;
- Up-front commitment to the full amount, with annual donor payments timed to build up the full amount by the time funds are expected to be needed;
- Up-front commitment to the full amount, with donor payments taking place only when actually required for compensation to developers.

Different donors may have different preferences, based on different considerations. This section looks at the main general advantages and disadvantages of these three different financing methods. Since an important consideration for the choice will be implications for an individual donor’s domestic authorisation and appropriation laws and procedures, the following section reviews the implications of the different methods for Norway in terms of Norwegian state economic regulations.

Canada is so far the only major donor that has signalled its intention to pay the full amount up front (option 1), while most other donors would be expected to commit to some variation of option 2. So far it appears that the US appropriation system does not lend itself to multi-year commitments.

4.1.1 Full front-loaded financing

Under this option the donor makes its entire commitment available from the beginning, i.e., at the point the AMC is established. This would not necessarily have to be done in the form of cash, but could be accomplished via deposit of promissory notes, letters of credit “or other instruments that provide for the payment over a certain time span” (Tremonti 2005a, p. 14). The money or other instruments presumably would be kept in a trust fund until needed.

The main advantage of this option is likely to be maximum credibility in terms of donor commitment: Potential developers will be reassured to know that the money is clearly

available. However, if all commitments were bundled into a single financial instrument, potential vaccine developers may look more closely at how this single instrument is secured rather than at how each individual commitment within it is structured. Moreover, the perceived reliability of the World Bank will probably go at least some way in compensating for possible doubts about the reliability of specific governments' pledges.

On the other hand, the greater the total amount of cash provided up front by all donors, the less it is likely to cost to bundle the pledges into a single financial instrument, since the available cash could be used to provide insurance for the remainder. It therefore would seem advantageous from the viewpoint of the AMC as a whole to have at least some donors provide money up front in order to help guarantee the amount to be paid later by others.

This option would be the best alternative in the event that vaccine development occurs earlier than expected, especially in the case of a late-stage vaccine, such as that for pneumococcal disease. However, the second financing option (periodic build-up) and even the third (payment when needed) could probably handle this eventuality sufficiently as long as some sort of bridging financing had been arranged.

This option would have the greatest opportunity cost, since the full amount of money would be unavailable for other activities for the full period of the AMC (although use of smaller up-front contributions based on net present value could minimise this in theory). It would consequently also result in a large idle cash balance that would have to be invested in order to partially offset the opportunity costs.

4.1.2 Financing through periodic contributions

Under this option, a donor would commit to the full amount at the establishment of the AMC and provide a stream of payments on an annual basis, with the aim of reaching the full commitment amount by the time vaccine development is expected.

This option lowers the potential problem of excessive idle cash noted under the first option. Opportunity costs are also smaller, and could be further minimised by "back loading", i.e., starting with smaller annual contributions and increasing them over time.

As noted above, eventual early vaccine development could be handled through a contingent facility for bridge financing. Moreover, expected regular monitoring of industry activity by the AMC secretariat could provide some advance warning if and when additional funds may be needed, giving donors some opportunity to increase annual contributions if required (WB & GAVI 10/2006, p. 36).

AMC planners note that this option is likely to be the most amenable to most donors' budget and appropriation systems, following "well established precedents for most countries" of full authorisation followed by annual appropriations (WB & GAVI 10/2006, p. 51).

This option might also be most amenable to financing via a sales tax, e.g., the tax on airline tickets originally proposed by France and now being considered by a number of other countries. To protect against the effects of an eventual downturn in the commerce in question, e.g., air travel, annual flow estimates from this source (ideally supplemented by a fixed amount from the regular budget) could be set conservatively,

so that in practice the commitment may be fulfilled early under a normal tax collection scenario.

4.1.3 Financing when disbursement is required

Under this option, the donor would commit to the entire amount up front, but disburse money only when needed, i.e., when developers are paid for actual vaccine sales. As under the other options, however, the donor would still need to make small annual payments to cover the operating costs of the AMC.

The main advantage of this option would be minimisation of opportunity costs, i.e., the money would not be standing idle and so be available for other development priorities.

Depending on how structured, it may not be very flexible in the case of earlier-than-expected vaccine development. However, as noted above, monitoring of industry activity by the AMC secretariat could help provide advance warning about when funds may be needed.

AMC planners note that this option could be particularly appropriate for early-stage vaccines, for which the expected date of future payments is distant and hence relatively uncertain (WB & GAVI 10/2006, p. 52). On the other hand, this option may provide the least assurance to industry, while the need assurance may be greatest for early-stage vaccines, due to greater risks.

It is thought that this option may be difficult for many donors in practice because their budgeting systems may not “lend themselves to making credible and legally sound financial commitments, contingent upon a future event” such as the production of a vaccine that meets particular requirements. While governments often undertake to buy goods at some future date, “there is much less precedent where the goods in question do not yet exist and when the supplier is not defined” (WB & GAVI 10/2006, p. 52).

4.2 Implications of Norwegian budgetary regulations

Article 6 in *Bevilgningsreglementet*, “Decisions on commitments for future budgetary years” (Vedtak om forpliktelser for framtidige budsjettår) notes that the State (an administration) can incur commitments to be honoured/covered after the budgetary year only if special consent (særlig samtykke) has been given by *Stortinget*. The phrasing suggests special procedures for such allowances to be made. In addition, if consent is to be given, it will be so only for a given/specified year (for det enkelte budsjettår) and for a certain amount. This seems to be an obstruction for the third alternative, i.e., a commitment to finance only when disbursement is necessary, since it is not known when vaccines are to be developed and/or demanded.

One complicating factor with AMCs is the conditionality clause, which states that money committed and/or already paid out will not be used in case vaccines are not developed or demanded. *Bevilgningsreglementet* does not give any clear answers as to whether committed money could later be used for other (development) purposes if not used to purchase vaccines. Article 5 (*Bevilgningsvedtak*) does state that funds allocated to a particular purpose (*utgiftsbevilgninger*) cannot be exceeded or used for purposes other than they were intended for. That does not immediately exclude the possibility that money set aside for a fund but left unused can be used for other (closely related)

development issues, but this depends on how narrow the definition of the intended use of allocated funds needs to be.

Article 3 concerns which expenses and revenues the budget should include. It states that expenses and revenues should be included in the budget when they are to be paid in cash. Therefore, money allocated to AMCs apparently will count as a budgetary expense only when money is paid out to a fund and not at the time of commitment (if option 2 or 3 are used).

To conclude, in so far as all three financing alternatives imply that funds will not be paid out in the same budgetary year as that in which the commitment is made, special consent from *Stortinget* apparently would be needed for each option. In order for *Stortinget* to give such consent, a specific amount and year for disbursement must be specified. In our opinion, this would favour contributions upfront or periodically into a fund (options 1 and 2). Such an arrangement bears similarity to the current setup for funding from Norway to the International Development Association (IDA): the government decides to pay money over periods to an account in Norges Bank, from which the IDA can draw the funds in accordance with an agreed schedule. (This arrangement also required special consent from *Stortinget*.)

4.3 DAC ODA scoring

This section looks at the when donor support to an AMC can be counted as Official Development Assistance (ODA) under the rules of the OECD Development Assistance Committee (DAC). ECON consulted with the DAC on this issue.

In general, two conditions must be fulfilled in order for donor support to count as ODA:

1. There must be an official expenditure.
2. There must be a cross-border flow in balance of payments terms.

Contributions into a fund, either fully front-loaded (option 1) or periodic contributions (option 2), would satisfy the first criterion. Even promissory notes usually can count as ODA at the time they are deposited, since the balance-of-payments accounting system is accruals based, meaning that income is recorded when earned and not necessarily when received.

However, pledges and guarantees are not scored until they are paid. Thus the third alternative of ‘financing when disbursement is required’, without any contributions to a Fund in advance, will likely not meet the first requirement at the time the pledge is made.

To conclude, the first two financing alternatives meet requirement one, while financing alternative three does not meet requirement one.

The second requirement for ODA scoring is more difficult in terms of AMC because of the conditionality clause, which effectively introduces an element of uncertainty regarding whether or not the funds deposited ultimately will be used for development. According to the OECD, the issue would be to determine when there the flow of benefit to developing countries occurs. Since there is likely to be a safeguard clause to cover the eventuality of no vaccines being purchased, one cannot determine a flow at the point of funding the AMC. Thus it appears no financing alternative will meet requirement two at the time of commitment, providing there is such a safeguard clause for alternative use of

funds. Due to the fungibility of funds (e.g., cuts could simply be made elsewhere in the budget), this is even likely to be true if the safeguard clause noted generally that any alternative use of the funds would also be for development.

This information from DAC conflicts with the more positive assumptions made in some reports that may not have taken into account the apparent implications of the conditionality clause.

From the discussion above it appears that the earliest time that ODA scoring of contributions that have already been made, e.g., to a trust fund held by the World Bank, is after a vaccine has been developed, approved and demanded. However, the OECD representative to which we spoke believed that donations to cover the administrative costs of the AMC could be counted as ODA, providing that the AMC is intended solely to benefit developing countries.

Although some reports have indicated that there are discussions within the Development Assistance Committee (DAC) on the application of scoring criteria in relation to innovative financing mechanisms, DAC indicated that this was not the case.

4.4 Bundling the financial commitments

A brief evaluation of possibilities to "bundle" contributions into one package that is flexible enough to cover out-payments and to pay a return (Kort vurdering av mulighetene for å "bundle" bidragene til en pakke som er fleksibel nok til å dekke utbetalinger og forrente seg).

The main goal of the AMC is to encourage the private sector to invest in vaccines for developing-country diseases by assuring private investors that there is a viable market for such vaccines. This goal would be undermined if potential developers had to assess each donor's pledge individually, including differences in timing and underlying legal foundations. On the other hand, it is important to have a financial structure that is flexible enough to accommodate donors' different commitment preferences, including their different legal and budgetary requirements.

The current proposal by the Technical Working Group is to give the World Bank responsibility for managing AMC funds. However, donors reportedly still have yet to officially ask the World Bank to take on this role, which would have to be approved by the Bank's Board.

The "key role" of the World Bank as the AMC's financial intermediary would be to "act as the single contact point for industry by bundling together donor financing into a single financial asset that provides clear, coherent and legally-binding financial underpinnings to the legal obligations set out in the Framework Agreement" of a particular AMC (WB & GAVI 10/2006, p. 52). In fulfilling this role, the World Bank would hold donor commitments, manage and invest liquid assets, ensure timely payments to suppliers, smooth timing mismatches between commitments and payments, and mitigate related risk (London 2006b, Rome 2006e, Droop 2006, WB & GAVI 10/2006, p. 49).

However, the precise details of the financing arrangements "cannot be specified at this point, since much will depend on the nature of donors' pledges" (WB & GAVI 10/2006, pp. 48, 53). Once the pledges have been made, "a period of detailed discussion between

donors and the World Bank will be necessary to define the arrangements”. Nevertheless, “possible elements of a solution might include” a third-party guarantee by a commercial entity, e.g., a sort of re-insurance, and the use of cash from eventual up-front and annual payments by some donors to help underwrite the risks associated with future payments by the others (Ibid).

In principle, if the World Bank were to provide the bundling directly, it should be less expensive than if a commercial provider were to do so, since the World Bank is not a for-profit institution. The use of a “commercial wrap” for an AMC fund administered by the World Bank is also being investigated. While there do not seem to be particular difficulties with this solution, it would be the first time that the World Bank would engage a commercial bank to provide such cover. The main reason for the additional use of a commercial entity would be to add another degree of certainty for potential developers.

Developers would be expected to take into account the share of funding and credit standing of AMC donors in assessing payment risks. Consequently, a cushion amount might need to be added to an AMC to cover that expected discount.

Given the different payment profiles of different donor pledges, each commitment probably will need to be converted into net-present-value (NPV) terms in order to calculate actual donor shares in an AMC (WB & GAVI 10/2006, p. 53). Since donors ultimately will be responsible for “assuring credible funding, including the cost of bundling” (WB & GAVI 10/2006, p. 8), it also may be necessary to come up with rules for apportioning bundling charges according to the perceived risk profile of a particular pledge. However, using NPV shares to do this would effectively penalise donors that provided a large portion of their pledge early. One simple way to apportion the costs of covering risk and administration might be to pro rate such charges according to the face value of each commitment. This would have the effect of charging higher insurance rates to those donors that chose to make their payments later.

4.5 The need for start-up funds to get AMCs “up and running”

The need to make public development funds available to get the AMCs “up and running”. (Behovet for offentlig medvirksomhet med bistandsmidler for å få AMCs “opp og stå”)

The AMC pilot proposal prepared by the World Bank and GAVI notes that “the costs of implementing the AMC are expected to be low, with GAVI and the World Bank building on existing capacity and requiring relatively modest support” (WB & GAVI 9/2006, p. 7)

According to a representative of GAVI we spoke to, start-up costs for the pneumo AMC are likely to be around US\$2.5 million, which he calls a “modest percentage” of the estimated AMC size of US\$1.5 billion. These start-up costs would cover work to develop the TPP, hold initial IAC meetings, structure the finance, hire two new staff at GAVI and cover the “significant” legal costs involved in developing the agreement.

Although some of the costs, such as hiring of two dedicated staff, might come initially from the regular GAVI budget, GAVI expected that donors would be asked to contribute new money to cover the start-up funds. However, it was not clear whether

this would be part of a coordinated appeal or a separate appeal by each of the relevant organisations involved, i.e., GAVI and World Bank. It was also not clear when this would happen, though GAVI noted that it could be in February when countries would be asked to make commitments to the longer-term AMC costs.

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Annex 1: Terms of reference

Prosjektbeskrivelse

Prosjektet består av en hurtigutredning av såkalte Advance Market Commitments (AMCs) for Vaccines, som foreslått av Italia, Storbritannia og Canada. Følgende problemstillinger vil være sentrale:

- AMCs evne til å kompensere for ”markedssvikt” ift utvikling av nye medisiner/vaksiner
- Behovet for offentlig medvirkning med bistandsmidler for å få AMCs ”opp og stå”
- Hva man oppnår med AMCs som ikke oppnås ad andre kanaler for helsebistand
- Mulige effekter av AMCs på andre kanaler, spesielt produkt-relaterte offentlig-private samarbeidsprosjekter (Product Development Partnerships – PDP)
- Hvordan sikre seg at man går for de ”riktige” preparatene ift u-lands behov?
- Hvordan være sikre på ”riktig prising” av ennå ikke utviklede preparater?
- Den tilhørende risikoen for uheldig offentlig subsidiering av farmasigiganter
- Risikoen for de facto støtte til monopolisering i internasjonal farmasøytisk industri
- Hva skjer dersom man *ikke* lykkes i utviklingen av ”bestilte” vaksiner/medisiner?
- En vurdering av foreslåtte styringsmekanismer for *pneumokokk* AMC, inkludert relasjon til GAVI-alliansens styringsmekanismer

Prosjektet skal dessuten munne ut i en *pro-et-contra* vurdering av de tre finansieringsalternativene for AMCs:

1. "up-front" innbetaling av hele summen
2. årlig innbetaling av et avtalt beløp fra år 1
3. innbetaling først ved implementering (f. eks innkjøp og levering av vaksine), kanskje 10-12 år fram i tid (for *pneumokokk* tidligere, kanskje allerede fra 2011-2012)

Under antakelse om at deltakende givere vil velge å bidra på ulikt vis, kan man i prosjektet med fordel også kort vurdere mulighetene for å ”bundle” bidragene til en pakke som er fleksibel nok til å dekke utbetalinger og forrente seg.

Samtlige opsjoner bes vurdert ift Statens økonomireglement.