

Concerns Regarding the Center for Global Development Report “Making Markets for Vaccines”⁺

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+ The opinions expressed here are those of the authors and do not necessarily reflect the views of the organizations with which the authors are affiliated. Further copies of this policy briefing can be found at <http://www.who.int/intellectualproperty>.

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I. Introduction

The recently-launched and heavily-promoted Center for Global Development report “Making Markets for Vaccines,”² proposes “Advance Market Commitment” (AMC) subsidy programs for discovering and developing new vaccines, especially for HIV, malaria, and tuberculosis. After a careful review of the CGD report and of its earlier drafts – indeed, all of us advised on it – we conclude that the CGD model for these vaccines is unworkable, inefficient, and inequitable towards the wide range of potential developers and suppliers of such vaccines. This policy briefing summarizes a range of our concerns.

Many of these concerns center around the weaknesses and failings of the two-stage contracts appended to the CGD report. Contracts are at the core of AMC thinking, and yet crucial contractual details – such as the treatment of liability risk; the terms of treatment of new, emerging entrants to the vaccine industry; the methodology for assuring long-term price and supply; the rules for distributing the AMC subsidy over multiple vaccine developers to generate the complex subsidy pattern being presumed; etc. – are simply missing. Other contractual details – largely because of the extreme paucity of information in advance about vaccines yet to be discovered – are set on the basis of inappropriate evidence, unrelated to the distinctive complexities of discovery, manufacture, and delivery of such vaccines. That all these fundamental flaws still persist more than eight years after the idea first surfaced³ (though only very recently taking on the guise of an “Advance Market Commitment”) and after a great deal of effort by a great number of individuals – not to mention of a great deal of funding – says something

² “Making Markets for Vaccines: Ideas into Action”, Center for Global Development, Washington D.C April 2005. Also, “Frequently Asked Questions”, Center for Global Development, April 2005.

³ The Sabin Vaccine Institute colloquium held at Cold Spring Harbor, New York, 5 – 7 December 1997 identified many of the issues and reservations still unresolved in the CGD’s 2005 report (see Muraskin, W. “Vaccines for Developing Economies: Who will Pay?” Albert B. Sabin Vaccine Institute, New Canaan, CT, USA., 2001).

about the underlying problems of relying on such programs to drive R&D for these vaccines.

Problems in setting key contractual terms mean that, ironically, far from being 'market-based', the CGD model of AMCs ends up being heavily 'committee-based'. Frequent references in the report to a 'market' and to 'competition' seem inappropriate and appear to be inserted only to make the proposals more broadly appealing. Since setting terms 15-30 years in advance is impossible, a great deal of discretion has to be left in the hands of a committee – suggested in the report to be of as few as five individuals – vested with the power to distribute the funds. The tension between the need to be credible and the need to be flexible creates great risk to investors, especially to those investing into early parts of the research process. The capture of the subsidy program by larger, and more influential, developers and by those later in the development process is a particular risk.

Such subsidy programs have never been used before – even for the most basic of cases. Thus no evidence is provided in the report to reassure us that the complex mechanism being proposed will work, and that it will not simply absorb a great deal of valuable time and energy in an essentially costly experiment, while detracting attention from other more efficient and proven – but currently underfunded – approaches.

II. Concerns

There is insufficient space to cover all concerns here. Interested readers might like to consult further background material that covers a wider range of issues⁴.

II.1. Complexity and Change – Closing the Door on Later Innovators

The contractual arrangements for an AMC call for the sponsor(s) and for all actual and potential vaccine developers to sign-on to the ‘framework’ contract within 36 months of the initiation of the program, and for all developers to agree to be monitored by the committee running the program and to abide by its rules and its use of discretion when determining the distribution of the payments many years later at the end of the process. Those conducting current vaccine trials and failing to sign-on, and those initiating future vaccine trials without prior permission from this committee, will be barred access to the ‘eligible’ markets controlled by the committee. Entry of later developers to the program will be controlled through the committee.

However, the development, introduction, and manufacture of vaccines are extraordinarily complex processes that take place over many years and involve many organizations. In addition, the global state of the development and manufacture of vaccines is rapidly changing, with centers in developing and emerging countries such as India, China, and Cuba becoming increasingly important. At a very early stage in the development of a vaccine, it would not be possible to identify all those who may

⁴ Farlow, A.W.K., “The global HIV enterprise, malaria vaccines and purchase commitments: what is the fit?” Commission on Intellectual Property Rights, Innovation and Public Health, March 2005 (www.who.int/intellectualproperty) and forthcoming, *Innovation Strategy Today*; Light, D.W., “Making practical markets for vaccines: revisions needed and problems with the Center for Global Development report, Making Markets for Vaccines”. Stratford, NJ: University of Medicine and Dentistry of New Jersey, April 2005 (<http://www.bioethics.upenn.edu>); Widdus, R., “Key Stakeholders and Funding of HIV and Malaria Vaccines: Considerations in selecting appropriate instruments for accelerating public health impact of vaccination in poorer countries,” Initiative on Public-Private Partnership for Health (IPPPH) at the Global Forum for Health Research, Geneva, Switzerland, April 2005, paper prepared for the UK Department for International Development, submission to Commission on Intellectual Property Rights, Innovation and Public Health, May 2005 (www.who.int/intellectualproperty).

potentially take part in such a program in ten to twenty, or even more, years time. Nor is it clear why the incentives of later innovative research teams should be stymied by contractual arrangements that unnecessarily constrict competition by forcing them to go through large multinational pharmaceutical companies.

II.2. The Lack of an Evidence-Based Methodology

The CGD report proposes that payment be set in the contracts at \$3 billion per disease for HIV, malaria, and tuberculosis, with a complex technical specification, and rules for the treatment of vaccines of different specifications, contractually set in advance. The \$3bn is described as a “crucial detail” – one would expect to be set with some care and related to the vaccines at hand – and yet it is now pitched much lower than in draft versions of the report of even just a few months ago, with no rationale provided to explain this, other than political expediency.

To price an AMC appropriately – both the overall size of the fund, and the level of the initial high guaranteed price and the number of sales at that price – a thorough analysis of the history of the introduction of various kinds of vaccines would be required to provide an evidence-based method for computing payment, technical specification, and rules for each vaccine. This would take into account, amongst other things, the *expected* complexity of the underlying science, nature of production technologies, time to when the vaccine will emerge, and epidemiology – all factors in industry calculations, which also include the cost of capital. No such methodology has been employed here. Its absence is even openly promoted as some sort of a virtue. The fact that by getting terms wrong, an HIV vaccine might therefore fail to materialize, is dismissed by observing that if for HIV an AMC “does not succeed, there is no cost to the sponsors.”

The methodology on which the \$3 billion *is* based relates to matching the sales of developed country ‘blockbuster’ drugs, not past successful vaccines, and may grossly overestimate the innovation costs likely incurred by developing and emerging country

developers and suppliers, even while it may underestimate the costs of development of complicated early-stage vaccines by developed country developers. In particular, given the extreme scientific risks, the long periods of discovery time, and the huge risks of the AMCs proposed in the CGD report, the vast majority of the \$3bn would go into the costs of capital rather than into any out-of-pocket R&D – making the AMCs described in the report a very inefficient way to support such R&D.

One should also reflect on practical evidence, such as that of the hepatitis B vaccine. If a program such as this had been in place for the development of that vaccine, it would have led to the payment of \$3 billion to one or two developed country producers who are not today major suppliers of hepatitis B vaccine for developing countries. Such a program would certainly not have been favorable for China, India, and Korea, who are today's suppliers. The hepatitis B case was included in draft versions of the report but has been removed in the final report perhaps because, as a case-study, it shows that the original vaccine developers were not the ones who developed and maintained the lower price market, and because the competitive situation for hepatitis B today – a key component in achieving long-term sustainable low prices and secure supply – reflects poorly on the non-competitive model being put forward here.

II.3. Problems with the Long-Term Price and with Secure Long-Term Supply

The CGD contracts call for determining, at the time of signing, the 'guaranteed' long-term near-marginal-cost-of-production price, and for the obligation of a company to supply *at that price* in the long-term, in return for having had the short-term advantage of initial sales at high, heavily subsidized, guaranteed prices. This is described in the report as a "critical component of the advance market commitment". If it were possible to make computation of such a price, the report should have referred to a proven, transparent methodology. Instead, this "critical component" is missing from both the report and from the contract term sheets.

To our knowledge no such methodology exists. The CGD Working Group heard expert advice that production costs could range anywhere between \$0.50 to \$15.00 per course, depending on the manufacturing complexity of the vaccine discovered, and that no such guarantee could therefore be inserted into contracts. This advice was ignored. The Working Group should have reviewed the extensive exploration of this issue undertaken by the NIH in the early 1990s, which concluded that it was extraordinarily difficult to compute or even lay out a methodology for computing the price of an unknown product, and that competition policy and commercial law may well preclude engaging in activity that could be seen as price fixing and/or a subsidy to a favored firm.

A mechanism that relies on this presumption holding in order for it to work and in order to secure long-term vaccine supply, should be treated with a great deal of caution, indeed skepticism – even more so when one sees that the contract term sheets have also left blank those sections specifying remedies in the event of a breach of this condition. The risk is that all the sponsor’s funding is absorbed by the first developer and the long-term low price is not achieved, or even that the long-term ‘eligible’ market is abandoned in preference for serving a more valuable ‘non-eligible’ market. Crucially, the design of the CGD model precludes competition among different suppliers to develop more efficient production methods and lower vaccine prices to poor nations, as happened in case of the Hepatitis B. Thus the central goal of an AMC to buy out an effective vaccine so that it becomes available thereafter at a low price cannot be achieved by the route suggested in the CGD report.

II.4. Promoting the Lowest Common Denominator

The CGD model calls for the setting of minimum requirements for a vaccine at the start, and a small distribution committee with the power to lower those standards yet further when determining how to distribute the funds – but never, under any circumstances, to raise standards. However, predicting an efficient technical specification resembling the ultimately useful vaccine – or, indeed, the series of ever-improving vaccines to reward a

series of developers – would be impossible to set years in advance for HIV, malaria, and tuberculosis. The Working Group was advised of this difficulty, yet chose to ignore the advice.

It is also becoming increasingly clear that requirements would be set at the very lowest level that would be of any epidemiological value. In successive drafts of the CGD report, the requirements for a malaria vaccine gravitated ever-lower, standing in the final report's contract term sheets at a suggested 50% efficacy for 24 months from up to four doses, with room to lower the requirements even further. There was no clear rationale to support this lowering of requirements. It may have been a response to a malaria candidate vaccine making the headlines in late 2004. Unfortunately, though promising, this candidate is based on a single component of one stage of the life-cycle of the parasite causing malaria, and may not have enough efficacy to be worth using widely. Even if it is successful in upcoming trials – by no means a foregone conclusion – there will be need to encourage the design of subsequent generations of better vaccines with much broader activity and higher efficacy. Blindly pitching minimum requirements ever lower simply works against this long-term goal.

The consequence is that the CGD model provides no incentive for competing teams to develop vaccines that exceed the minimum requirements, because the first company to satisfy the requirements would have a huge incentive to try to harvest the full \$3bn from the small portion of all potential sales that get the high subsidized price, even if its vaccine is later abandoned and follow-on vaccines are also stymied. No follow-on innovator would invest the additional time and resources into a superior vaccine if the development of that vaccine would take several years longer than the minimum requirement vaccine and risk 'missing the subsidy'. Because the discretion to lower standards is especially risky to smaller and less powerful developers, and because the risk of political capture is high, most of the world's research teams and venture capitalists would be put off from investing private funds in the first place.

To make matters worse, the greatly reduced reward obtained from exploiting improvements in technology to generate higher quality products, destroys incentives to make such breakthroughs in the first place; there is no relevant price signal. The design of the program also encourages the hoarding, rather than the sharing, of vital R&D information, and so does not work well when vaccine development is not 'linear' and static but, instead, highly dependent on feedback loops and collaboration – something typical of these particular vaccines. Funding collaborative efforts is much more likely to speed the discovery of effective vaccines, and at much lower costs.

Therefore, from many different angles, the CGD model would actively discourage the development of highly effective and safe vaccines.

II.5. Liability Risk

Any program involving billions of dollars, large organizations, global institutions, and medical technologies must apportion and deal clearly and effectively with issues of liability risk from the start. The report calls for the sponsor(s) to fully indemnify the distribution committee running the program – even though the sponsor(s) lose all control over their funding to a committee with wide discretion – and then for the eventual designated supplier to “defend and indemnify” the sponsor and members of the committee. The former is impossible to imagine; what firm would want the PR disaster of suing the World Bank, the Gates Foundation, or a PPP? The proposal with respect to the supplier is not an impossible requirement to fulfill, although it does mean that only the world’s largest companies will be able to participate in the program.

Failure to contractually cover liability risk has doomed previous such proposals and indeed is an important component of private sector worries about investing in early-stage vaccines, such as those for HIV, malaria, and tuberculosis. The report even recognizes this in the case of Project Bioshield, a project that no longer treats liability risk

in the fashion that this report now proposes should be applied to developers of HIV, malaria, and tuberculosis vaccines.

Sponsors of any proposed purchase program also have a responsibility to undertake 'due diligence' to check if the proposed mechanisms are economically valid for the types of candidate vaccines they target and if they are in fact likely to have the claimed effects. If the AMC mechanism collapses through no fault of those firms taking part in it but because of the negligence of those setting it up, the sponsors would have some obligation for the losses.

It is hard to imagine – supposedly in order to achieve 'credibility' of the program – that sponsors, especially foundations and their legal advisors, would permanently relinquish key decisions to a distribution committee with wide discretion, fail to work out the exact legal status of these new institutions alongside already existing institutions, and yet leave the issue of liability risk entirely unresolved. The contract term sheets leave all these issues blank.

II.6. Intellectual Property (IP)

The development of vaccines involves a continual process of IP accumulation and assembly. Developers have to identify the need for patented purification techniques or for patented adjuvants or for patented antigen synthesis methods. Any developers that have signed an AMC contract would be forced to 'share' the expected value of the \$3 billion payoff and thus would be constantly remortgaging a future income, thereby reducing the value of the payoff. There is no clear methodology in the report for preventing this from reducing the 'additionality' of the AMC, severely diminishing its power.

Furthermore, the contracts call for a supplier to turn over its IP to the sponsor if the supplier "prefers" to abandon the 'eligible' market in the long-term. However, this does

not take into account that the supplier may not have the right to sublicense all the IP it has obtained by license or that the production of a vaccine is as much, or more, a matter of know-how than of access to patented technologies. This is, therefore, not a credible way to discipline suppliers. It risks severe supply shortages and damaging delays in access to vaccines; and the very knowledge that the threat might actually be used would undermine incentives to invest in vaccine delivery systems in the first place. The strategy also creates a huge range of conflicts and of further supply problems given that the supplier nevertheless retains IP rights to 'non-eligible' markets. Consideration of "other penalties" is suggested in the contract term sheets attached to the report; however, other than unspecified "liquidated damages provisions", the details are left blank. Such "damages provisions" themselves inflict disincentives on firms to carry out R&D – even more so if the provisions are as vague as they are here.

IP and know-how barriers have been principal causes of delays in achieving flexible, cost-effective manufacturing and in getting vaccines to poor countries quickly in the past. Yet this practical issue is not addressed in the report either. All the emphasis is put on getting the \$3bn to the supplier of the first 200m 'eligible' treatments. Long-term price, and indeed secure long-term supply of these vaccines, is thus left totally unresolved in this report.

II.7. A Proposal That puts Most Risk onto Biotechs

The AMC described in the report also puts risk disproportionately onto the shoulders of biotechnology firms. The report states that biotechs engaging in research on early-stage vaccines expressed much less interest in AMC programs compared to large pharmaceutical companies with vaccines coming to market soon. Biotechs even asked for major modifications to be made to the contracts. These were not made, partly because it would have proved too difficult to do so, but also perhaps because it would have exposed the manifest weaknesses of the contracts. Yet, confusingly, the accompanying "Frequently Asked Questions" document claims that biotechs had been

“particularly enthusiastic about this idea”. The CGD report goes on to assert, without any evidence, that the program would initially motivate biotech companies while larger pharmaceutical firms – most of whom have abandoned the vaccine market, and are not likely to return for just one early-stage vaccine – would only get involved after “further advances in the science...perhaps led by biotech firms”. This is all very incoherent, and ultimately unconvincing.

The claim is that the expected decisions of the distribution committee will work all the way back to very early rounds of biotech investment. But this is where the difference between a genuine market and a committee-driven program bites. ‘Mechanism risk’ is extremely high for early investors into an AMC. The further away from the ultimate committee decision, the greater the chances that the program will not work as intended – or that it may even collapse. There is a large investment ‘option price’ to be priced in by venture capitalists when investing early, a price that is especially high if a program is highly uncertain. If the program collapses – indeed, biotech reactions to just such a possibility may make this largely self-fulfilling – it is biotechs and their investors, and not large pharmaceutical firms, who will pay the heaviest price. Furthermore, given the huge degree of discretion at much later stages of the program, the risk of ‘dynamic inconsistency’ – of decision makers taking advantage of firms’ already sunk investments to drive an even better ex post deal – is especially high for early investors. For these reasons – and also because of the greater difficulties in internalizing the value of early investments compared to later investments for such highly complex vaccines – early developers will have a very high required rate of return. At a fifteen to twenty-plus year horizon, with highly uncertain science, a \$3bn AMC for HIV starts to have extremely weak pulling power, if any at all.

The report presumes that biotechs would be prepared to take on board much more risk than any evidence suggests that they would be prepared to bear. Their rapid (and needed) reaction in order for the program to work is based more on hope than on any

solid evidence. To reassure early investors that the program would not be wound up early, it might be thought that the program could be made 100% permanently fixed. However, it is not clear which would be worse – having a reversible program that is not motivating biotechs because of the possibility of reversal, or being stuck with a non-reversible program the terms of which are set badly such that biotechs are not motivated by it.

II.8. Predicting the Future

For early-stage vaccines, the program seeks to put into place today an arrangement that will guide investments that will not mature for many years. In the case of HIV, such an arrangement would have to take into account all of the possible variations in the epidemiology and treatment of the disease, as well as the question of whether the search is for a therapeutic vaccine or a prophylactic vaccine. The delivery of a therapeutic vaccine would be fundamentally different than for a prophylactic vaccine. For example, a therapeutic vaccine would be delivered to a population of infected individuals among mainly adults, whereas a prophylactic vaccine might be administered to all individuals at an early stage of life. The two markets would be very different.

The report also repeatedly asserts the centrality of long-term political commitment to make the program work, yet it is hard to imagine investors and senior executives in pharmaceutical firms making such political predictions and trusting multiple overlapping political administrations as far as the mid 2020's when launching major and expensive privately-funded R&D programs.

II.9. The Role of Developing Country Recipients

The Working Group did not seek out the perspectives of countries that are supposed to benefit and implement the program. Neither do the contractual arrangements include them as signatories. These countries would make their 'commitments' to the program, via purchases, only after a vaccine is cleared by the distribution committee, and they

would pay only about 10% of the initial procurement price (currently set at \$15). Such an arrangement provides them, in essence, with a veto over the success of the program. Their small, marginal, contributions would be essential to make the whole program, involving billions of dollars, work, and therefore they could use their position to achieve additional benefits. In return, the supplier (or the supplier's country) would come to realize the value of 'subsidies' to developing countries – in whatever forms those 'subsidies' might take – targeted at winning the \$13.50 per-treatment subsidy on the first small tranche of treatments. The system of long-term multi-institution and multi-country monitoring and policing of such behavior does not bear thinking about, even if investors would need to be reassured in advance that such monitoring and policing would actually take place.

Meanwhile, 'non-eligible' countries, even if still very poor, pay much higher prices for much longer. Neither were the views of these countries especially sought.

II.10. The Problems of Developing Country Innovators

The report states that the program would be equally accessible to developed and developing country innovators. However, developing country innovators face a number of barriers that their developed country counterparts do not face to anywhere near the same extent – including lack of personnel, facilities, and the 'deep pockets' needed to see projects through extremely long gestation periods without any payment and, indeed, with risk of non-payment. Since the distribution of AMC funds comes at the end of a very long process, such programs would do little to help developing country innovators. Similarly, building regional capacity in both development and production is a major practical issue not taken up by the CGD report.

II.11. The Problems of Vaccine Delivery

Huge practical difficulties beset the delivery of vaccines to millions of people in developing countries. Field reports to the Gates Foundation and others detail problems

of organization, qualified personnel, political interests, cultural barriers, and knock-on costs. Tackling these practical difficulties is not taken up in the CGD report. Nor is the knowledge of such problems, and lessons from past delays, used in the report to help design more realistic, practical AMCs that would help recipient countries to actually deliver vaccines. Indeed, many of these grave practical difficulties are deliberately fed back on to vaccine developers through the payment mechanism proposed in the CGD report. The Working Group did not contain a single person with hands-on practical experience in delivering vaccines in developing countries.

II.12. Attention Deflected Away from Currently Existing Vaccines, and the Dangers of Encouraging Cuts in Funding for Vaccine Research

Increasingly, the attention of the CGD Working Group was shifted away from late-stage vaccines (such as pneumococcal and rotavirus) and currently existing vaccines (such as hepatitis B, influenza, cholera, etc.) toward much more speculative, unknowable, and experimental applications of AMCs to HIV, malaria, and tuberculosis. Indeed, these are the only vaccines currently making the headlines being generated by the Center for Global Development. This is in spite of the fact that many of those running the project doubted, even less than a year ago, that the approach could ever be used for such vaccines.

The report, and surrounding press releases, argues that we now have a powerful new instrument for incentivizing R&D into vaccines for HIV, malaria, and tuberculosis, even though we have never used such programs for anything – not even for the most trivial of cases – before. The report makes no attempt at quantifying the response. Theoretical and empirical evidence suggests that such programs will be very weak at incentivizing fresh private R&D into such vaccines. Meanwhile, these exaggerated claims run the very real risk of feeding the current heavy budgetary pressures to cut funding for vaccine research, without worrying about the long-term damage to the discovery of such vaccines.

II.13. The Failures of Command and Control

Despite its rhetoric of “making markets”, the suggested CGD program has all the hallmarks of failed command and control mechanisms. Rather than being ‘market-driven’, the program is ‘committee-driven’, and should not be graced with language that suggests otherwise. The CGD report discusses the great difficulty of monitoring the performance of the program – particularly with respect to early development – in the absence of periodic reporting by developers over very long stretches of time. However, this heavy dependence on monitoring, evaluating, and approving activities creates clear incentives to distort evidence and to corrupt the decision-making process, and it seems somewhat ironic given that one of the initial arguments made in support of AMCs over alternatives was that AMCs would avoid many of these interventions.

The report proposes reliance on a potentially very small committee making critical decisions at a few key points in time, with the opportunity for large mistakes. Indeed, it is suggested that important decisions about specifications and eligibility of vaccines be taken out of the hands of the sponsors themselves and put into the hands of as few as two or three individuals. An alternative approach that spreads power and decision-making through time and puts decisions into more hands in a more democratic process would allow for more checks and balances, and for greater chances for mistakes to be discovered and averaged out. Giving to a few members of an already small committee the power to make or break an expensive research strategy is a big risk to many firms – especially if such firms are unable to influence the committee.

Such top-down, committee-driven, approaches are incapable of the subtle, complex, adaptive adjustments required for developing vaccines for HIV, malaria, and tuberculosis. Past experience teaches us that such highly-centralized, and heavily-discretionary, systems do not incentivize private efforts, and would work against private competition to produce a diverse range of vaccines, which improve over time.

The report also concedes that “it would be extremely costly” to create a distribution committee that was fully capable of doing all that would be required of it, and hence allows the committee to rely on third parties, such as the WHO and its procedures. Yet, it is not clear why the WHO or others, including PPPs, would perform such acts and yet relinquish all decision-making power, with all of its consequences for liability, to such a committee. And it is not clear why there is need for yet more layers of committees and decision-makers with potential conflicts of responsibility and consequentially complicated IP, institutional, and legal tangles of unclear jurisdiction.

II.14. Concerns About the Manner in Which the Report was Compiled

Finally, we have serious concerns about the way in which the report was compiled. Advice – by specialist experts and firms alike – was routinely picked over so as to find those parts that bolstered the report, while more difficult and critical commentary was discarded. Increasingly, simplistic spin took over from rational and self-critical analysis. Crucial contract details that were signaled as “To Be Inserted” in early drafts of the report, receded into the “To Be Determined” in the final report. To an extraordinary and unrealistic degree, push efforts to foster research and development were kept separate from the deliberations of the Working Group, and the group was forced to focus just on what pull strategies could contribute. The myth of no trade-off between push and pull efforts was thus built into the project design from the start. The Working Group should also have been much more impartial, global, and inclusive, especially with respect to developers and sponsors in Asia, Latin America, and Africa.

III. What Next for AMCs?

As we read the report, we are increasingly concerned about what appears to be a program that cannot be implemented in the way it is portrayed. This leads us to the conclusion that there is the possibility of certain agreements being reached under the umbrella of the program which may not represent actual responses to the type of program being proposed in the report.

For example, we can visualize an early announcement of an agreement between a European country and a major vaccine manufacturer of an accord on an AMC for a malaria vaccine. It seems likely that a new malaria vaccine will not become available for at least a decade if not more. The company and other organizations have already made substantial commitments to the development of this vaccine, and detailed development plans are in place. One then wonders what value-added contribution the AMC would have made, which there must be for the company to be involved.

Nevertheless, given the proposed contractual arrangements, it is hard to visualize that such an early agreement would not at some point hit serious difficulties. It is not clear that other potential malaria vaccine developers would, or could, sign a contract in the window of opportunity given to them before being locked out. An early agreement with one company would be seen as bouncing (if not blackmailing) other developers into signing on to an ill thought-through program that entails unclear risks, and into agreeing to be monitored by – and to abide by the rules and discretionary decisions of – a distribution committee of a highly uncertain nature. If others refuse to sign, this increases the chances of the program locking in to just a few big companies (even just the one), or of collapsing. It would not help the promoters of AMCs to go into the difficult US budget process if they have a program that had transparently already been used to ‘benefit’ just one large EU company, and that had also set extremely low minimum requirements for that company.

A second possibility is of an announcement on rotavirus, and possibly HPV, vaccines. The rotavirus vaccine has recently entered the market, and the HPV vaccine is scheduled to enter next year. US companies have already made virtually all of the financial commitments necessary to bring these products to market. Thus an AMC would be a means for funding and empowering the Vaccine Fund to negotiate with the companies to obtain the best price - a mechanism that already exists and that the AMC would have done little specifically to advance. A European company has a rotavirus vaccine on the market and has indicated willingness to sell the vaccine to the public sector at \$10 per dose. It would be interesting to see what price the company would offer under a simple long-term purchase agreement for, say, 100 million doses per year.

A third possibility is the announcement of an agreement between a US company and the US government concerning a pneumococcal vaccine. Again this pneumococcal vaccine is already in the market in the United States and clinical trials in Africa have demonstrated that it may have value in developing countries even though it is not against the major strains of pneumococci that exist in developing countries. Again an AMC would represent funding of a procurement system for this vaccine and would have done little extra to incentivize research and development on the part of a US company or any other entity.

Following one or more of these announcements, the promoters of AMCs could claim these as proof of their value. This could provide an appearance of success, while the stated purposes of AMCs, i.e. to incentivize R&D for early-stage and late-stage vaccines, would largely not have been achieved via this route, and the mechanisms in the CGD report and its contract term sheets would not have been used. Indeed, the results would more likely have been driven by the new International Financing Facility for immunizations.

On a more positive note, it could just be that the high profile of the AMC idea and the willingness to tolerate such poor-quality and highly uncritical analysis, has been because of its usefulness as a device to help raise the visibility and legitimacy of companies, of PPPs, and of all those involved in vaccine issues in general. In which fortuitous case, it may yet turn out to be a useful stepping-stone for heading off in a different direction.

IV. A Different Direction

If the goal is to save the greatest number of lives, and reduce unnecessary suffering, in the shortest possible time, the first priority is to greatly increase funding for the existing product procurement/donation mechanisms run by foundations, companies, non-governmental organizations, and international bodies for the procurement of currently existing vaccines – such as those for hepatitis B, rotavirus, influenza, cholera, HPV, Japanese encephalitis, typhoid (a new conjugated vaccine), meningitis C, and pneumococcal infections – and for investing in vaccine delivery systems. Besides doing the greatest good for the greatest number in the shortest time, this has many other advantages, including:

- 1) It sends the clearest possible signal to industry that sponsors are truly committed and that the market for vaccines is real. This is good for vaccine divisions of large pharmaceutical firms when they make their case for their share of overall R&D budgets, but it also helps to unlock the constraints of developing and emerging country and biotech firms;
- 2) It enables the terms of multi-year contracts to be based on solid information about R&D costs, manufacturing costs, technical characteristics, and delivery problems. For very recently launched vaccines, such as those for rotavirus and pneumococcal, competition is likely in 0-4 years but supply capacity is only now being decided, and there is a chance to influence those decisions now. The efficacy of the vaccines is known, the benefits are known, and the production technology (hence rough cost) is known. Rather than generating institutional conflict, such purchases can also be incorporated into public-private processes for the joint planning to accelerate vaccine introduction;

- 3) It helps to overcome some of the targeting problems of AMCs. By targeting only some of the players, the AMC approach reinforces many structurally-generated vaccine R&D problems, such as an overly-narrow research focus, a very low (and shrinking) global vaccine production capacity, and the same few large companies researching vaccines and drugs for the same conditions. A large increase in funding for the procurement of currently existing vaccines, investment in vaccine delivery systems, more direct investment into biotechs, and greater levels of funding for successful PPPs – would be far better at unlocking the constraints of developing and emerging economy and biotech firms, releasing their innovation potential, while helping to tackle these other problems too;

- 4) It can be carried out in a market of current vaccine owners at much less than \$3 billion.

When it comes to discovering *new* vaccines, the scientific challenges and great uncertainties create irresolvable difficulties for AMCs to deal with, and they will have negligible impact on commercial decisions, and – by leading to cutbacks elsewhere – could even damage incentives. Evidence for the supposed strength of AMCs is based on unrealistic models and speculation.

Discovering vaccines for HIV, malaria, and tuberculosis are critical priorities, but they can and are best pursued through the excellent partnerships that the Bill and Melinda Gates Foundation and others have forged, and through directly funding both basic research and trials, and developing synergies among researchers working together. Many key components of a mechanism for the development and delivery of such vaccines are already in place, honed over many years for the task, and they are a known quantity rather than something theoretically dubious and empirically unfounded. This will be faster, smarter, more effective, and cheaper than using AMCs to discover new vaccines. Sadly, previous promises from policymakers on funding for many of the

components of the current mechanism have been betrayed. It is now time to dramatically increase the low levels of resources going into some of the existing global/regional consortia/PPP's⁵ and emerging Vaccine Enterprises, and to make good on those previous promises, rather than to issue yet more way-off financial promises of an even more dubious and indeterminate nature.

Our primary concern is that the current heavy lobbying for AMCs risks the creation of elaborate new institutional and regulatory structures, to implement an unproven, experimental, mechanism based on contracts that have not even been modified to be remotely appropriate for the early-stage vaccines being targeted, that may absorb a huge amount of policy energy, divert attention from those things that really could be making an impact on saving lives, and distort known effective mechanisms for supporting global efforts to develop, introduce, and use new and improved vaccines: support of good research and development; encouragement of competition among developers; the implementation of global procurement programs; and the establishment of effective delivery systems in developing countries.

The CGD report states that “if thirty years pass and no substantial progress has been made on the product of interest, a vaccine commitment may not be the most useful approach, and the policy would be worth reevaluating.” This is a truly terrible way to evaluate a policy instrument, never mind one involving so much human suffering. Life-and-death policy instruments should be critically evaluated now – not later when they prove to have been a mistake. We call for much more careful reflection before moving forward with AMCs for HIV, malaria, and tuberculosis.

⁵ Just for current activities, PPPs are estimated to need an *additional* \$1–2 billion over the next two to three years. Sander, A. and Widdus, R. “The emerging landscape of public-private partnerships for product development”, IPPH, 2004.

Appendix: About the Authors

Andrew W.K. Farlow, is an economist in the Department of Economics, University of Oxford, and Director of Economics, Oriel College, University of Oxford. He has provided extensive feedback to the Center for Global Development and others warning that the AMC approach is very problematic in the cases of HIV, malaria, and tuberculosis. He has written a number of recent papers on the economics of vaccines and of the role of purchase commitments.

Donald W. Light is Professor of Comparative Health Care Systems at the University of Medicine and Dentistry of New Jersey, a Senior Fellow at the Leonard Davis Institute Of Health Economics at the University of Pennsylvania, where he is also a Senior Fellow at the Center for Bioethics. He was a member of the Center for Global Development Working Group for “Making Markets for Vaccines”, and worked hard to improve the final version of the report but felt it was still too flawed to endorse.

Richard T. Mahoney is Research Professor at the BioDesign Institute of Arizona State University, acting CEO of the Centre for the Management of Intellectual Property in Health Research and Development, Oxford, England, and a consultant to the Rockefeller Foundation. He was heavily involved in setting up the Hepatitis B vaccine programs of the 1980s, and his papers on vaccine introduction into developing countries have considered in detail many of the issues discussed here.

Roy Widdus is Former Project Manager of the Initiative on Public-Private Partnerships for Health (IPPPH) at the Global Forum for Health Research, Geneva, Switzerland. He worked on the Children's Vaccine Initiative, as Executive Director of the U.S. National Commission on AIDS, on the Global Programme on AIDS, and the Tuberculosis Programme of the World Health Organization Director of the Division of International Health, and at the Institute of Medicine of the U.S. National Academy of Sciences, where he managed a number of major studies on vaccine development priorities, national vaccine policy, and HIV/AIDS. He was involved at the early stages in the creation of the International AIDS Vaccine Initiative, the Aeras Global TB Vaccine Foundation, and the Malaria Vaccine Initiative.