

Amsterdam, 15 April 2009

Response to the Expert Working Group on Alternative Financing

This response has been prepared by Health Action International (HAI). HAI is a non-profit, growing, global network of consumers, public interest NGOs, health care providers, academics, media and individuals with over 25 years experience in representing the voice of civil society, and poor and marginalised people in medicines' policy debates.

Our authority rests on our integrity and independence from commercial and political party interests, our research excellence and evidence-based advocacy.

- HAI promotes increased access to essential medicines, the essential medicines concept and the rational use of medicines.
- HAI advocates for greater transparency in all aspects of decision making around pharmaceuticals, for example, by reducing industry secrecy and control over important clinical data.
- HAI promotes the rational use of medicines; that all medicines marketed should meet real medical needs; have therapeutic advantages; be acceptably safe and offer value for money.
- HAI works for better controls on drug promotion and the provision of unbiased and independent information for prescribers and consumers.

Summary

The Expert Working Group (EWG) is faced with a great opportunity and a great responsibility, and therefore it should be ambitious. There are many relevant proposals on alternative financing that should be duly considered and analysed. It is paramount to explore and discuss the Biomedical Treaty on Research and Development (R&D). Within this framework of global norm setting, we wish to highlight the importance of not limiting the scope of diseases being tackled and of allowing recipient countries to prioritise their R&D needs themselves. Furthermore, it also represents a timely opportunity to reassess the set up of phase III clinical trials, particularly with regard to medical ethics. Moreover, it is essential to guarantee, overall, very high standards of transparency. An essential component or complementary part to such a treaty would be the establishment of innovative models stimulating R&D for neglected diseases. One of these ideas, the Advanced Market Commitment concept, requires reassessment. A redesigned AMC model is needed; one with the potential to strongly encourage R&D and thus, to deliver its promises.

Impaired Access to Medicines

Target Four of Millennium Development Goal (MDG) 8 specifically acknowledges the need to improve the availability of affordable medicines for the world's poor. It also calls for international cooperation, including pharmaceutical companies, to provide access to affordable drugs in developing countries.

Access to essential medicines in developing countries remains inadequate and is a challenge that must be faced urgently. In countries for which data is available, only one third of essential medicines are available in the public sector, and two thirds in the private sector. Affordability also remains a significant challenge. Recent data indicate that the price paid for the lowest-priced generic in the public and private sector is 2.5 to 6.5 times the international reference prices, respectively.

Rationale for a Biomedical R&D Treaty

HAI considers it essential that steps are taken towards the establishment of a Biomedical Research and Development Treaty. The importance of health in the United Nations development agenda is reflected in the fact that four out of the eight MDGs are, directly or indirectly, related to health (MDGs 4, 5, 6 and 8). While substantial progress is being made towards achieving the MDGs, serious shortfalls still exist in human development and health. These are most evident in sub-Saharan Africa and South Asia. Despite the scaling up of both external and national aid, the performance in health-related MDGs has not improved as far as developing countries are concerned. With this in mind, it is important that any design for a financing mechanism for R&D in the developing world does not suffer from the same short-comings in implementation and performance. The current financial crisis will cause additional strains for budgets in developed and developing countries. In the past, economic downturns have led to reductions in overseas development aid from developed country governments and a rollback of public spending by developing county governments. There will be a temptation to shift the burden of R&D financing to private sources and to cut back support programmes for poorer countries. Hence, it is the responsibility of WHO to engage in the management of the funds jointly with national governments to ensure the sustainable financing of innovation and access. The EWG has received a clear mandate to explore the establishment of a Biomedical R&D Treaty. HAI Global strongly recommends the members of the EWG to take up this important responsibility to catalyse and sustain this process.

Elements of the Biomedical R&D Treaty

The biomedical treaty will inevitably have to consider a number of problematic issues and specifics. However, the overarching function of the treaty should be its role as a 'global norm setting' instrument. Given that it has the capacity to impact on the health of billions, it is vital to adopt global principles and standards. The World Health Organization should take the lead in establishing a Biomedical R&D Treaty as they are best-placed to facilitate dialogue and stimulate international cooperation on these issues.

In this response, we will focus on four key elements: *Flexibility and Priority Setting, Global Financing of Clinical Trials, Transparency, and Medicines Procurement* before presenting a response specifically dealing with Advanced Market Commitments (AMC) concept.

Flexibility and Priority Setting

A narrow mandate that focuses on R&D financing for specific diseases may prevent the fund from supporting other conditions that could become prevalent at different times and in different countries. It will be difficult for countries to effectively coordinate such programs if vertical funding is established for each and every disease. Therefore, HAI recommends horizontal funding streams that will grant sufficient flexibility for countries to focus on diseases according to their own priorities and needs.

Global Financing of Clinical Trials

Medicines are evaluated as to their quality, safety and efficacy. In phase III trials, the safety and efficacy of the drug is compared to its “gold standard” in large patient groups, usually in randomised trials across several study centres. Due to their design, length, intricacy and cost, this type of trial tends to be funded mainly by private sources, i.e. pharmaceutical companies.

Bringing phase III trials of R&D into public hands would be one major innovation and improvement the Treaty could bring, as this would signify a move towards a more inclusive model. Donor nations and foundations could play a pivotal role, offering the financial help that developers need. Apart from the obvious advantages for small scale developers and research institutes who cannot cover the costs of phase III trials; this approach would bring other important benefits by stimulating independent research and adding therapeutic advantage as another criteria in medicines’ evaluation.

Phase III Trials & Medical Ethics

The evaluation of a medicine involves a multi-faceted decision that weighs the treatment benefits against the treatment harms. Successful phase III trials are decisive factors for drug regulatory agencies when evaluating medicines before authorising their entry into the market. That decision must be based on independent and relevant information devoid of commercial interest.

The treaty should avoid perpetuating suboptimal practices entrenched in the current model of financing, such as distorted study results, perverse incentives, undeclared conflicts of interest, promotion of off-label use (beyond approved indication), and disguised promotion by key-opinion leaders, among others.

Phase III trial results are fundamental to the rationale behind medicines’ approval decisions and originator companies are dependent on their outcomes. Consequently, these studies should be conducted by an independent actor, with no interest linked to a positive or negative study outcome and not by those whose profits depend on the results.

Therapeutic Advantage as Key Criteria

In addition, the R&D Biomedical Treaty should ensure that real therapeutic advantage is added to the current three evaluation criteria of efficacy, safety and quality when granting marketing authorisation. The therapeutic advance would be appraised in comparison with existing treatments and demonstrated by relevant clinical data collected from comparative clinical trials.

Transparency

Overall transparency in R&D is essential and a set of criteria or norms ensuring transparency should be instituted by the Treaty at a global level.

Currently, a major barrier to transparency is commercial confidentiality of drug safety, effectiveness, and pricing data. Publicly available data on actual production costs would prevent citizens from being overburdened or denied potentially life-saving treatments by unreasonably high prices. ‘Commercial confidentiality’ is not a legitimate reason to withhold data about medicines.

Greater transparency in medicines’ pricing is necessary, with information available on the prices of medicines throughout the world. Unlike other products, medicine prices have fundamental implications for public health, since they determine access to necessary medical care.

Decisions on pricing and reimbursement should remain with individual States. However, the criteria through which a medicine's effectiveness is appraised should be harmonised as not all States require pharmaco-economic evaluations.

The role of the regulatory agencies is to act as firm gatekeepers of public health. This role should include a duty to publicly disclose all data related to the efficacy and safety of medicines, which is of clear public interest. It should be a priority to ensure that all information on drug safety and effectiveness submitted to regulatory authorities is publicly available, including all pre-market laboratory and clinical data and post-marketing studies.

Health agencies should be entirely transparent about how and when they are funded by, or in partnership, with pharmaceutical companies. The same holds for 'scientific advisors' whose engagement with industry should be carefully monitored to prevent agencies from becoming a service provider devoted to the pharmaceutical industry and diverted from their evaluative mission and the safeguarding of public health.

Medicines Procurement

Governments purchasing medicines to be given or sold to their citizens through cost-recovery schemes possess a range of policy options to increase access and reduce prices, such as establishing a national essential medicines list and tendering. When procuring medicines, price transparency must be a priority. Pooled procurement with other national buyers and the use of international price comparisons to fix prices of originator products may also help governments to negotiate better deals. For single source products, governments can make a case for differential pricing and use of TRIPS flexibilities to stimulate generic competition. Governments are also in a strong position to exempt themselves from tariffs and taxes. Throughout the procurement process, assurance of transparent and quality price monitoring and public information is necessary.

REDESIGNING THE ADVANCED MARKET COMMITMENT (AMC) MODEL

While affordable prices are a key determinant in improving Access to Medicines, adequate, sustainable and equitable financing of medicines is also required. The original AMC concept espoused the use of donor commitments to provide incentives to pursue R&D to produce vaccines for developing countries. However, the implementation of the AMC pilot has been reduced to a simple purchase agreement. The AMC model must incorporate other aspects of distribution, supply and financing as part of an integrated medicines' policy.

Ensuring the sustainability of such financing mechanisms is crucial: if initial AMC prices are set too high, countries will be unable to adequately finance new purchases and hence, fail to meet national needs. Prices should be adapted to the purchasing power of governments and households in lower-income countries so that they receive the best possible prices for life-saving vaccines, rather than being based on the highest price that consumers are willing and able to pay in affluent markets. There also needs to be greater transparency in pricing decisions by manufacturers to contribute towards the disclosure of all price components and to enable purchasers to explore all options that will ensure sustained and improved access to affordable medicines in their country.

Serious design problems¹

Having identified some problems with the current AMC pilot project, we will outline possibilities for improvements to the AMC that could make its contribution to innovation and access more effective. These adjustments would also support the development of local R&D and production in the South and overall generic competition. However, these aspects were not taken up in the current pilot project, thereby excluding many other actors aside from large originator companies.

Despite wide endorsement and enthusiasm for the current AMC model, there are reasons for concern about the way the project is designed. Too many uncertainties and contingencies in the AMC design may deter some researchers from initiating projects to discover new vaccines.

Because the current AMC concept provides no funding until a new vaccine is fully developed and considered necessary by developing countries, it discourages all but a few large companies to participate because the investment costs are extremely high. Secondly, its competitive design could undermine cooperative efforts and grant-based 'push' funding. Thirdly, by favouring large companies over biotech companies and teams of researchers at universities or non-profits institutes that require more interim funding, the AMC could actually decelerate R&D. Finally, even the sharply discounted post-buyout prices would still not be affordable for developing country markets, and past experience with AIDS drugs shows that manufacturing in developing countries would supply medicines at much lower prices. The Treaty should pursue alternative approaches that could address these and other design problems such as:

- The AMC is not likely to stimulate basic research, since the output/outcome of basic research is often difficult to specify in advance
- There are no incentives for collaboration/knowledge sharing
- The AMC model leaves the IP protection intact in the face of major international debate on this at the WHO during the IGWG on the Global Strategy and Action Plan on Public Health, Innovation and Intellectual Property.

Design Improvements²

An earlier AMC model considered a variety of alternatives for how to structure advanced purchasing. A better design could complement push funding, encourage the synergies of cooperative research and mobilise research teams in all sectors. It could address the IP obstacles and include technology transfer. The following ideas should be considered in order for the AMC concept to structurally contribute to R&D and Access.

- **Milestone payments:** A matrix of prizes would motivate a wider range of research teams as they could be structured to provide much needed funding at each stage. These prizes would also support partnerships and collaborative projects.
- **Coordination with push funding:** Adjusted advanced market commitments could complement funded research to increase the discovery of diseases prevalent in developing countries.
- **Required licensing/sharing of IP technology:** More flexible approaches are needed that require sharing or licensing of intellectual property and know-how.

¹ Donald W. Light. Advanced Market Commitments, Current Realities and Alternate Approaches; 2009, Health Action International/Medico International.
<http://www.haiweb.org/31032009/27%20Mar%202009%20AMC%20Current%20Realities%20%20Alternate%20Approaches%20FINAL.pdf>

² Ibid.

Other improvements to the AMC could include:

- patent buyouts
- cooperative payback with push funders
- higher technical requirements for follow on vaccines
- bonuses for vaccines that are easier to administer or store
- helping developers to fund late stage trials

In the current model these ‘flexibilities’ have been put aside. Donors do not have to pay anything for years, which is not very favourable to smaller scale developers as they would find it impossible to fund a 10-15 year R&D process.

Issues of delivery

AMCs need to strengthen the public health systems on which sustained vaccination programs depend as well as pursue manufacturing at prices countries can afford. It cannot provide an equitable solution to increasing access to medicines unless it reflects a holistic approach; equal attention needs to be given to efficiency in the supply and distribution chain, as well as adequate pricing schemes. Building manufacturing capacity in developing countries would considerably reduce production costs, thereby ensuring sustainability of supply as well as establishing national infrastructures for sustained R&D.

Mechanisms should be found to provide medicines in public sector health facilities, where medicines are usually provided at low cost or free of charge. These facilities are especially important in the provision of health care to the poor. The transparency and efficiency of the distribution system for such medicines need to be as carefully analysed as the purchase agreement itself. The role of pharmaceutical companies, ranging from multinationals to generic manufacturers to national distributors, is critical in this effort. The pilot project, which constitutes simply a procurement commitment, risks failing to respond to the needs of people in developing countries as it is limited to purchasing a fixed volume of vaccines without any guarantees of effective and high-quality delivery to those who need them.

Innovation inducement prizes

A redesigned AMC model that takes into account all the above-mentioned elements, i.e. a ‘flexible’ or ‘systemic’ AMC model’ (as it has the potential to structurally adjust the system) actually shares many characteristics with the prize fund model. The latter is also designed to allow a move away from the monopoly system, which currently stifles innovation, by allowing interim prizes, requiring open licensing, and rewarding the knowledge sharing, and thus providing incentives for collaboration.