2.1.4. Advance Market Commitments: a new mechanism to help development?

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Introduction

Many low-income countries, especially in Sub-Saharan Africa, have considerable difficulties in investing the amount of money required to cover essential needs in health. On the other hand, rich countries do not seem to have any real intention of providing the missing funds. Some of the chapters in this report deal with these questions, analysing the various mechanisms that overseas development assistance (ODA) policies have experimented in the attempt at bridging the gap. In particular, the provision of essential medicines (drugs, vaccines and diagnostic tools) demands a clear strategy to respond to the lack of sufficient investments in medical research aimed at the needs of poor countries. The other question to be tackled is the long time lapse between availability of the same essential medicine to patients in rich countries and those in poor ones. Moreover, it is necessary to secure predictable and long-term funding aimed to health systems strengthening according to public health needs, so that once the drugs, vaccines and diagnostic tools do become available, they can reach patients and be used by individuals and populations in most urgent need. This short chapter intends to analyse one of the most recent mechanisms developed by the international community to overcome the issue of incentivizing innovation and access to new vaccines of prime importance for developing countries: the advance market commitments (AMC).

Advance Market Commitments: what they are and how they came into being

One of the key findings of the 2006 report by the WHO Commission on Intellectual Property Rights, Innovation and Public Health (CIPIH)[1] is that the mere market function is unable to combine medical innovation and access to essential medicines for people living in poor countries. In other words, the market's hand is not invisible, rather it is completely absent, when it comes to responding to the needs of the most vulnerable. It is only too clear that the pharmaceutical and the bio-tech industry should be reluctant to invest in research and development (R&D) on health tools aimed at those countries whose markets, with their limited purchasing power, simply do not serve their profit logic. There are no appropriate incentives to this end. In addition, measures are required to address the need for a significant political commitment. What can be done, then, to cajole the private sector into this terrain if not artfully create the potential of an attractive market based on low-income countries' needs?

In the wake of suggestions made during the annual meetings of the G8 Finance Min-

isters[2,3], this idea found its way and took shape in January 2005, when the G8 Finance Ministers launched a consultation process aimed to jump-start one AMC pilot project. This is in practice, an anticipated commitment by governments – as proposed by Giulio Tremonti (Italy) and Gordon Brown (UK) – to purchase products (vaccines) in an attempt to stimulate the interest of the pharmaceutical industry. Italy worked at the feasibility study seeking to identify the technical aspects and the institutional organisation of the proposal, through a disease-focussed pilot project. This study was successfully presented in London in December 2005. Following to that, one *ad hoc* group, chaired by the Health Minister of Malawi, selected the range of pneumococcal diseases as the target for vaccine development in the pilot project. As a matter of fact, pneumococcal diseases are one of the main causes of infant mortality in Africa, with almost 2 million deaths per year. After many consultations and diplomatic steps – among them, a letter sent by Italy's Prime Minister Romano Prodi to over 50 governments in developing countries – the pilot project was launched in Rome in February 2007.

What is it all about? The five donor countries (Italy, Canada, UK, Norway and Russia) commit to a public contribution of US $ 1.5 billion in nominal value to re-launch the research effort on anti-pneumococcal vaccines, with exclusive focus on the serotypes affecting poor countries' populations. The basic idea is to extend market incentives to serve developing countries. This would promote expanded research on vaccines that are already at an advanced stage of clinical development, so as to respond to poor people's needs. The underlying concept is to anticipate the vaccine price negotiation accordingly, and subsidize poor countries' procurement of these vaccines, once they are produced.

Wyeth introduced its anti-pneumococcal vaccine for children, Prevnar, in 2006 and is currently experimenting a new generation of 13-valent paediatric vaccine. Merck has a adult vaccine, Pneumovax 23, and GlaxoSmithKline has a version of the vaccine, which covers a wider spectrum of pneumococcal diseases, at an advanced stage of development. These are the firms bound to benefit from the AMC initiative, including the plan to set up new production sites (in the case of GlaxoSmithKline). The Global Alliance for Vaccines and Immunisation (GAVI) – the entity coordinating the management of AMCs – talks of a market opportunity open to all potential producers. Yet, the thick and impenetrable forest of patent protections makes it objectively hard, if not impossible altogether for firms in developing countries, which do exist, to undertake the route leading to vaccine research and development.

The assumption here is that Big Pharma will take the bait and decide to go into the uncharted territory of producing vaccines for the poor![4] Indeed, from the companies' point of view, the conditions required for the disbursement of AMC public funds are rather uncertain. These depend on the virtual discovery of vaccines that are appropriate to meet poor countries' needs. At the same time, a sufficient demand must come from developing countries, which are themselves asked to contribute to a small part of the agreed purchase vaccine price. Much more oiled are the market dynamics in the US and Europe for the multinational companies, where they are already making incredible profits, with their unprecedented vaccines prices.

On 20th May 2008, donor countries met in Ottawa, Canada, to finalise the agreement on this first pilot project, but consultations with the pharmaceutical companies were

said not to be easy. Discussions in any case continue behind closed doors. In this way, the promoting governments can maintain a regime of extreme reserve on how to resolve the difficulties that are intrinsic in the architecture of this new funding mechanism.

Some open questions

The one million dollar question, at this point, seems inevitable: are we truly convinced that AMCs are going to provide an adequate solution to the problem? Signs of perplexities are ill received, yet scepticism is widespread, even among officials of those very governments that have joined the project. Some basic questions emerge, starting from the controversial fact that this injection of public funds into pharmaceutical companies to stimulate research, and to beneficiary countries to purchase the vaccines for a binding ten year period is itemised as ODA[5]. This situation has created a number of difficulties in the dialogue between interested ministries within the Italian government, just to mention one example. Given the rich countries' current deadlock in terms of their ODA, and their failure to meet the objective of 0.7% of their GDP to development cooperation, this is at best a controversial choice, and one which immediately raises questions about the cost/benefit analysis of the intervention, and about potential alternative interventions aimed to reduce infant mortality in low-income countries, that would be comparatively more immediate, efficacious and sustainable.

- Whichever vaccine is selected as the agreed target for an AMC, the range in which its cost may fall is bounded between two conflicting extremes: on the one hand, by the "cost-effectiveness" and the accessibility of the vaccine; on the other, by the need to incentivize and motivate R&D. The crux of the matter is finding a balance between financial investment and research outputs, in the face of health needs. The nearer the bargaining mechanism can push the cost of the vaccines down to the bottom of the range, the more budget will be available to expand the immunization programmes. There is a risk in delegating the entire operation to private industry. If the value of an AMC is set too high, it motivates wasteful R&D, which will reduce resources available for other vaccines and the health system. If the AMC is set too low, it motivates too little R&D, which could grind research to a halt, and finally no vaccine would be developed. Since it is giants like Merck, GlaxoSmithKline and Wyeth to lead the dance, "how big must this carrot be?" is the question raised by *Médecins Sans Frontières*, which has added its voice to the chorus of critics[6] Research work suggests that poverty-related disease R&D is better conducted through collaborative and more cost-effective public and private ventures, rather than by industry alone approaches*,[7].
- The price of the vaccine in the AMC scheme is negotiated with the pharmaceutical companies, that do perceive developing country markets as both low value and risky. Here, too, the risk is that prices may be more set to overcome industry's reluctance than to realistically respond, with sustainable and adapted thresholds, to the pur-

* M. Moran, *The New Landscape of Neglected Disease Drug Development,* Pharmacuetical R&D Policy Project, London School of Economics, The Wellcome Trust, September 2005.

chasing capacity of individual recipient countries, which bind themselves to a ten-year financial commitment once the vaccine has been produced. The process of determining prices has so far been arduous and somewhat obscure. With time, the price has decreased and has now been set at US $ 5-7 per dose in the first years, down to a tail price of US $ 2 after a set period. In any case, it would be the most expensive vaccine for poor countries ever. You only have to compare this price with that for the meningitis A vaccine, produced by the *Serum Institute of India*, and currently used in clinical trials in Africa as part of the *International Meningitis Vaccine Project*. This vaccine will be marketed at US $ 0.40 per dose. Unlike the anti-pneumococcal vaccination, the meningitis A vaccine does not have any market in rich countries. Leaving the specificity of the two vaccines aside, it may be worth investigating the reasons behind the two different prices attentively[8,†]. At an important meeting in 2007, held at the WHO, experts estimated that the cost of producing a single conjugated vaccine on a large scale amounted to about US$ 0.26, and that "with a highly efficient process, any additional costs incurred by adding serotypes would be minimal"[9].

- Even admitting that selling vaccines to poor countries through the mechanisms provided by AMCs could effectively stimulate research initiatives by the pharmaceutical companies, this effort does not provide any margin of flexibility when it comes to patent protection. In other words, exclusive IP rights will be granted for R&D of vaccines carried out using exclusively public funding. In recent years, R&D collaborations with the private sector on diseases that predominantly affect low income countries pursued by public-private partnerships have started to adopt a more open attitude towards IP, providing such rights for not-for-profit use, or non exclusive agreements, i.e. the exclusion of any patent protection for the new drug. This is a fundamental condition if free access to treatment is to be ensured[‡], as well as the wide promotion of productions to respond with more commercial partners to the health needs. The industry alone, market incentive mechanism provided by AMCs entails a return to more secretive, IP focussed and non collaborative approaches that feature purely commercial R&D[§]. From this point of view, AMCs are running counter to the international debate on medical innovation and access, skewed towards more innovative policies such as open licensing, collective management of intellectual property or patents donations, to favour widespread essential medical innovation aimed at producing public goods**.

If these are the main concerns, they are not the only ones. Other considerations could be made about the overall opacity of the AMC operation, primarily discussed and conceived in the not-exactly-inclusive rooms of the G8. Only at a much later stage

† Jonathan Miller's investigation of the AMC plan for anti-pneumococcal vaccine was shown on Channel 4 News (UK) on the 19 November 2007

‡ See for example the partnership *Drugs for Neglected Diseases Initiative* with Sanofi Aventis which was set up in 2004, to produce ASAQ antimalaria treatment (artesunato/amodiachina) for the African continent, and was launched on the 1st of March 2007 www.dndi.org

§ Ibidem.

** See the WHO negotiation which has produced the Global Strategy on Public Health, Innovation and Intellectual Property Rights, http://www.who.int/gb/ebwha/pdf_files/A61/A61_R21-en.pdf

has a dialogue with civil society organisations started, not without confusion, the result being that, still today, many of the interested NGOs keep demanding more transparency in the process[10].

Italy's role

Italy has thrown herself wholeheartedly into the initiative and is, though hard to believe, the largest donor of all the countries involved in the pilot AMC. Italy's contribution amounts to US $ 635 million, Great Britain US $ 485 million, US $ 200 million from Canada, US $ 80 from Russia and US $ 50 from Norway. The 2008 budget law formally authorized the Italian participation in the AMC, and from 2008 onwards funds will be made available accordingly over the next 7 to 10 years.

Given Italy's leading role, perhaps time has come to urge all Italian organisations involved in global health issues to keep a closer eye on the AMC process. And to propose alternative paths. The anti-pneumococcal vaccine is a pilot project. It would be appropriate to carefully monitor the solidity of the framework set up so far, before venturing off into new expensive AMC projects for other vaccines. Lastly, it will be equally appropriate to honestly recognise that the AMCs represent a mere governments' adaptation to the current R&D regime (in deep, and documented, crisis).

The objective of developing effective policies for needs-driven medical research and better access in poor countries should move beyond the current market incentives. A public dialogue on these issues, totally absent in Italy today, becomes at this point extremely urgent.

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[10] T. Von Schoen-Angerer, *op. cit.*