Time for the EU to lead on innovation

EU policy opportunities in biomedical innovation and the promotion of public knowledge goods.

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Acronyms/Abbreviations

ACTA	Anti-Counterfeiting Trade Agreement
ARV	Antiretroviral
CEWG	Consultative Expert Group on Research and Development Coordination and Financing
DG	Directorat-General
EFPIA	European Federation of Pharmaceutical Industries and Associations
EMA	European Medicines Agency
EPARs	European Public Assessment Reports
HAI	Health Action International
GDP	Gross domestic product
GSPoA	WHO Global Strategy and Plan of Action (GSPoA) on Public Health, Innovation and Intellectual Property
IMI	Innovative Medicines Initiative
INN	International Non-proprietary Name
IP	Intellectual property
LDC	Least developing countries
NIH	National Institutes of Health
OSDD	Open Source Drug Discovery Initiative
PDP	Product Development Partnership
PEPFAR	United States President's Emergency Plan for AIDS Relief
R&D	Research and Development
TACD	Trans Atlantic Consumer Dialogue
TB	Tuberculosis
TRIPS	Trade-Related Aspects of Intellectual Property Rights
USTR	Office of the United States Trade Representative
WHA	World Health Assembly
WHO	World Health Organization
WIPO	World Intellectual Property Office
WTO	World Trade Organization

Executive Summary

The production of knowledge that leads to innovation has always been crucial to social, political and economic development, and nowhere is this more true than in the discovery, development and production of pharmaceuticals. However, the contemporary model of biomedical research tends to enclose knowledge by means of intellectual property rights (IPRs), awarded in exchange for the results of research and development. Indeed, this model has successfully incentivised numerous key medicines in several disease areas. However, in many others it has failed, and it is becoming increasingly clear that the present model of incentives to innovation is not compatible with any vision of the economic sustainability of global healthcare and it woefully neglects the health needs of the world's poor, who enjoy very limited access to essential medicines.

One of the most critical limitations of an innovation model based on patent monopolies is the reliance on high prices of the resulting technologies. In short, it allows the innovator to recoup R&D costs through high prices while protected against competitors. In addition, the reported paucity of innovation in pharmaceutical companies' development pipelines has resulted in fewer and fewer innovative drugs of any true therapeutic value reaching the market. Originator companies have gradually shifted their focus from health-needs innovation towards marketing, wide patenting, and litigation against competitors. At the same time, the current innovation model shrouds the results of clinical trials and other health research data in secrecy, leading to a potentially unethical situation in which patients are sometimes being exposed to the harmful secondary effects of medicines where the risks are known but not revealed due to commercial confidentiality.

The globalisation of stringent intellectual property (IP) standards and the accompanying high prices have contributed to limited access to essential medicines in the Global South. Crucially, in the context of this paper, market-driven innovation, extended patents and high prices, add to the financial burden of already over-stretched European public health systems, in the midst of a global economic and public debt crisis.

For all the above reasons, debates on alternative and complementary approaches to innovation for health products have been taking place at the World Health Organization (WHO). The European Union (EU) has also committed itself to exploring alternative models, through its development and health policy objectives.

The WHO Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property (GSPoA) of May 2008, and the EU Council Conclusions on Global Health in May 2010 both called for needs-driven innovation and for further exploration of innovation models

that de-link the cost of research and development (R&D) from the price of medicines to encourage both needs-driven research and more affordable access to essential medical technologies. The ‘de-linkage’ of R&D costs from the price of medicines addresses three weaknesses of the current model of medical innovation: unaffordability, unavailability and unsuitability. Many of the new proposals in this paper have recently been recommended by a special WHO Consultative Expert Working Group on Coordination & Financing of Biomedical R&D (CEWG) that will deliver these recommendations to the World Health Assembly (WHA) in May 2012 (WHO, 2012).

In respect of publicly funded medical R&D, one of the core questions is whether knowledge generated by EU financed medical research (in other words, supported by European taxpayers) should continue to be predominantly guided by the current business models of large private actors or whether EU health research policy should contain clear social conditionality. In other words: Should the billions of Euros’ worth of EU funding continue to be awarded without any strings attached such as commitments to social responsibility or openness? Should market-driven innovation be promoted by the EU to the detriment of greater access to effective and affordable health treatment?

The *Horizon 2020 EU Research and Innovation Framework* provides the EU with an opportunity to make socially responsible choices that lead to new sustainable models of innovation which contribute to the public good. The EU needs to be an investor that makes sure that EU citizens reap the benefits of its investments through improved public health. It is time for the EU to be a leader in the exploration of biomedical innovation strategies that promote both affordable access to R&D outcomes, and the creation of public knowledge goods.

Various proposals and projects have been developed by governments, civil society, academics and industry which attempt to promote both access and innovation. Some are relevant to patients within the EU, while others focus entirely on developing countries and/or diseases that predominantly affect developing countries. A new paradigm of innovation in medical technologies which is gaining ground is based around the sharing of knowledge and data rather than shrouding it in IPR. While a number of these initiatives have already been implemented, others remain policy proposals. Among others, these include:

Socially Responsible Licensing (SRL) or Equitable Licensing - SRL encourages the non-exclusive or conditional licensing of patented technologies. The rationale is to generate the highest possible social benefit from publicly funded research. SRL could be the standard model for publicly funded biomedical research.

Open Source Research - Open Source mechanisms allow researchers to collaborate and

share knowledge with an open approach to IPRs. A number of Open Source initiatives have been launched in the medical field over the last decade. Open Source research can be an especially useful tool for neglected diseases, antibiotic research, or for certain conditions that are not properly addressed in a purely market-driven model.

Open Access - This refers to the provision of open access to published research. The high cost of medical journals and high data access fees prevent the sharing of knowledge and wide use of crucial health-related information.

Patent Pooling - The Medicines Patent Pool (MPP) supported by UNITAID aims to simplify and improve voluntary licensing negotiations with the aim of accelerating generic competition to lower the cost of patented medicines and stimulate the development of fixed dose combinations and paediatric forms for HIV/AIDS medications. In order for this to function, companies need to license their HIV/AIDS products to the MPP.

Product Development Partnerships (PDPs) - Aimed at developing new medicines and vaccines through a combination of resources from the public sector, philanthropy, and the pharmaceutical industry. PDPs usually encourage research and the development of products that target diseases which disproportionately affect developing countries.

Innovation inducement prizes - Prizes are an incentive system to induce R&D for new essential medicines, and can be implemented in a manner that ensures competition, affordability and widespread access. Innovation prizes can function to incentivize parts of the innovation process, to reward research outcomes that are not expected to result in commercially viable products. An ambitious version of innovation prizes would include open licensing of the end products.

Biomedical R&D Treaty or Convention - Proposals would secure and enhance sustainable financing mechanisms for R&D, in order to develop and deliver health products and medical devices which address the health needs of developing countries. The R&D Convention concept is predicated upon the principles of a de-linkage of product prices and R&D costs, open-knowledge innovation, competition among suppliers of products, access to and transfer of technology to developing countries. The WHO's CEWG recommends that formal intergovernmental negotiations on a binding R&D Convention should be initiated (WHO, 2012).

Recommendations

The EU could make a real difference in supporting global calls for an improved system of biomedical innovation. The EU aims to be a leader in technological innovation, yet the EU could and should be a leader in both innovation *and* access. For the EU to succeed, it needs

to look positively at new approaches to innovation and promising developments in the area of incentives and financing of R&D. The EU should consider innovative proposals, especially proposals that de-link the R&D costs from the price of final products, and become a key player in the development of new sustainable models of biomedical innovation and public knowledge goods. The need for a new approach to innovation is even more urgent where R&D is subsidized through public funds. EU policies should be guided by the notion that knowledge goods developed by means of public funds need to be affordable and accessible to all. The Common Framework Horizon 2020 policy is an ideal opportunity for the EU to take the lead in some of the issues described above.

HAI Europe and TACD call upon the EU:

In respect of research programmes and EU internal policy, to:

- Incorporate socially responsible principles as a condition for its biomedical research grants, most notably in Horizon 2020 grants.
- Establish clear rules in Horizon 2020 to mandate open access to EU financed health related research results.
- Promote meaningful technology transfer; Horizon 2020 should increase the level of incentives and support for researchers from developing countries as compared with FP7.
- Carry out feasibility studies and pilot programmes for various innovation inducement prizes, in particular concerning HIV/AIDs, cancer research, neglected diseases and antibiotics.
- Ensure access to clinical trial data of medicines registered with the EMA or national market authorities.

In respect of international policy, to:

- Constructively engage in negotiations for a Biomedical R&D Convention as to be recommended by the WHO Consultative Expert Working Group to the 65th World Health Assembly in May 2012.
- Encourage companies to join the Medicines Patent Pool granting voluntary licences to their patented technologies for better access in all developing countries.
- Rather than extend market exclusivities through IP protection in EU Free Trade Agreements, focus on stimulating therapeutically valuable and affordable innovation.

Introduction

Across the world, more than 2 billion people still lack access to essential medicines with the high cost of medicines being one of the most important factors that contributes to the lack of access. At the same time, pharmaceutical companies' production pipelines are drying up and few truly innovative medicines that add any real therapeutic value are reaching the market. The considerable financial costs and opportunity costs deriving from the current innovation model affect not only developing countries, but also governments and patients in the European Union (EU). Increasing pharmaceutical expenditure is one major reason why a number of EU Member States are seeing their public health budget burden increase. The unsustainability of this situation in the midst of a global economic crisis is forcing some governments to make decisions to the detriment of patients and consumers, limiting access to life-saving medical technologies.

In order to improve access to medicines and improve innovation, different strategies should be explored. One approach is to engage in strategies within the current system to provide access and improve innovation outcomes. Another approach should focus on investigating and utilizing alternatives to the current model of biomedical innovation. This longer term strategy is the approach that is explored here.

For more than two decades the international public health community has been calling for new models that promote needs-driven, rather than market-driven innovation. The problems regarding the lack of innovation by the transnational pharmaceutical industry (Big Pharma) have also been widely recognized by industry itself. Important underlying ideas to these discussions can be found in the conclusion of the 2006 World Health Organization (WHO) report of the Commission on IPRs, Innovation and Public Health (WHO, 2006, p.10). One conclusion is that in the absence of a profitable market, as is often the case in developing countries, the protection of IPRs in order to stimulate innovation becomes irrelevant.

More recently, the WHO Global Strategy and Plan of Action (GSPoA) on Public Health, Innovation and Intellectual Property of May 2008 (WHO, 2008), and the EU Council Conclusions on Global Health in May 2010 (Council of the European Union, 2010a) have both called for needs-driven innovation and the further exploration of innovation models that de-link the cost of research and development (R&D) from the price of medicines to ensure both innovation and access to essential medical technologies. Meanwhile, successful innovation initiatives, based on greater openness and collaboration, have sprung up around the world, indicating a new way forward.

Instead of playing a proactive role in the debate on new models that encourage innovation

and access to essential medical products, the EU has until now, contributed to the furtherance of strict intellectual property (IP) protection and enforcement measures across the globe, that actually limit access to medicines. However the *Horizon 2020 EU Research and Innovation Framework* provides the EU with an opportunity to make socially responsible choices that lead to new sustainable models of innovation which contribute to the public good[1].

In light of Horizon 2020 and the Innovation Union[2] agenda, this Policy Paper offers an overview of the most important contemporary discussions, initiatives and proposals on biomedical innovation, and provides recommendations to European institutions on how to become leaders in exploring new and complementary models that promote innovation. It proposes the establishment of a truly innovative research agenda while implementing commitments to Health Equity within the EU and to Global Health (Council of the European Union, 2010a). Not only are there clear moral reasons for policy-makers to explore the proposals being developed, but also economic imperatives. These aim not only to ensure broad access to medical technologies, but also ensure the sustainability of European health systems by rationalising public investment and improving innovation through efficient knowledge management. 'Business as usual' is no longer an option.

Although biomedical innovation is a crucial element for guaranteeing access to medicines, it is important to keep in mind that the lack of needs-driven biomedical research is only one factor among others in the access to medicines problem. Furthermore, it should be taken into account there will never be 'a pill for every ill' and medicines alone can rarely make a contribution to the health of the people if other crucial elements of health systems and social determinants of health are not in place.

[1] Public good is meant here as the collective ethical notion of decisions contributing to societal welfare. The economic notion of 'public goods' as in non-rivalry and non-excludable goods will be employed later in this paper.

[2] The Innovation Union, an EU flagship initiative, has recommended the exploration and implementation of innovative and efficient models for innovation.

The problematic current system of biomedical innovation

> '*Innovation can be a driving force for improving public welfare. Nowhere is this more stark than in the creation of drugs to treat fatal diseases. If you have the drug you live; without it you die. Whether you have the drug depends on two issues: has it been developed, and if so, do you have access to it? The conflict between these issues revolves around how to stimulate innovation and how to pay for it. Drugs are cheap to manufacture, but expensive to develop. Much of the underlying research comes out of academic institutions funded by government grants. Much of the development work is by pharmaceutical companies, which will not invest in research and development without incentives: in this case the patent system, which rewards a company that develops a successful drug with a 20-year marketing monopoly. Allowing monopolies leads to bad side effects and drugs are no exception.'*
>
> Tim Hubbard and James Love, *The Guardian*, 4 February 2004

How does it work?

The current pharmaceutical innovation model is based on patents and other forms of IP protection to innovator companies. The patent system however, has not always dominated the model for medicines R&D. Many European countries which built their industries without patent protection only started to grant pharmaceutical patents in the 20th century. Until recently, most of continental Europe only granted patents on a medicine's production *process*, not on the *product* as is now the case. Hence, once a medicine was discovered, other manufacturers could also produce it using different processes (Boldrin and Levine, 2008).

The current model has produced many key medicines for several disease areas (Munos 2009). Yet, this model also has fundamental limitations. The drying up of pharmaceutical companies' development pipelines has resulted in fewer innovative drugs of added therapeutic value reaching the markets. There are of course notable exceptions, but these are only a small percentage of all new products reaching the market (La Revue Prescrire, 2001). Companies have gradually shifted their business model from focusing on therapeutic innovation, towards marketing, wide patenting, litigation against competitors and the development of 'me too' medicines[3] of little therapeutic advantage (Boldrin and Levine 2008). Indeed, as analysed by magazine Prescrire, out of 97 new drugs or new indications of a known drug in 2010, only four provided a therapeutic advantage (Revue Prescrire 2011).

[3] 'Me too's' refers to medicines that are similar or just slightly better than an existing medicine and, with the help of adequate marketing, can take over a share of the market. 'Me too' medicines do present some form of competition in an otherwise monopolised market, thereby offering patients a greater variety of choice and slightly lower prices. In the absence of generic competition this therefore does improves welfare somewhat; this, however, comes with the opportunity cost of funds not being invested into innovative medical technology with actual substantial therapeutic benefit.

Meanwhile, pharmaceutical companies in the EU spend 23% of turnover on marketing, while only 17% is allocated to R&D (European Commission 2009). The 2009 Director-General (DG) Competition Pharmaceuticals Sector Enquiry report also concluded that the excessive focus on litigation is hampering generic competition and weakening innovation (European Commission 2009).This suggests the current incentives structure is problematic.

This intrinsic model of knowledge enclosure and secrecy is particularly problematic in the field of medical research, where non-disclosure of essential R&D health data means additional delays, bottlenecks and wasteful repetition in the development of life-saving drugs. The secrecy extends to the data resulting from clinical trials, which are not fully disclosed. This establishes an unethical situation where patients are exposed to the harmful secondary effects of drugs where the risks are known but not revealed due to commercial confidentiality. This is exacerbated by the fact that the European Medicines Agency (EMA) in its European Public Assessment Reports (EPARs) only summarises the data and grounds for granting market authorisation for a medicine. Thus it allows only limited public access to the data presented by companies in order to gain market approval.[4] Here as well, a move towards openness is required.

The promise that the current patent system and the granting of monopolies would encourage massive investment in health-driven R&D has failed to materialise. Medicines and other medical technologies are expensive and the IP system is often misused. Furthermore, the current predicament of both decreasing levels of effective innovation and the forthcoming expiration of many lucrative patents in Europe have led companies to seek higher revenues in developing countries and emerging markets through the implementation of higher standards of IP protection around the world.

Globalising IP Protection

In 1994,WTO Members set global standards on IP through the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) (WTO, 1994). Effectively this agreement globalised EU and US IP standards and reduced the possibility for middle and low income countries to either produce or import generic medicines from, for example, India which has a large generics industry and did not previously grant product patents. India has acted as the

[4] Why is it important that the EPAR be complete, accurate and transparent?

- Healthcare professionals: to know the size of effect of newly licensed medicines for prescribing reasons
- Researchers: to use data in the EPARs for meta-analysis and access data that may never be published in journals
- Consumers: to understand and monitor the drug approval process

More information regarding EPARs may be found at the following link: http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/landing/epar_search.jsp&murl=menus/medicines/medicines.jsp&mid=WC0b01ac058001d125

'pharmacy of the developing world', providing low cost medicines to the poor. Recognising the need for checks and balances in a system that was likely to impact adversely on developing countries, the TRIPS agreement does provide for *flexibilities* and public health safeguards (Correa, 2000). For instance, under TRIPS flexibilities countries are legally allowed to overcome patent barriers for public health purposes in order to either produce their own generic versions of patented medicines or import them. However, these flexibilities have proved very difficult to implement, as developing countries that attempted to use them often faced heavy political pressure from companies and foreign governments to do otherwise. In the Doha Declaration on the TRIPS Agreements and Public Health (WTO, 2001), WTO members re-affirmed that TRIPS 'can and should be interpreted and implemented in a manner supportive of WTO Members' right to protect public health and, in particular, to promote access to medicines for all' (WHO, 2001). When used, TRIPS flexibilities have significantly contributed to increased access to medicines in middle and low income countries.[5]

Nevertheless, the IP protection and enforcement agenda of the EU and the United States are leading to a further deterioration and undermining of TRIPS flexibilities, and are in fact creating additional IP barriers to generic competition. The most important elements of this agenda include Bilateral and Regional Trade Agreements containing strong IP chapters with TRIPS plus provisions; the WTO Accession conditions; the Anti-Counterfeiting Trade Agreement (ACTA); the Office of the United States Trade Representative (USTR) unilateral Special 301 Report; the EU enforcement watch-list; as well as national legislations and regulations (e.g. anti-counterfeiting legislations) (HAI Europe, Oxfam, 2009). Together, these measures restrict the limited policy space available for developing countries to prioritize public health over the protection of IPRs. [6] This same policy space will be further restricted when the transition period for TRIPS implementation ends. By 2016, the least developed countries (LDCs) are expected to have fully implemented the TRIPS agreement (unless further extensions in the transition period are granted). In 2005, India completed the implementation of TRIPS, making it very difficult to develop generic versions of new

[5] Compulsory licensing has been applied by Thailand and Brazil to increase access to second line ARVs as well as by several other countries ('t Hoen, 2008).

[6] Examples of TRIPS plus provisions that can undermine the flexibilities:

- Data Exclusivity
- Impose obligations concerning the subject matter or standards for granting of patents
- Limit patent opposition processes
- Patent - Registration Linkage
- Patent Term extensions
- Enforcement measures like border measures, criminalisation of infringements, high damages, limitations to exceptions, injunction measures.

medicines coming to the market, unless it applies rarely utilised TRIPS flexibilities. Once LDCs comply with TRIPS they will also face IP barriers when they seek to import the affordable generic versions of newer medicines.

European health budgets & health inequity

In Western Europe, most healthcare systems provide universal access to essential medicines. However, high prices for medicines represent an enormous cost to healthcare budgets and insurance companies, which are coming under increased pressure. In light of the global financial crisis, an ageing European population, and the cost of chronic diseases treatments like cancer and diabetes, governments no longer have sufficient financial means to fully support healthcare systems, especially if some of the new technologies offer little additional therapeutic benefit. In Central and Eastern Europe, where healthcare budgets are even more limited and do not provide for access to all essential medicines, more patients tend to (co)pay for their medication out of pocket. For example, in 2005, the percentage of out of pocket paid for 'medical goods dispensed to out patients' in Bulgaria was 79%. Correspondingly in Cyprus this was 81%, in France 16% and in the Netherlands 26% (Van Mosseveld, Kawiorska and De Norre, 2008). The effect of high prices on access to medicines is therefore likely to be more catastrophic. These problems are exacerbated by the fact that Central and Eastern Member States that joined the EU since 2004 were obliged to adhere to the same IP regulations as Western European Member States despite a significant relative difference in the gross domestic product (GDP) per capita. Moreover, in March 2004, prior to their accession, the EU regime on data exclusivity[7] was also changed, providing extra market exclusivity to originator pharmaceutical companies in these emerging markets. The Health Ministers of the accession countries raised concerns about higher prices after accession but commercial interests were upheld, with a negative effect on medicines prices and public health budgets.

Several EU countries recently introduced price limits on originator (or brand name) drugs. In Spain, a law was recently passed whereby doctors may only prescribe active ingredients, referring to the International Non-proprietary Name (INN) instead of any brand names. This effective way of lowering costs had already been adopted by other EU countries. Various reforms which encourage greater use of generic medicines and tougher negotiations on prices for patented drugs are of course necessary and beneficial, but they do not address structural flaws of the current system. These shortcomings include inefficient incentives to

[7] "Data exclusivity refers to a practice whereby, for a fixed period of time, drug regulatory authorities do not allow the registration files of an originator to be used to register a therapeutically equivalent generic version of that medicine." (MSF (2004) technical brief 'Data exclusivity in international trade agreements: What consequences for access to medicines?')

invest in R&D, excessive secrecy and too little sharing of knowledge, data, materials and technology, and unequal and rationing of access to new patented medicines.

Within the context of the current EU public debt crisis, many public hospitals in Southern Europe are unable to pay for their pharmaceutical expenditure (Ornelas, 2012).This has even led some large pharmaceutical companies, such as Roche, to stop supplying several cancer medicines to Greece (Daley, 2011). Other Southern and Eastern EU Member States may soon face the same predicament and be forced to remove a number of medicines from the list of treatments reimbursed by the State. While European governments are already facing difficulty in increasing their health budgets to accommodate rising pharmaceutical expenditure, this is likely to be amplified with the ageing populations. Access to medicines varies greatly among patients across Europe, and bearing in mind the current political and economical developments, disparities within and between countries are likely to grow. Therefore, the question of whether the current R&D system is sustainable or even desirable must be addressed. If the answer is no, what are alternative models of medical innovation to be considered?

In order to convert its policies into real action, and demonstrate its commitment to ‘Equity and Health in all Policies’, the EU must reform its internal market and innovation policies to increase its coherence with these goals. One avenue that has not yet been explored is the promotion of alternative incentives to innovation.

International debates on medical innovation & EU commitments

The WHO´s global call for a new innovation model

The EU's research and innovation policy still does not reflect the international community's recognition of the need for new medical innovation models, as highlighted in May 2008 during the World Health Assembly (WHA) where all countries, including EU Member States, agreed to a comprehensive Global Strategy and Plan of Action (GSPoA) on Public Health, Innovation and Intellectual Property. The GSPoA calls on all stakeholders to 'explore and promote a range of incentive schemes for R&D, including addressing the de-linking of the cost of R&D and the price of health products' (WHO, 2008). Specifically, section 2.3c of the GSPoA calls to 'encourage further exploratory discussions on the utility of possible instruments or mechanisms for essential health and biomedical R&D, including inter alia, an essential health and biomedical R&D treaty*'* (WHO, 2008, p.11).

A Consultative Expert Working Group on R&D Coordination and Financing (CEWG) was established to analyse various proposals for innovative mechanisms. The WHO working group through a process of public consultations has received various proposals from WHO Member States, civil society, academics, industry and other stakeholders. Proposals that have been considered include:

Innovation Inducement Prizes (both prizes for final products as well as milestone prizes); Open Source R&D models; Priority Review Vouchers; New indirect taxes; Medicines Patent Pools; Equitable and humanitarian licenses; Biomedical R&D treaty; Pooled funds related proposals; Advance Market Commitments, Health Impact Fund, Green Intellectual Property.

Following their three meetings in April, July and November 2011, as well as regional consultations, the CEWG in April 2012 gave recommendations on the proposals which best met the criteria.[8] The CEWG characterizes most promising proposals as 'open knowledge innovation', defined as research and innovation that generate knowledge which is free to use

[8] These WHO criteria are the following:

- Public health impact
- Efficiency/ cost effectiveness;
- Technical feasibility;
- Financial feasibility;
- IP management issues;
- Delinking;
- Equity/distributive effect, including on availability and affordability of products and impact on access and delivery;
- Governance and accountability;
- Impact on capacity building in, and transfer of technology to, developing countries.

without legal or contractual restrictions. The recommended proposals are for a Global Framework on Research and Development; Open approaches to research and development and innovation[9]; Pooled funds; Direct grants to companies; Prizes and Patent pools.

Importantly, the report states: 'The time has now come for WHO Member States to begin a process leading to the negotiation of a binding agreement on R&D relevant to the health needs of developing countries, and this would be under Article 19 of the WHO Constitution' (WHO, 2011, Ch.6).

While many of these proposals were initially drawn up with the needs of the developing world in mind, today these initiatives have become increasingly relevant for developed countries like EU Member States, and will be discussed in detail the next chapter and in the Annex

De-linkage principle - separating R&D costs from medical product prices:

According to this principle, innovation models should aim at ensuring broad and affordable access to medical products by avoiding time limited legal monopolies that have the effect of increasing price**.** If implemented correctly, de-linking R&D costs from the price of medicines can address many of the weaknesses of the current model of medical innovation: unaffordability, unavailability and unsuitability for purpose.

De-linkage can be used as a tool to promote R&D funding toward needs-driven, affordable and socially responsible health products. As such there would no longer be the need to rely on the expectation of high prices and monopolies to incentivise innovation. Choosing which health problems to be addressed in research should not only be a question of markets but one concerned with social needs. De-linkage is a key factor for policies which allow broader generic competition for life-saving essential medicines and the safeguarding of the fragile financial sustainability of health care systems. Manners in which the de-linkage principle can be applied is discussed in the Proposals section of this document.

Unaffordable: Existing medicines, vaccines and diagnostics are often too expensive for individuals and broad public coverage including within many EU Member States.

Unavailable: For certain diseases very few or no medicines or diagnostics are being developed as there is no profitable market. Very little research is devoted to creating new antibiotics and scarce attention is given to 'neglected diseases'[10] affecting the global South. The low **productivity** of the current R&D paradigm is not limited to neglected diseases and

[9] Includes, inter alia, precompetitive research and development platforms, open source, open access and equitable licensing.

[10] Neglected diseases are diseases that disproportionately affect the populations of developing countries and which do not represent a commercially viable market for pharmaceutical companies, because the populations are generally too poor.

antibiotics, even though these are among the most glaring shortcomings. The de-linkage reforms could also be used to accelerate the development of new treatments for diseases such as cancer and Alzheimer's.

Unsuitable: Often, the development of new drugs is guided by the needs of well-financed hospitals in the most advanced developed countries, while the social, infrastructural, epidemiological, climatic and demographic conditions of the rest of the world's populations are not taken into account.

EU commitments on global health and new models for innovation

The EU has a clear stance in favour of universal access to health and access to essential medical products, as highlighted in its Global Health Council Conclusions and through its consensus to the adoption of the WHO GSPoA Intellectual Property on Public Health, Innovation and IP. Unfortunately, to date, these stated commitments have not been transformed into political and financial support for concrete EU policies in the field of medical innovation.

Even so, the EU admits there is need for major changes. In June 2010, the EU Council adopted the Conclusions on Global Health 'to promote effective and fair financing of research that benefits the health of all. Towards that aim the EU will ensure that innovations and interventions produce products and services that are accessible and affordable' (European Council, 2010, Art.18). The Conclusions also recognised that one mechanism would be to 'explore models that dissociate the cost of R&D and the prices of medicines in relation to the WHO´s GSPoA on Public Health, innovation and IP' (European Council, 2010, Art.18c). For the first time, the EU here openly voiced support for the de-linkage principle. The WHO Global Strategy has established a clear pathway on how to change the medical R&D model into one that favours globally accessible health technologies while at the same time it eases the burden of pharmaceutical expenditure in European Member States´ public health systems. Furthermore, the EU´s 2020 flagship Innovation Union proposal speaks of introducing a more 'open approach to innovation', 'increased open access to the results of EU financed research' and the promotion of 'patent pools and innovation brokering'. It also points to inducement prizes as a way forward (European Commission 2010).

Knowledge generated by EU financed medical research (in other words, supported by European taxpayers) should not predominantly lead to returns for large private actors but maximise the general public good, as laid out in recent EU policy declarations[11]. Today, the question at stake for European Parliamentarians, the European Commission, EU Member

[11] Innovation Union and Horizon 2020 commitments.

States and other policy makers is whether the EU will seriously explore these new innovative proposals, or act as if “business as usual” is the only path with only minor token exceptions. Fundamental to meeting these commitments is the design of incentives, regulations and financing mechanisms. The principles of openness, knowledge sharing and de-linkage or disassociation of the R&D costs from the price of products should be the underlying principles. The EU´s research and innovation funding programmes like Horizon 2020 should reflect these important factors in order to ensure the sustainability of the medical innovation model.

Public risk-taking must have a clear return for common or public good

Economist Mariana Mazzucato (2011, p.109) explains how the generation of knowledge is socialised, with the public bearing the costs, while the commercialisation of publicly financed knowledge is privatised: ‘In finance, it is commonly accepted that there is a relationship between risk and return. However, in the innovation game, this has not been the case. Risk-taking has been a collective endeavour while the returns have been much less collectively distributed. Often, the only return that the State gets for its risky investments are the indirect benefits of higher tax receipts that result from the growth that is generated by those investments. Is that enough?’

In the model of public risk taking, private benefit has been accepted as a necessary measure to spur innovation and support (European) industry. Moreover, mounting evidence leads to questions about the viability and efficacy of policies which increase exclusivity-based commercial exploitation of publicly funded research results in Europe (Tinnemann, Özbay, Saint and Willich, 2010). An ever increasing number of voices in both academic and scientific communities are convinced that inventions from publicly funded research should be made more publicly accessible. The United States have already taken a leadership role, mandating Open Access publication of the National Institutes of Health (NIH) funded R&D. This is currently not the case with the knowledge obtained from EU-financed health research. A growing number of universities in the United States promote equitable or socially responsible licensing for their patents in biomedical research, to ensure that as much social benefit as possible comes from the exploitation and product development of publicly financed innovation. In the EU, funding worth billions of Euros cannot continue to be awarded without any strings attached and with little consideration for the creation of public goods[12] in the benefit of global health.

[12] The economic notion of ‘public goods’ is meant here as in non-rivalry and non-excludable goods.

Antibiotics and the need for alternative incentives

One important example of why new approaches to biomedical research are needed is the growing public health concern regarding antimicrobial resistance and the growing inefficacy of currently available antibiotics. Every year, EU citizens suffer 400,000 antibiotic resistance infections leading to 2.5 million days of hospitalisation. Up to 25,000 deaths are attributed to antibiotic resistant infections annually. Such infections annually cost an estimated EUR1.5 billion in healthcare expenditure and productivity loss across Europe. Failure to tackle this growing and dangerous public health challenge is a clear demonstration of market failure. Over the past decades there has been insufficient investment in new antibiotic treatments while many resistant bacteria have emerged, thus radically reducing the chances of curing infections with the available therapeutic arsenal.

There are currently no effective financial incentives or regulatory mechanisms to promote industry or public investment in this important field. This lack of investment stems from the fact that antibiotics do not usually generate substantial profits. Efforts to conserve antibiotics through rational use guidelines curb the opportunity to expand markets. Moreover, antibiotics are typically only used for short periods of time as opposed to treatments for chronic diseases. Consequently, as there is no expectation of high volume sales and revenues, a monopoly-based incentive model becomes obsolete. As with neglected diseases, relatively low anticipated returns on investment have deterred firms from investing in developing novel antibiotics over other products. Meanwhile, antibiotic resistance remains a global problem with a vast health impact. Several de-linkage proposals for antibiotics are currently being discussed in the EU and the United States (see Annex).[13]

[13] Read:

Jack, A., 2011. 'Prize' system urged to boost antibiotics research. 7 July. *Financial Times*. Available at http://www.ft.com/intl/cms/s/0/dcead16e-a7fa-11e0-afc2-00144feabdc0.html#axzz1oFxjWodp

The Economist, 2011. The spread of superbug. 31 March. *The Economist.* Available at: http://www.economist.com/node/18483671

Proposals promoting affordable access to medicines & needs driven innovation

Parallel to intergovernmental policy discussions and international debates, various proposals and projects that promote innovation and affordable access have been developed by governments, civil society, academics and industry. Some are relevant for patients within the EU, while others focus entirely on developing countries and/or neglected diseases, which are relevant to EU policies and commitments in Development and Global Health. This section briefly describes some of the proposed mechanisms that are relevant for EU policy, some of which are currently being implemented.[14] For more detailed descriptions and analysis of these mechanisms please see the Annex of this policy paper, where an extensive overview is given.

Open innovation in health research

Open Source research, open science and open medicine are all variations of an alternative paradigm of innovation in medical technologies which is gaining ground and is based upon the sharing of knowledge rather than enclosing it by means of IP protection or otherwise. Open Science or Open Source research is an approach to research that allows scientists to share problems and interests freely, regardless of organisations, disciplines or borders. This novel culture of innovation is based on the successful experience of Open-Source software. Collaborative research and networks may be more efficient and lower costs in innovation (So, 2011). The pharmaceutical industry has also been resorting to open innovation methods (CEWG, 2012). There is a wealth of Open Science and Open Access initiatives taking place across the world, not least in the innovation ecology environment of the California Bay Area - Silicon Valley - where an important part of the biotech industry is based.[15]

An Open Source product is one where the design is freely available for anyone to use, modify and distribute, and is created through collaboration between researchers and an open approach to IPRs. When health needs are great but funds are scarce, Open-Source biomedical research could help pool resources to create low-cost business models, especially where public finance is involved. Open Source medicine can be an especially useful tool for neglected diseases, antibiotic research or for certain conditions that are not properly addressed in the pure market-driven model. A number of open source initiatives

[14] Push and pull mechanisms: Financing of R&D requires inputs from both ‘push’ and ‘pull’ mechanisms. Push mechanisms generally refer to supply measures which involve governments and other funding agencies or industry actively encouraging certain R&D directions; ‘pull’ mechanisms refer to the dynamics of market demand or similar incentives for R&D in certain health-related innovations.

[15] During the yearly Open Science & Open Medicine Summit researchers, industry and other stakeholders share their experiences and discuss the future of collaborative science and innovation. http://opensciencesummit.com/

have been launched in the medical field over the last decade. An important example of open source initiative in biomedicine is the Open Source Drug Discovery (OSDD) Initiative for tuberculosis (TB) which has had impressive results in developing novel compounds.[16]

Open Access is the practice of providing unrestricted access via the internet to peer-reviewed scholarly journal articles. Open Access publishing has seen a rapid growth over the last years, and studies published in 2010 showed that roughly 20% of the total output of peer-reviewed articles published in 2008 was openly accessible (Björk, 2010). Current expensive medical journals and high data access fees all prevent timely and wide use of crucial health-related information. As the journal *Open Medicine* states 'Open access to, and wide use of, research data will enhance the quality and productivity of science systems worldwide' (Murray, 2008).

Socially responsible licensing

An important approach is the socially responsible licensing of R&D and innovations generated with public funding. The rationale behind this form of licensing is to generate the highest possible social benefit out of publicly funded research. The concept of 'socially responsible' licensing is especially appropriate in case of public (research) institutions licensing publicly funded results to private companies, but some socially responsible licensing principles could equally apply to use of research results by private companies receiving public funding for their R&D.

Socially responsible licensing conditions aim to ensure (a) accessibility and affordability of biomedical products – especially for low and middle income countries and (b) to ensure that publicly funded research remains free for use for further (clinical) research, professional education and training, validation of test results, etc. Under this concept of social licensing, a specific proposal has been further developed: 'equitable access licensing', also referred to as 'humanitarian use licensing'. This refers to all kinds of contract clauses and licensing forms that secure the possibility for inventors and technology suppliers to share their IP with people in need, most notably in low and middle income countries. For example, by carving out specific applications or territories and allowing non-exclusive use or lower royalty rates for these regions/applications. This is to ensure that knowledge and technology remain available for humanitarian use, while at the same time allowing for commercial exploitation of the research results in high-income countries.

[16] "As of September 2010, the OSDD identified 18 targets, conducted 19 virtual screens, and is currently optimizing two lead novel compounds as potential TB drugs. This initiative, led by India's Council on Scientific and Industrial Research, receives public funding and taps into a network of universities, companies, contract research organizations, and volunteers.'' (So, A.,D., et al., 2011, p.93)/ Open Source Drug Discovery Initiative web site. New Delhi, Council of Scientific and Industrial Research, 2011 (http://www.osdd.net/)

Socially responsible licensing is promoted in the United States by the National Institutes of Health (NIH) (Innovation Strategy Today, 2005) and by several leading technology offices of US universities, including UC Berkeley which has implemented the 'Socially Responsible IP Management Program' (IPIRA, 2011). Through this programme UC Berkeley has collaborated with several companies on licensing agreements to ensure affordable pricing in low-income countries for products stemming from university research. Projects with agreements under this programme include, among others, TB vaccine research, malaria artemisinin-combination therapies (ACTs) research and research for a possible HIV treatment (IPIRA).

In recent years, a number of European universities have also started to endorse new licensing programs. In 2011, the University of Dundee joined the Re:Search project which is a database run by the World Intellectual Property Office (WIPO) to push R&D for neglected diseases. Dundee University agreed to provide its IP which can now be used without royalties by all licensees who wish to develop products for neglected diseases.

Socially responsible licensing can also be an effective way of achieving health **technology transfer.** Technology transfer here refers to the manners and means through which companies and organisations acquire technology from foreign sources. Local production of pharmaceuticals, vaccines and diagnostics may contribute to sustainable and long-term solutions to the challenges posed to health innovation and access in developing countries. The EU has committed to technology transfer in the TRIPS and in WHO commitments like the GSPoA on Public Health, Innovation and IP. Taking into account the disappointing results of technology transfer up to now (Moon, 2011), Horizon 2020 should include incentives for companies and research institutes, as well as support for researchers from developing countries, that are stronger, more targeted and more effective than those in Framework Programme 7 (FP7).

Innovation inducement prizes

> *"A medical prize fund would not provide a panacea, but it would be a step in the right direction, redirecting our scarce research resources toward more efficient uses and ensuring that the benefits of that research reach the many people who are currently denied them."*
>
> Joseph Stiglitz, 2007, Project Syndicate

Prizes are an incentive system to induce R&D for new essential medicines, and can be implemented in a manner that ensures competition, affordability and widespread access. Innovation prizes are least controversial when they are proposed as systems for incentivizing parts of the innovation process, to reward research outcomes that are not expected to result in commercially viable products, or designed to replicate Big Pharma payments for reaching

benchmarks in a larger innovation program. A more ambitious version of innovation prizes would include open licensing of the end products. In the open licensing approach, cash prizes would be a substitute for exclusive rights to sell products and monopoly prices. In some proposals, innovators would be awarded large monetary prizes based in part or in whole on the improvements to health outcomes over existing products. This would dramatically reduce incentives for the marketing and promotion of medicines that are used irrationally, or that are no better than the benchmarked alternatives. Other proposals would link prize payments to non-specified product performance criteria, such as the accuracy and cost of a point of care diagnostic test.

A variety of proposals for prize schemes to reward innovation for new drugs, vaccines or diagnostic devices already exists (Love and Hubbard, 2007). The most ambitious prize fund approaches combine several different prize mechanisms. These include (1) end-product prizes that are awarded to the developers of products that are registered for sale and used by patients, (2) open source dividend prizes, which reward upstream open sharing of knowledge, data, materials and technology, and (3) prizes for earlier or interim development, such as achieving specific product development benchmarks or identifying biomarkers.

In order to further advance discussions on prize fund models, government- and donor-backed research must be carried out to investigate the costs, benefits and feasibility of various implementation schemes. This could focus on several of the specific proposals that have been put forward to address very specific R&D and access needs. The EU could play an important and leading role in this exploration. DG Research & Innovation plans to launch a prize for heat stable vaccines in April 2012.This is a step in the right direction, but unfortunately no conditions for accessibility or affordability seem to be put in place, nor for a non-exclusivity in the license.

For Specific Prize Proposals, please see the Annex.

Other alternative incentive mechanisms

The Health Impact Fund, the Priority Review Voucher and Advance Market Commitments are also schemes that employ alternative mechanisms to induce innovation or bring products to the market. These proposals, although allowing for broad access once the product is available, do not necessarily encourage knowledge sharing, transparency, sustainable public investment or generic competition. The proposals are described in the Annex.

Product Development Partnerships

The past decade saw the launch of numerous product-development partnerships (PDPs) aimed at developing new medicines and vaccines through a combination of resources from

the public sector, philanthropy, and the pharmaceutical industry. PDPs research, develop and support accessibility of new health technologies that target diseases which disproportionately affect developing countries.[17] Thankfully, the R&D pipeline for neglected diseases is now beginning to show signs of life, with PDPs managing almost 150 projects in pre-clinical and clinical development (DNDi, 2011).

The Medicines Patent Pool (international policy)

The Medicines Patent Pool focuses on HIV/AIDS and was created to increase access to quality assured, safe, efficacious, appropriate and affordable medicines. Here, patent holders share their IP with the Pool which then licenses it to other producers in order to facilitate the production of affordable generic medicines for use in resource-poor settings. In addition to reducing the prices of medicines, the Pool aims to facilitate the development of HIV medicines that are better-adapted for resource-limited settings: examples include medicines that do not require refrigeration, special formulations for children, and ‘ fixed-dose combinations’ that combine multiple medicines into one pill and ease treatment for patients and treatment providers alike (Medicines Patent Pool 2011). Producers may pay royalties to patent owners in order to manufacture patented medicines and sell them in countries well before the expiration of the patent term.

Recently, the Pool obtained a licensing agreement with Gilead as well as sublicensing agreements with generic producers for second line antiretroviral (ARV) treatments.[18] The medicines covered are three of the 19 prioritised as especially critical to public health by the WHO’s HIV/AIDS Department. Subsequently, sublicences with generic companies were negotiated, presenting a major step forward in the development of an effective Pool as these licences will have a tangible impact on the lives of many patients. The license between the Pool and Gilead has recently been the subject of criticism in regards to the scope of the license. The terms of the licence are not as inclusive as many had hoped, yet compared to other voluntary licence it is an important improvement. It is key that more companies license their patents to the Pool allowing for a broad scope for both production and importation.

[17] Examples of PDPs in the health field include: the TB Alliance, Aeras Global TB Vaccine Foundation, the Drugs for Neglected Diseases Initiative (DNDi), the Global Alliance for Vaccines Initiative (GAVI), the International Partnership for Microbicides, Medicines for Malaria Venture (MMV), the International Aids Vaccines Initiative (IAVI), the Institute For One World Health, the International Vaccines Initiative, PATH, Malaria Vaccine Initiative, the Innovative Vector Control Consortium, and others.

[18] The licences cover: tenofovir (TDF), cobicistat (COBI), elvitegravir (EVG), and the Quad, a fixed-dose combination of TDF-COBI-EVG-emtricitabine. There is also a covenant not to enforce emtricitabine (FTC) patents, and the ability to make other fixed-dose combinations involving these compounds. One major down-side of this licence is that India is the only country eligible to produce, and the geographical scope for beneficiaries also excludes many countries.

R&D Convention or Treaty (international policy)

In May 2012, during the 65th WHA, the WHO's CEWG will recommend that formal intergovernmental negotiations commence on a binding R&D Convention. Negotiations on such a binding intergovernmental instrument would take place under the auspices of the WHO. It is important that the EU takes a proactive role in the development of such an instrument.

The R&D Convention as proposed by the CEWG would have a significant impact on public health as it would create a new global framework for supporting priority medical R&D that is based upon the equitable sharing of the costs of R&D and incentives to invest in needs-driven R&D. The R&D Convention concept is predicated upon the principles of de-linkage of product prices and R&D costs, open-knowledge innovation, competition among suppliers of products, access to and transfer of technology to developing countries. This would involve norms and obligations on both national governments and international institutions. See the Annex for details on the R&D Convention or Treaty.

"There is a danger that industry subsidies might sometime be little more than corporate subsidising an already rich industry ,or, worse, paying for something that industry would otherwise have done for itself." Jim Murray, 2001, former head of BEUC.

The Innovative Medicines Initiative

The European Commission has led a European initiative to foster European R&D through the Innovative Medicines Initiative (IMI), a public-private partnership with the European Federation of Pharmaceutical Industries and Associations (EFPIA). The IMI highlights that the pharmaceutical industry is willing to cooperate and to share results provided they benefit from this. The objective of the IMI is to develop knowledge sharing tools and methods that will facilitate the development of better medicines. The IMI has a budget of EUR 2 billion for the period 2009–13, with the EU providing EUR 1 billion and the pharmaceutical industry the other half. The IMI supports pre-competitive collaborative research in order to address research bottlenecks in the drug development process. Its main objectives are to improve the efficiency of the drug development process with the long-term goal of producing safer and more efficient drugs and also to improve education and knowledge management in R&D. The chief focus areas of the Initiative are brain disorders and cancer, as well as metabolic, infectious and inflammatory diseases.

Unfortunately, the Initiative missed out on the opportunity to contribute towards societal welfare and guarantee affordable access to the developed medicines. While the IMI

ensures that public money contributes towards more efficient R&D, benefits which stem from this research are mainly privatised while there are no clear conditions laid down in regards to affordability, accessibility and the general public interest. The following quote by EFPIA is quite telling in this regard: “IMI projects replicate work that individual companies would have had to do anyway”[19] (EFPIA, 2011). Another criticism is that the agenda is predominantly set by industry, with researchers having little say. Meanwhile, there has been a great deal of controversy surrounding IP issues as a vague definition of IP ownership currently leaves academic partners vulnerable and disadvantaged. Their concerns indicate that industry stands to gain most from this partnership.

The EU could take action to improve the licensing practices of IMI and future initiatives, ensuring greater public benefit from the EUR 1 billion that has been invested. One way of addressing this problem would be to apply the Rules of Participation (art. 45) of the Horizon 2020 programme that refers to the ‘access of EU institutions and member states to the results of Community financed projects’ (European Commission Proposal 2011/0399 (COD)).

[19] “Large pharma will also benefit, along with the other participants, from the discoveries made in projects that are worth many times the value of each individual company’s contribution. In some cases, this offers tremendous cost savings, as the IMI projects replicate work that individual companies would have had to do anyway.” This information was retrieved on 28 October 2011 at the following link, but has now been removed by the EFPIA: http://www.efpia.org/Content/Default.asp…

How can the EU be a leader in new innovation approaches?

The way innovation is currently being rewarded is putting the economic sustainability of EU health budgets and research financing at peril. Furthermore, it is undermining access to appropriate and affordable medicines worldwide. There is a clear need to support and explore alternative and complementary models of innovation which will produce public knowledge goods. The EU cannot limit itself to 'planting the seeds' of innovation and then naively expect growth, private re-investment in socially relevant projects, and the blossoming of innovation. EU Member States that are greatly stressed by dwindling public resources cannot be expected to contribute generously to innovation programmes that, in some cases, convert the State into venture capitalists with little or no possibility of recovering their risky investments. The following questions remain unanswered and should be addressed by the European Commission, the European Parliament and the Member States:

- What new instruments will be created for the EU´s innovation policy to be coherent with the objective of ensuring relevant, affordable and accessible innovation?
- Will the rules and regulations managing IP in EU research programmes reflect the Innovation Union's "open approach to innovation, innovation brokering and patent pools"?
- In the midst of a financial crisis affecting many public health systems and the general stagnation of medical research progress, will EU taxpayers continue to hand over billions of euros to large commercial interests with very little competitive or social conditionality?
- Will the EU support the exploration of initiatives being discussed at the WHO and other international fora that aim to structurally reorient biomedical R&D towards a more needs-driven approach, allowing people worldwide to have access to the medicines they need?

Horizon 2020 programme and public funding for the public good

The Common Framework Horizon 2020 policy is an ideal opportunity for the EU to take the lead in some of the issues described above. The Research programme has a budget of EUR 80 billion, unequalled by most public research budgets globally. Europe 2020 has recognised crucial challenges: low growth, insufficient innovation and a diverse set of environmental and social challenges. The EU aims to address societal challenges and promote smart and inclusive innovation which leads to equitable benefits. The notion of sustainable and efficient innovation that responds to public health needs can be entirely coherent with EU objectives of promoting a vibrant and competitive market for medical products, defending public health and the protection of jobs in the health sector. The flexibility and openness that has driven the most dynamic technological sectors of our economy, such as software, telecom and IT

could also be applied to the medical innovation field. So at a time when funds are scarce and the EU finds itself in a crisis, innovation and competitive businesses should be stimulated, while public money provided by taxpayers needs to be invested wisely, promoting economic and social returns for the public interest.

International developments and the EU's position and influence

European R&D policy is not just a matter of investing in a given research project. The EU is also a very influential player on the world stage, where multiple policy developments regarding biomedical innovation take place. On the one hand, the EU could make a real difference in supporting global calls for an improved system of biomedical innovation. Once the final recommendations of the WHO´s CEWG are delivered in May 2012, it will be up to the international community to take them forward and implement them. Negotiations regarding a global binding instrument for the coordination and financing of R&D will be key in this respect. We hope the EU will engage itself constructively in these negotiations and accept the broad challenges facing global health. On the other hand, the EU's IP policy both in its own market and third country markets still focuses on getting increasingly extended market exclusivity periods on medicines. The EU should seriously re-evaluate how this is contributing to innovation.

Recommendations

The EU aims to be a leader in technological innovation, yet the EU could and should be a leader in both innovation *and* access. For the EU to succeed, it needs to look positively at new approaches to innovation and promising developments in the area of incentives and financing of R&D. The EU should consider innovative proposals, especially proposals that de-link the R&D costs from the price of final products, and become a key player in the development of new sustainable models of biomedical innovation and public knowledge goods. The need for a new approach to innovation is even more urgent where R&D is subsidised through public funds. EU policies should be guided by the premise that knowledge goods developed by means of public funds need to be affordable and accessible to all.

Open Innovation

EU research programmes need to actively promote a new scientific ecology in which a vibrant open innovation sector is allowed to compete and cooperate alongside more traditional Big Pharma and biotech industries. EU health research programmes need to more strongly support transparency and knowledge sharing; this will promote academic integrity, reduce the potential for scientific fraud or wasteful repetition of research, and generally foster greater public faith in scientific endeavours.

Societal benefits and the public good

The EU´s Horizon 2020 project should condition any transfer of knowledge property to a plan that conforms to ethical, social and environmental objectives in accordance with the public interest. This entails establishing participation rules for EU research programmes that include possible mandatory conditions for licensing that preserve public objectives.

New incentive mechanisms

The EU should support concrete incentive mechanisms to promote R&D that is needs-driven and affordable. The principle of de-linking the cost of R&D from the price of products should guide the design of new incentive mechanisms.

HAI Europe and TACD call upon the EU:

In respect of research programmes and EU internal policy, to:

- Incorporate socially responsible principles as a condition for its biomedical research grants, most notably in Horizon 2020 grants.

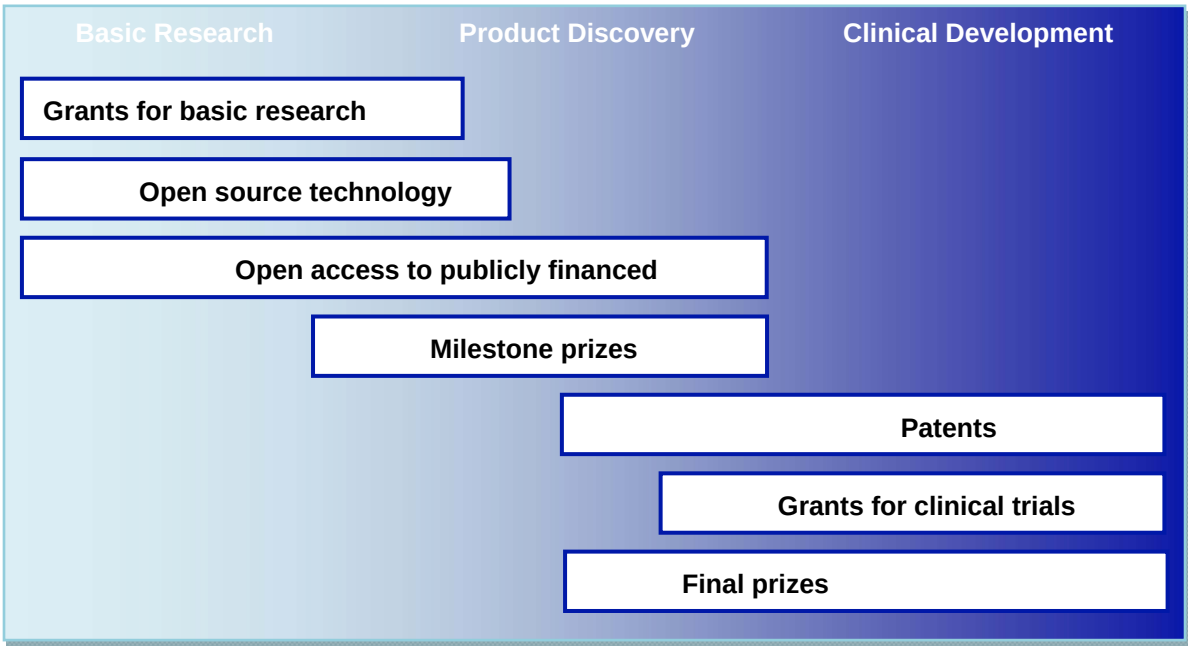
- Establish clear rules in Horizon 2020 to mandate Open Access to EU financed health related research results.
- Promote meaningful technology transfer; Horizon 2020 should increase the level of incentives and support for researchers from developing countries as compared with FP7.
- Carry out feasibility studies and pilot programmes for various innovation inducement prizes, in particular concerning cancer research, HIV/AIDs, neglected diseases and antibiotics.
- Ensure access to clinical trial data of medicines registered with the EMA or national market authorities.

In respect of international policy, to:

- Constructively engage in negotiations for a Biomedical R&D Convention as will likely be recommended by the WHO Consultative Expert Working Group to the 65th World Health Assembly in May 2012.
- Encourage companies to join the Medicines Patent Pool granting voluntary licences to their patented technologies for better access in all developing countries.
- Rather than extend market exclusivities through IP protection in EU Free Trade Agreements, focus on stimulating therapeutically valuable and affordable innovation.

ANNEX of specific proposals regarding biomedical innovation and EU policy opportunities

Figure 1



Interaction between proposed research and development incentives in connection with the development of new drugs for neglected diseases. (Based on Årdal, C., Iversen, J.,H. And Myhr, K., 2011, p. 2017)

Push & Pull mechanisms

Financing research and development (R&D) requires inputs from both “push” and “pull” mechanisms. “Push” mechanisms: financing or other incentives provided to innovators up front, which reduce risks or costs of R&D. “Pull” mechanisms: financial rewards or other incentives provided to innovators for progress or completion of research, development, or scale-up of production, which enhance market opportunities.

Figure 2

Push mechanisms	Pull mechanisms
R&D grants	Extended market exclusivity
Open access to publicly funded research	Government-guaranteed future procurement
Open source drug discovery	Purchase funds
Tax reduction for R&D	Patents
	Prizes
	Tax deduction on sales income
	Accelerated regulatory review

Push and pull mechanisms for stimulating research and development (R&D) of new medicines (Based on Årdal, C., Iversen, J.,H. And Myhr, K., 2011, p. 2017)

Socially Responsible Licensing

In order for publicly financed research to revert back into the public good, a new European Union (EU) legal framework is needed to assure that licensing and exploitation of publicly funded research results fulfil broad social objectives.

We propose socially responsible licensing conditions to be attached to the rules of participation of the EU Programme for Research and Innovation – Horizon 2020, specifically to grants funding biomedical research. We recognize that specific licensing conditions between research institutes and private parties need to be determined on a case by case basis. However, this does not preclude the Commission from formulating and implementing clear guidelines, and where appropriate mandatory rules, regarding the use and licensing of research results generated under an EU grant.

We recommend particularly far-ranging social and equitable licensing conditions for R&D generated by publicly funded research for biomedical research, and within this field most strongly in the field of neglected diseases and antibiotics.

An appropriate set of such socially responsible conditions should include non-exclusive licensing as a default. Non-exclusive licensing would generally allow for broader access to health technologies and products, as it allows for more than one company to exploit the innovation, thereby enabling generic competition and as a consequence lowers prices of health technologies and products. If an exclusive licence is negotiated, the owner of an

invention (research institute, etc.) or funding authority may retain the right to intervene in case of unmet market or public health needs.

The licensee may further be obliged to use different tools for improving access to the products in middle- and low income countries: the humanitarian use licensing conditions. For example, by implementing the obligations for companies that commercially exploit a product derived from public funded research to implement a differential pricing scheme to ensure affordable access to the health technology in developing countries. Alternatively such licensing conditions can dictate the obligation to allow for open, non-exclusive licenses to enable competition in developing countries that will lower the price of biomedical products. Other elements that can be included are clear obligations to engage in meaningful technology transfer, and including access and training programs (Godt, 2011).

To sum up, licensing conditions for EU-grants for biomedical research under Horizon 2020 grants could include the following principles:

1. No unjustified transfer of ownership of (intellectual property rights protected) research results from research institutes to private companies, and non-exclusive use of publicly funded research results as the default principle.
2. In case of non-exclusivity, licensees should be prevented from using additional or follow-on IP claims on licensed inventions to constrain or block competitive exploitation of licensed research results.
3. In case of exclusivity, the right to use research results and practice the inventions for research and/or educational and teaching purposes should be retained.
4. In the condition for EU grants, socially responsible licensing could also mandate certain conditions requiring the affordability and accessibility of products produced with research results financed by EU funds. For example, when an overriding social demand exists, the European Commission and EU member states should retain the right to exploit the research results on a royalty-free basis or to permit exploitation by third parties in order to confront unmet market needs or to confront clear societal challenges, such as public health.
5. The EU can establish, when appropriate, specific conditions for pricing, open competition and accessibility for the public procurement of the commercial exploitation of EU financed research results in order to fulfil EU policy objectives.
6. Horizon 2020 should further establish clear humanitarian use licensing conditions to improve access and affordability of biomedical products in middle- and low income

countries. For example by making non-exclusive licensing mandatory for exploitation of research results in this region, or, in case of exclusive licenses, by requiring the implementation of meaningful differential pricing or other access schemes resulting in low- or no-cost access.

7. Horizon 2020 should establish specific conditions to ensure that EU financed research contributes to meaningful health technology transfer to developing countries in fulfilment of EU policy objectives with regards to global health and access to medicines.

Innovation Inducement Prizes

The HIV/AIDS Prize Fund & the Medicines Patent Pool

The Prize Proposal for HIV/AIDS treatment addresses the problem of the rising costs for HIV/AIDS treatment and the large number of people in need of treatment. Finance mechanisms and donor funded treatment initiatives such as the Global Fund, UNITAID and PEPFAR depend upon generic competition to maximise the purchase of cheap/affordable treatment. At present, more than 90% of donor funded AIDS medications to developing countries are supplied by Indian generic manufacturers (Waning, Diedrichsen and Moon, 2010). However, with the cost of treatments rising as patients are switching to second line and third line antiretroviral (ARV) treatment, while at the same time generic competition is restrained, the Global Fund and other donor funded institutions may not be able to maintain their current levels of treatment for 5.2 million persons, nor address the needs of the remaining 9.7 million individuals still awaiting treatment.

The Donor Prize Proposal presents a possible solution to this ongoing problem, addressing the need for donors to purchase medicines at competitive generic prices, while providing rewards to innovators.

The Prize proposal asks donors to place a fraction of their budgets for purchasing medicines into a fund that would be used to reward companies who license their patent to the Medicines Patent Pool. When patents are licensed to generic suppliers, donors would be able to buy the medicines at marginal cost. Because the prize fund rewards are tied to licensing practices, companies would have strong economic incentives to license to the patent pool, and accept whatever broad scope of distribution was required, including middle income countries. One suggestion for the fraction of budgets is 10 percent of all drug medicines purchases.

More information regarding the HIV/AIDS Prize Fund may be found at the following link: http://www.who.int/phi/Bangladesh_Barbados_Bolivia_Suriname_DonorPrize.pdf

Prize fund proposals for Antibiotics

Antibiotic resistance is a major public health problem. The current (irrational) incentives to sell as many antibiotic units as possible and increase market share, have led to the development of antibiotic resistance and failed to stimulate innovation. The public health community and key business leaders have identified the field of antibiotic innovation as one requiring alternative models, which could include the de-linking of price from R&D costs.. For more information please read the following articles:

So, A.,D., et al., 2011. Towards new business models for R&D for novel antibiotics. *Drug Resistance Updates,* 14, pp. 88-94. Available at: http://www.sciencedirect.com/science/article/pii/S1368764611000161

Outterson K., Pogge T., Hollis A. (2011) Combating Antibiotic Resistance Through the Health Impact Fund. June 22. *Boston Univ. School of Law, Law and Economics Research Paper No. 11-30*. Available at: http://papers.ssrn.com/sol3/papers.cfm?abstract_id=1866768

Chagas Disease Prize Fund

Chagas disease (T. cruzi infection or American Trypanosomiasis) is a tropical parasitic disease commonly transmitted to animals and people by insect vectors that are found only in the Americas (mainly, in rural areas of Latin America where poverty is widespread). The disease may also be spread through blood transfusion and organ transplantation, ingestion of food contaminated with parasites, and from mother to foetus. It is estimated that as many as eight to 11 million people in Mexico, Central America, and South America have Chagas disease, most of whom do not know they are infected. If untreated, this chronic disease is often fatal. According to the WHO, the annual impact of Chagas disease is estimated 13,000 deaths. There is currently no adequate treatment for Chagas disease.

For information regarding the proposal by Bangladesh, Barbados, Bolivia and Suriname: Chagas Disease Prize Fund for the Development of New Treatments, Diagnostics and Vaccines please go to the following link: http://www.who.int/phi/Bangladesh_Barbados_Bolivia_Suriname_ChagasPrize.pdf

A Milestone Prize

A milestone prize allows rewarding developers as they complete specific milestones along the neglected disease product development process. The proposal submitted by BIO Ventures for Global Health for consideration by the WHO/CEWG regarding a milestone-

based Prize to stimulate R&D for point-of-care fever diagnostics is available at the following link: http://www.who.int/phi/news/phi_18_BVGH_CEWG_proposal_en.pdf

Tuberculosis Diagnostic Prize Fund

One major gap in the treatment of tuberculosis (TB) is the lack of a simple, effective, and affordable test to rapidly and accurately diagnose TB, and which can be used as close as possible to a patient's bedside – at the point of care (POC). Today, the most commonly used test in developing countries, the sputum smear microscopy (SSM), detects less than half of all TB cases, and performs even worse in children and people living with HIV who either have difficulties producing enough sputum, or do not have sufficient or any mycobacteria in their sputum to be detected under the microscope. This test also completely fails to detect the extrapulmonary form of TB. One of the major scientific hurdles to the development of a TB POC test lies in the identification of a biomarker – something that when it is detected shows that a person is infected with TB.

In a submission to the World Health Organization (WHO) Consultative Expert Working Group on R&D Coordination and Financing (CEWG), Bangladesh, Barbados, Bolivia and Suriname proposed a TB Diagnostic Prize Fund of at least USD 100 million for the development of a low-cost rapid diagnostic test. The proposal discusses the need for a TB POC diagnostic test which can be used where health practitioners may not have access to laboratories that can analyse sputum smears. The Prize, administered by WHO, would be awarded once a submission meets the minimum criterion specified by the fund.

The proposal by Bangladesh, Barbados, Bolivia and Suriname for a Prize Fund for the development of low-cost rapid diagnostic test for TB is available at the following link: http://www.who.int/phi/Bangladesh_Barbados_Bolivia_Suriname_TBPrize.pdf

Médecins Sans Frontières' proposal for a TB Diagnostic Prize Fund as submitted to the CEWG is available at the following link: http://www.who.int/phi/MSF.pdf

The Openness Dividend

Prizes can contain an Openness or Open Source Dividend, to reward parties that openly share the knowledge, materials and technology that was critical to the success of the development of the products that qualify for the prize money. For example, the Product Prize Fund shall set aside up to five percent of its prize fund payments to this end.

To qualify for the Openness Dividend, knowledge, materials and technology must be made freely available on a non-remunerative basis. To the extent IPRs exist, the knowledge, materials and technology must be licensed on a royalty free basis for a field of use and

geographic region that is consistent with the field of use and geographic region covered by the Prize Fund rewards.

Variations on Open License Innovation Inducements Prizes

Although the following proposals allow for broad access once the product is available, they do not necessarily encourage knowledge sharing, transparency, sustainable public investment or generic competition. This is dependent on how they address IP management and monopolies.

The Health Impact Fund (HIF)

The full proposal is available at the following link:
http://www.yale.edu/macmillan/igh/pilot.html

Priority Review Voucher (PRV)

For more information about PRV please go to the following link:
http://www.nejm.org/doi/full/10.1056/NEJMp0806684?ijkey=40867983409f7a8a73b1ba1e848fd14ef5ba8af6

Advance Market Commitment (AMC)

For more information about AMC please go to the following link:
http://www.haiweb.org/31032009/27%20Mar%202009%20AMC%20Current%20Realities%20&%20Alternate%20Approaches%20FINAL.pdf

R&D Convention or Essential Health and Biomedical R&D Treaty

In a joint submission to the WHO CEWG in June 2011 on a possible essential health and biomedical R&D Treaty, Health Action International (HAI) Global, Initiative for Health & Equity in Society, Knowledge Ecology International (KEI), MSF, and Third World Network (TWN) outlined the rationale, objectives and possible elements for such a Treaty or Convention.

The purpose of the R&D Convention would be to create a new global framework for supporting priority medical R&D that is based upon the fair and equitable sharing of the costs, access, and benefits of R&D. This would involve norms and obligations on both national governments and international institutions.

The Objectives promote a sustainable system of medical innovation that would:

1) ensure adequate and predictable sources of finance for needs-driven medical treatment relevant in particular to diseases and conditions which disproportionately affect developing countries **2)** allocate fairly the costs of supporting needs-driven medical treatment, in particular, to meet the health needs of developing countries; **3)** identify priority areas of needs-driven; **4)** explore and promote a range of incentive schemes for health-needs driven research addressing the de-linkage of the costs of and the price of health products; **5)** encourage the broad dissemination of information and sharing of knowledge and access to useful medical inventions including the facilitation of access to publicly funded research**; 6)** promote transparent and ethical principles for clinical trials involving human beings as a requirement of registration of medicines and health-related technologies**; 7)** enable medical researchers to build upon the work of others**; 8)** support diversity and competition; **9)** utilize cost effective incentives to invest in promising and successful research projects that address health care needs; **10)** enhance the transfer of and building of technological knowledge and R&D capacity to further social and economic welfare and development in developing countries; and **11)** promote equitable access to new medical technologies, so that all share in the benefits of scientific advancement.

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