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Consultative Expert Working Group on Research and Development: Financing and Coordination

In line with World Health Assembly resolution WHA63.28, the Director-General has the honour to transmit to the Sixty-fifth World Health Assembly the final report of the Consultative Expert Working Group on Research and Development: Financing and Coordination, attached as Annex.

ANNEX

REPORT OF THE CONSULTATIVE EXPERT WORKING GROUP ON RESEARCH AND DEVELOPMENT: FINANCING AND COORDINATION

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PREFACE

The issue we were asked to investigate was identified at least two decades ago. Market mechanisms, and also publicly-funded research, collectively result in far too little investment in research and development on diseases that mainly affect developing countries. This means that poor people suffer and die because there are no effective health technologies like medicines, vaccines or diagnostics. Markets fail because intellectual property rights are not an effective incentive in these circumstances, and public investment is also dominated by the rich world and its own health needs. This is the challenge for the world as a whole which has guided our discussions and deliberations. We have framed our recommendations to indicate that finding solutions is the responsibility of all of us in this interdependent world, in developed and developing countries alike.

The search for new, innovative and sustainable sources of funding, and making better use of existing resources for research and development for the specific health needs of developing countries, was an unfinished agenda of the negotiations that led to the Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property (GSPA-PHI) agreed in 2008. Those negotiations themselves were the response of WHO Member States to the report, published in 2006, of the Commission on Intellectual Property Rights, Innovation and Public Health (CIPIH) which was established in 2003. We in turn were asked by Member States to review the work of the Expert Working Group on Research and Development: Coordination and Financing, established on the recommendation of the GSPA-PHI, which reported in 2010. We therefore felt an obligation to produce a solid report, based on empirical evidence, while also ensuring that our processes were as transparent and open as possible. The report from this Consultative Expert Working Group seeks to bring this long-running debate, if not to closure, to a head.

We hope our analysis of the current situation of R&D for health needs in developing countries, our assessment of various proposals for better financing and coordination, and our conclusions and recommendations will move this debate forward in a significant way. We believe our recommendations deserve serious consideration by WHO Member States, in particular the idea of securing implementation of our key recommendations through a binding international instrument. Agreement on this could have far-reaching effects on people suffering from all types of diseases in developing countries – now and into the future. In face of such complex challenges, a stronger multilateral response will help to improve millions of people's lives.

It has been a pleasure and honour for us to chair the work of the Consultative Expert Working Group on Research and Development: Financing and Coordination. We had three face-to-face meetings in April, July and November of 2011, and we communicated regularly from April 2011 onwards, and almost daily in the last couple of months. The result is this report and a lot of good memories of a productive group of engaged and concerned experts from different countries and backgrounds. All members contributed actively to the analysis of the proposals on our table. We learned from, and learned to know, each other, and the atmosphere was always constructive.

Differences of opinion are inevitable in such a diverse group. However, differences of opinion enrich and help to deepen the discussions. This diversity was therefore also our most valuable asset. The challenge therefore lies in how such differences are handled to make the final outcome bigger than the sum of its parts. We can confidently say that the members of this group showed a lot of understanding, wisdom and magnanimity in accommodating each other's perspectives and arguments; and all this without compromising their own fundamental values and core positions. We are thankful to all our colleagues in the group for their cooperation, commitment and guidance.

Our time and resources were limited and the mandate was comprehensive, but very specific. Despite these limitations we sought to ensure the maximum possible input into our work from all parties

interested in this agenda. We held a day-long open forum as part of our first meeting, invited submissions on new ideas and proposals, conducted regional consultations, held open sessions at the end of each of our three meetings, and posted on the WHO web site all relevant documents and outcomes of the meetings all along. Not only have we been open in our process, but we believe we also managed any conflicts of interest in a transparent and appropriate manner. We hope that this work will not only be remembered for what it produced but also how it was conducted – a truly collective process with inputs from many different stakeholders which has provided a global public good in a way similar to how we recommend more of research should be organized.

We should like to emphasize that, although we have been nominated by our governments and then appointed by the Director-General of WHO at the request of the World Health Assembly, we have been given absolute freedom to analyse the issues in the way we believed to be appropriate and to reach our conclusions and recommendations without interference. We should like to thank the WHO secretariat and all staff involved for the excellent support given to our process and work. The Director-General, Dr Margaret Chan, has shown a keen interest in our work and participated in the opening meeting. Assistant Director-General, Dr Marie-Paule Kieny, provided excellent oversight and followed the work closely. Dr Zafar Mirza directed the secretariat and has been a strong support, and Dr Charles Clift has been instrumental and invaluable in committing our analysis and conclusions to paper in the form of this report.

In finishing we would also, on behalf of the group, like to thank all organizations and professionals who submitted innovative proposals that we benefitted from and which were critical to our intensive learning process.

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TERMS OF REFERENCE

The terms of reference for the CEWG are set out in World Health Assembly resolution WHA63.28, the text of which follows (without footnotes):

Establishment of a consultative expert working group on research and development: financing and coordination

The Sixty-third World Health Assembly,

Having considered the report on public health, innovation and intellectual property: global strategy and plan of action, and the report of the Expert Working Group on Research and Development: Coordination and Financing;

Considering resolution WHA61.21 which requests the Director-General "to establish urgently a results-oriented and time-limited expert working group to examine current financing and coordination of research and development, as well as proposals for new and innovative sources of funding to stimulate research and development related to Type II and Type III diseases and the specific research and development needs of developing countries in relation to Type I diseases, and open to consideration of proposals from Member States, and to submit a progress report to the Sixty-second World Health Assembly and the final report to the Sixty-third World Health Assembly through the Executive Board";

Noting that although the Expert Working Group made some progress in examining proposals for financing of, and coordination among, research and development activities, as called for in resolution WHA61.21, there was divergence between the expectations of Member States and the output of the Group, underlining the importance of a clear mandate;

Considering that, in its recommendations, the Expert Working Group states the need to conduct an in-depth review of the recommended proposals;

Recognizing the need to further "explore and, where appropriate, promote a range of incentive schemes for research and development including addressing, where appropriate, the de-linkage of the costs of research and development and the price of health products, for example through the award of prizes, with the objective of addressing diseases which disproportionately affect developing countries";

Noting previous and ongoing work on innovative financing for health, research and development and the need to build on this work as relevant;

Emphasizing the importance of public funding of health research and development and the role of the Member States in coordinating, facilitating and promoting health research and development;

Reaffirming the importance of other relevant actors in health research and development,

1. URGES Member States:

(1) to support the work of the Consultative Expert Working Group by:

(a) providing, where appropriate, information, submissions or additional proposals;

(b) organizing and/or supporting, where appropriate, regional and sub-regional consultations;

(c) proposing names of experts for the roster;

2. REQUESTS the Director-General:

(1) to make available electronically by the end of June 2010:

(a) all the proposals considered by the Expert Working Group including their source;

(b) the criteria used to assess the proposals;

(c) the methodology used by the Expert Working Group;

(d) the list of the stakeholders that were interviewed and those who contributed information;

(e) sources of statistics used;

(2) to establish a Consultative Expert Working Group that shall:

(a) take forward the work of the Expert Working Group;

(b) deepen the analysis of the proposals in the Expert Working Group's report, and in particular:

(i) examine the practical details of the four innovative sources of financing proposed by the Expert Working Group in its report;

(ii) review the five promising proposals identified by the Expert Working Group in its report; and

(iii) further explore the six proposals that did not meet the criteria applied by the Expert Working Group;

(c) consider additional submissions and proposals from Member States, any regional and subregional consultations, and from other stakeholders;

(d) in carrying out the actions in subparagraphs 2(b) and 2(c), examine the appropriateness of different research and development financing approaches and the feasibility of implementation of these approaches in each of the six WHO regions, with subregional analysis, as appropriate;

(e) observe scientific integrity and be free from conflict of interest in its work;

(3) to provide, upon request, within available resources dedicated to the financing of the Consultative Expert Working Group, technical and financial support for regional consultations, including meetings, in order to seek regional views to help inform the work of the Consultative Expert Working Group;

(4) (a) to invite Member States to nominate experts whose details, following consultations with regional committees to achieve gender balance and diversity of technical competence and expertise, shall be submitted to the Director-General through the respective regional directors;

(b) to establish a roster of experts comprising all the nominations submitted by the regional directors;

(c) to propose a composition of the Group to the Executive Board for its approval, drawing on the roster of experts and taking into account regional representation according to the composition of the Executive Board, gender balance and diversity of expertise;

(d) upon approval by the Executive Board, to establish the Group and facilitate its work including its consultation with the Member States and other relevant stakeholders, where appropriate;

(5) to put particular emphasis on the transparent management of potential conflicts of interest by ensuring full compliance with the mechanisms established by the Director-General for that purpose;

(6) to ensure full transparency for Member States by providing the Consultative Expert Working Group's regular updates on the implementation of its workplan, and by making available all the documentation used by the Consultative Expert Working Group at the conclusion of the process;

(7) to submit the workplan and inception report of the Consultative Expert Working Group to the Executive Board at its 129th session and a progress report to the Executive Board at its 130th session with a view to submitting the final report to the Sixty-fifth World Health Assembly.

EXECUTIVE SUMMARY

The Consultative Expert Working Group on Research and Development: Financing and Coordination (CEWG) was established by the World Health Assembly in 2010 by resolution WHA63.28 with the principal task of deepening the analysis and taking forward the work done by the previous Expert Working Group on Research and Development: Coordination and Financing (EWG) which reported in 2010. Underlying both expert groups was the objective set out in the Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property (GSPA-PHI):

> "to examine current financing and coordination of research and development, as well as proposals for new and innovative sources of financing to stimulate research and development related to Type II and Type III diseases and the specific research and development needs of developing countries in relation to Type I diseases."

In undertaking our work we were mindful of the request that we "observe scientific integrity and be free from conflict of interest" in our work and we also decided to be as open and transparent as possible by providing an open forum during our first meeting, calling for submissions, providing open briefings after each of our meetings, and publishing as much as possible on our web site.[1]

Chapter 1

We describe the background to our work beginning with the establishment of the Commission on Intellectual Property Rights, Innovation and Public Health (CIPIH) in 2003 and set out how we interpreted our terms of reference and our approach to our task. Our focus is on the needs of developing countries for new products (including medicines, vaccines and diagnostics), but we recognize the importance of other kinds of health research relating to health systems, operational and implementation research, the effectiveness of interventions and health-related policy issues.

Chapter 2

We set out the reasons why action is required to address the fact that current incentive systems fail to generate enough research and development, in either the private or public sectors, to address the health-care needs of developing countries. In the case of developing countries, the market failure which intellectual property rights try to correct is compounded by a lack of reliable demand for the products generated by research and development (R&D). Thus the incentive offered by intellectual property rights fails to be effective in correcting the market failure. There is therefore an economic case, based on market failure, for public action. There is also a moral case. We have the technical means to provide access to life-saving medicines, and to develop new products needed in developing countries, but yet millions of people suffer and die for lack of access to existing products and to those that do not yet exist. This is also a matter of human rights as articulated, for instance, in WHO's Constitution, which states that "the enjoyment of the highest attainable standard of health is one of the fundamental rights of every human being without distinction of race, religion, political belief, economic or social condition".

We review recent trends in the pharmaceutical industry more generally, including the fall in the approval of new drugs, including those with new therapeutic effect, while, until recently, R&D expenditures have continued to rise and many existing top-selling medicines are going out of patent. We note the responses of the pharmaceutical industry, including a spate of mergers and acquisitions, a greater focus on emerging markets, and the search for new and better models of innovation often

[1] http://www.who.int/phi/news/cewg_2011/en/index.html

characterized as "open innovation" and involving more open collaboration with external partners. We compare these with the approaches we analyse in Chapter 3.

We review the evidence on health R&D relevant to developing countries, beginning with the pioneering work of the Commission on Health Research and Development (CHRD) in 1990 and subsequent estimates by the 1996 Ad Hoc Committee on Health Research, the Global Forum on Health Research, and latterly the estimates produced by G-Finder. We also review the evidence relating to new product development in the last decade, including products developed by public–private partnerships for product development. We note the importance of linking research strategies to access considerations and, in that context, the relevance of delinking the costs of R&D from the price of products.

We then review in outline the issues relating to financing and coordination of R&D. In respect of financing we note the various recommendations that have previously been made for increased financing of R&D, notably the call of the CHRD for 2% of health expenditures and 5% of development assistance for health to be devoted to health R&D. We also note the four innovative sources of financing reviewed by the EWG, and other proposals, such as the Financial Transactions Tax, which have been proposed as a source of finance for development, including health. As regards coordination, we note the diversity and complexity of the current R&D landscape and also previous recommendations regarding the need for better coordination, including improved priority-setting, coherence and efficiency.

Chapter 3

We focus here on the assessment of the proposals contained in the EWG report, combined with other proposals submitted to us as a result of our call for submissions, which we consolidated into 15 grouped proposals. Appendix 2 sets out our understanding of the EWG process and how we established our own grouped proposals. We then provide an assessment of each of our grouped proposals based on criteria we established, drawing on the more detailed reviews contained in Appendix 3, which are summarized under the headings of public health impact, and technical, financial and implementation feasibility. We also take into account the results of consultations held in five of WHO's regions.

We conclude that the following proposals met our criteria less well: **Tax breaks for companies, Orphan drug legislation, Green intellectual property, Priority review voucher, Transferable intellectual property rights, Health Impact Fund** and **Purchase or procurement agreements.**

This does not necessarily mean that countries or the international community should not adopt such measures, nor that it might not be in their interest to do so. Indeed several of these proposals (e.g. orphan drug legislation or procurement agreements) are already in existence and regarded by many as successful in achieving their objectives. It simply means that, in relation to our terms of reference, we do not think they do, or will, perform well in stimulating R&D needed by developing countries for health-care products for Type I, II and III diseases.

A second category consists of proposals that, irrespective of their other merits, are not principally contributing to improved financing or coordination of research and development. In that category we place **Regulatory harmonization** and **Removal of data exclusivity.**

The third category consists of proposals that we felt best met our criteria: **Global Framework on Research and Development, Open approaches to research and development and innovation,[1] Pooled funds, Direct grants to companies, Milestone prizes and end prizes and Patent pools.**

It would be possible to pursue each of these proposals individually but we see them as part of a wider package of measures that will promote R&D in ways that can also help address access issues. Delinking should be a fundamental principle underpinning open approaches to research and development and innovation. An absolutely necessary condition for implementing these approaches will be a sustainable source of funding.

Chapter 4

We review the four sources of financing assessed in the EWG report: **A new indirect tax, Voluntary contributions from businesses and consumers, Taxation of repatriated pharmaceutical industry profits and New donor funds for health research and development.** Having reviewed the four proposals against the available evidence, we reach the view that some form of taxation is the most fruitful avenue to explore in the search for new and sustainable sources of funding. However, it would be unrealistic, given the multifaceted nature of development needs, to think that one specific new source that would generate very significant amounts of money on a global scale would or should be devoted to the particular field of health R&D of relevance to developing countries. Rather we argue that from any new source of funding that might emerge a portion should be related to the improvement of health as an acknowledged development priority, and that another portion also should be devoted to currently underfunded R&D areas, including those within the CEWG mandate.

We then consider the evidence concerning different forms of taxation that might be suitable as the basis for raising taxes, including for health R&D. In looking at the various tax options we support the principle that taxes should be progressive, bearing more proportionately on the rich than the poor, particularly for sources unrelated to public health (e.g. an airline tax). On the other hand we recognize that particular forms of indirect taxation relevant to public health, such as "sin" taxes related to reducing lifestyle risks, are regressive in nature and that in these cases the public health benefits, particularly for the poor, should outweigh the possible adverse impact on income distribution. At the same time it is important that tax and benefit policies are looked at as a whole; in principle regressive impacts could be offset by changes in other taxes.

We look at the evidence for taxes on fat, sugar and tobacco and their potential for raising revenue. We examine various national examples where countries raise taxes specifically to fund health or health R&D. We consider various proposals for taxes that might raise finance for global purposes. We conclude that countries should first consider at **national level** what tax options might be appropriate to them as a means of raising revenue to devote to health and health R&D. We highlight, in particular, two possible taxes – the Financial Transactions Tax and the Tobacco Solidarity Contribution – that in addition to the airline taxes implemented in some countries could be used to generate funds to be channelled through an **international mechanism** to supplement national resources. We express our hope that such a tax could be agreed as part of an international commitment to finance global public goods, including for health and health R&D relevant to developing countries.

In the context of the overall funding of R&D by governments, we then review the performance against the various goals and targets that have been proposed for national financing of health and health R&D, such as the Abuja target for health spending of 15% of government expenditure, and the CHRD targets. In this respect, the limitations of current data are noted, particularly for developing countries.

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

However the available evidence suggests that most African countries, as also some other regions of the world, are a long way from meeting the Abuja target and the 2% target for health research. Developed countries, on average, meet or exceed both these targets and spend around 0.15% of gross domestic product (GDP) on health research. By contrast, we calculate that only 2.5% of development assistance for health is channelled to R&D, or 1.5% if we include both bilateral and multilateral assistance.

However, in reality, development agencies fund only 15% of total R&D devoted to Type II and III diseases by developed country governments, as the great majority is channelled through government-funded research organizations. For this reason we favour targets which relate R&D effort to GDP as the best available measure for contribution to global public goods. On this measure the largest public funder of relevant research is the USA at about 0.01% of GDP, but several developing countries are also significant spenders.

We conclude that proportionate targets related to health-related public expenditure or development assistance are not the best means of achieving the objective, principally because the denominator is itself not necessarily at its target level. We therefore propose an approach which sets targets that relate a country's effort in R&D spending, relevant to our mandate, to its GDP – a concept that is applicable to both developed and developing countries and takes account of the international public good that can be generated by each country's own R&D spending.

Our principal conclusion is that:

- *All countries should commit to spend at least 0.01% of GDP on government-funded R&D devoted to meeting the health needs of developing countries in relation to the types of R&D defined in our mandate.*

In addition we propose that countries should consider these targets:

- *Developing countries with a potential research capacity should aim to commit 0.05–0.1% of GDP to government-funded health research of all kinds*

- *Developed countries should aim to commit 0.15–0.2% of GDP to government-funded health research of all kinds.*

Chapter 5

We examine, in the light of the actions proposed in the GSPA-PHI, the history of coordination efforts in this field, including the Global Forum for Health Research – now part of the Council on Health Research and Development (COHRED) – and, in particular, the important role of WHO, various related initiatives in WHO, including TDR, and the Advisory Committee on Health Research (ACHR). It is also relevant that WHO has recently finalized its research strategy and new terms of reference for the ACHR, which include monitoring relevant parts of the GSPA-PHI. We also discuss what might be learned from the experience in international agricultural research of the Consultative Group on International Agricultural Research (CGIAR), noting however the very different construction of the health R&D field.

We conclude that coordination is likely to be most effective where it is associated with a funding mechanism that constitutes a significant part of total R&D funding for the disease areas of concern to us. We also believe, as proposed in Chapter 6, that a binding convention would make coordination more effective. Nevertheless, there is much that could and should be done to improve coordination within the existing structures and framework. We also think any proposed coordination, and indeed funding, mechanism should, wherever possible, build on existing institutional structures.

There are major challenges for WHO to address the conclusion of the Second World Health Assembly that "research and coordination of research are essential functions of the World Health Organization". In spite of these challenges, it is our belief that WHO should play a central and stronger role in improving coordination of R&D directed at the health needs of developing countries, and the current WHO reform programme means that this is an opportune time for defining WHO's appropriate role in relation to the coordination of global R&D. We strongly emphasize the need to consider this task as part of the WHO reform process with consequent action and allocation of resources. A key message is that, to do this properly, WHO requires a critical mass of people and resources. If that critical mass is not reached then the objectives will not be achieved. In addition, coordination policies (e.g. avoiding unnecessary duplication, addressing priorities) need to be effectively implemented through appropriate incentives and other measures. If these conditions are not fulfilled, useful things may be done but they will not amount to coordination as we define it.

The key elements of this coordination function under the auspices of WHO would include:

(1) ***A global health R&D observatory.*** *This would need to collect and analyse data, including in the following areas:*

- *financial flows to R&D*
- *the R&D pipeline*
- *learning lessons.*

(2) ***Advisory mechanisms:***

- **a network of research institutions and funders** that may include specialized sections according to the subject of research (e.g. type of disease), based on an electronic platform supported by WHO, and which may provide inputs to the advisory committee;
- **an advisory committee** that could be based on the current ACHR and also the ACHRs of the WHO regions, with suitably revised terms of reference and ways of operation (subcommittees could be established to tackle specific topics and facilitate regional inputs).

Assessing the costs of what we propose would require more detailed work, but would mean only modest allocations with a potentially high impact if R&D coordination is improved. In 2006 the governance and secretariat costs of the CGIAR were estimated at US$13.8 million. This was then about 2% of CGIAR spending on R&D. As a proportion of G-Finder estimated health R&D, it would be less than 0.05%. For comparison, the costs of G-Finder itself are about US$ 1.5 million annually and, as noted above, the estimated costs of the WHO research strategy US$4 million.

Chapter 6

We first summarize our recommendations on the lines noted above. We then state that it is time to consider new ways forward to achieve the objectives that WHO Member States have been grappling with for so long. There is a need for a coherent global framework that combines the different elements and recommendations into a concerted mechanism.

We look at how conventions have been used to pursue objectives in a number of fields, particularly in relation to the environment, and also in WHO's only convention to date – the Framework Convention on Tobacco Control (FCTC). This includes examination of funding mechanisms associated with conventions or their protocols, including the Multilateral Fund and the recently agreed Green Climate Fund. We also analyse the relative merits of "hard" and "soft" law as a means of meeting our objectives. We look at the various provisions in the WHO Constitution for producing agreements,

regulations or recommendations and express our preference for recommending *a binding agreement based on Article 19 of the WHO Constitution.*

The content of an agreement would be determined by the outcome of negotiations between Member States, but we set out the principles and objectives which we think should inform the negotiation process and some ideas about the next steps.

The framework for a possible convention has in many ways already been agreed between Member States in paragraph 14 of the GSPA-PHI.

The proposed convention aims at providing effective financing and coordination mechanisms to promote R&D. We see a convention not as a replacement for the existing intellectual property rights system but as a supplementary instrument where the current system does not function. R&D under the convention should focus on the development of health technologies for Type II and Type III diseases as well as the specific needs of developing countries related to Type I diseases.

We take it as granted that our suggestions are set in the context of a broader framework for health research and that the proposed financing mechanisms and the convention should: i) be supportive of health research in general, including on public health and health systems, ii) not imply resource shifts from other important areas of health research or iii) limit scope for financing of R&D on health needs in developing countries only to particular technologies or options.

To strengthen R&D capacity in, and technology transfer to, developing countries, we see the need for support to:

- Capacity building and technology transfer to developing countries.
- The promotion of partnerships and collaborations based on joint agendas and priority setting related to developing country health needs and national plans for essential health research.
- The development and retention of human resources and expertise.
- Institutional and infrastructure development.
- Sustainable medium- long-term collaborations.

We suggest that the following proposals be considered as part of the framework for a negotiation process for a convention:

Objectives

- Implementing States' obligations and commitments arising under applicable international human rights instruments with provisions relevant to health.
- Promoting R&D for developing new health technologies addressing the global challenges constituted by the health needs of developing countries by means that secure access and affordability through delinking R&D costs and the prices of the products.
- Securing sustainable funding to address identified R&D priorities in developing countries.
- Improving the coordination of public and private R&D.
- Enhancing the innovative capacity in developing countries and technology transfer to these countries.

- Generating R&D outcomes as public goods, freely available for further research and production.
- Improving priority-setting based on the public health needs of developing countries, and decision-making relying on governance structures that are transparent and giving developing countries a strong voice.
- Core elements under the convention should focus on development of health technologies for Type II and Type III diseases as well as the specific needs of developing countries related to Type I diseases.

Financing

- All countries should aim to achieve specified levels of public funding on health R&D relevant to the needs of developing countries.
- Countries could fulfil their financial commitment through contributions to a financing mechanism established under the convention, in combination with domestic spending on R&D undertaken to attain the convention's objectives, or through development assistance where applicable.
- A financing mechanism should be established based on contributions by governments. The convention may determine a level of contribution, taking account of countries' own investments in relevant R&D, either domestically or in other countries. We have suggested a contribution of 20–50% of their total funding obligation to a pooled funding mechanism.
- Such financing may be generated from existing taxpayer resources, from new national revenue-raising measures, or by channelling a portion of the resources raised from any new international mechanism to this purpose. Voluntary additional public, private and philanthropic contributions to a pooled funding mechanism can also be envisaged.
- The convention and its financing mechanisms for the more defined objectives of R&D need to be supportive of the broader context of overall allocation of public financing to health research and the sustainability of financing in other areas of health research.
- The convention should define which research entities in the public and private sectors, in public–private partnerships, and in developed or developing countries, should be eligible for funding.
- Funding should be directed so as to promote cost-effective R&D in ways that will also promote subsequent access to technologies in developing countries, in particular using the tools identified in our report which best meet these criteria, such as open knowledge innovation.
- Funding should also be directed in ways that promote capacity-building and technology transfer to the public and private sectors in developing countries.

Coordination

- A coordination mechanism would help to promote, in particular, the objectives in Element 2.3 of the GSPA-PHI ("improving cooperation, participation and coordination of health and biomedical research and development"), and could be based on the ideas we put forward in Chapter 5.

- The coordination mechanism would need to improve the measurement of the volume, type and distribution of relevant R&D and the evaluation of R&D outcomes, in particular so that progress against commitments and compliance could be measured. This will depend in part on data and reports provided by parties to the convention.

Compliance mechanisms also need to be devised, including through cooperation of the parties to the convention.

Next steps

The issues that will need to be addressed in a negotiation of a binding agreement are many and complex. One of the reasons that the negotiations on the GSPA-PHI took so long was that there was very little preparatory work. We suggest therefore that the World Health Assembly should consider, first, establishing a working group or technical committee composed of two members from each WHO region to undertake preparatory work on the elements of a draft agreement, soliciting inputs as necessary from other Member States, relevant intergovernmental organizations, funders, researchers, the private sector, civil society and academics as necessary. Alternatively, as was done with the FCTC, an open-ended intergovernmental working group could be established with appropriate technical support. The World Health Assembly should also provide for the establishment of an intergovernmental negotiating body open to all Member States to be established under Rule 42 of the World Health Assembly's Rules of Procedure to draft and negotiate the proposed R&D agreement following on from the report of the proposed working group.

CHAPTER 1. INTRODUCTION

This Consultative Expert Working Group (CEWG) was established after a succession of initiatives by WHO Member States going back to 2003. These initiatives were in response to the concern that insufficient resources were being devoted globally to research and development (R&D) to address diseases that principally affect developing countries. This concern centred in particular on the failure of intellectual property rights to stimulate innovation in healthcare products needed by developing countries, and in relation to the constraints created by such rights for access to needed products, especially by the poor.

We set out here the background to our establishment as it is important in understanding the current situation and the nature of our task.

Origins

At the Fifty-sixth World Health Assembly in 2003, the WHO Secretariat presented an information document on intellectual property, innovation and public health. This noted that:

> "...a significant proportion of the world's population, especially in developing countries, has yet to derive much benefit from innovations that are commonplace elsewhere. The reasons range from weak supply systems to unaffordable prices. The factors that drive innovation are often biased against conditions that disproportionately affect the populations of developing countries. ... Innovation to address conditions primarily affecting poor people is held back by a combination of market failure and underinvestment by the public sector. The process of bringing a new product to the market is both expensive and lengthy. Because of the resource implications and the uncertainties involved, creating an environment conducive to successful innovation is essential."(*1*)

The document focused on the need to look at mechanisms for stimulating innovation and the relationship with intellectual property and public health. It reflected issues raised in various recent studies and reports which investigated empirical and policy questions relevant to the relationship between intellectual property rights, innovation and public health.[1]

Drawing on this paper the World Health Assembly adopted a resolution which asked the Director-General to establish "an appropriate time-limited body to collect data and proposals from the different actors involved and produce an analysis of intellectual property rights, innovation, and public health, including the question of appropriate funding and incentive mechanisms for the creation of new medicines and other products against diseases that disproportionately affect developing countries". This body was to submit a final report "with concrete proposals" to the Executive Board (*2*).

In pursuance of this resolution, the Commission on Intellectual Property Rights, Innovation and Public Health (CIPIH) was established in early 2004. In its report, published in April 2006 (*3*), the CIPIH made some 60 detailed recommendations, but its central recommendation was that "WHO should develop a Global Plan of action to secure enhanced and sustainable funding for developing and making accessible products to address diseases that disproportionately affect developing countries."

In response to the CIPIH report, the Fifty-ninth World Health Assembly agreed in 2006 "to establish ... an intergovernmental working group ... to draw up a global strategy and plan of action in order to

[1] For example, the Commission on Macroeconomics and Health (2001) and the United Kingdom Commission on Intellectual Property Rights (2002).

provide a medium-term framework based on the recommendations of the Commission; such strategy and plan of action would aim, inter alia, at securing an enhanced and sustainable basis for needs-driven, essential health research and development relevant to diseases that disproportionately affect developing countries, proposing clear objectives and priorities for research and development, and estimating funding needs in this area."(*4)*

The Intergovernmental Working Group on Public Health, Innovation and Intellectual Property (IGWG), involving over 100 Member States, met three times between December 2006 and May 2008. In May 2008, after protracted negotiations in the IGWG, the Sixty-first World Health Assembly adopted the global strategy and plan of action on public health, innovation and intellectual property (GSPA-PHI) (*5*). The GSPA-PHI has eight elements and a large number of action points for governments, international organizations and other stakeholders. One of the key elements from our perspective is the seventh element: "Promoting sustainable financing mechanisms". The key action in this element was to "establish a results-oriented and time-limited expert working group under the auspices of WHO and linking up with other relevant groups to examine current financing and coordination of research and development, as well as proposals for new and innovative sources of financing to stimulate research and development related to Type II and Type III diseases and the specific research and development needs of developing countries in relation to Type I diseases".[1]

The Expert Working Group on R&D: Coordination and Financing (EWG), composed of 24 members, was established in November 2008 and had three meetings in 2009 before delivering a summary of its report to the Executive Board in January 2010 (*6*) and its final report (*7)* to the Sixty-third World Health Assembly in the same year.

At the consultation prior to the Sixty-third World Health Assembly in 2010, some Member States, mainly those from developing countries, indicated that the report of the EWG had failed to meet their expectations. Some countries considered that proposals they had submitted had been rejected without due consideration or explanation. Other specific concerns included:

- Insufficient attention had been paid to the need to delink the costs of research and development from the price of health products.
- The criteria used to evaluate proposals did not take proper account of the relevant aspects of intellectual property rights.
- The proposals for innovative financing mechanisms were common to those made for financing health and development in general.
- Little attention had been paid to research into the broader health systems barriers that limit access to care.
- Proposals to improve limitations in current coordination mechanisms were absent.

At the consultation, several Member States acknowledged the limitations of current coordination mechanisms in the field of R&D. While mechanisms existed in relation to specific diseases, a mechanism that provided a comprehensive overview in terms of activities and resource flows remained elusive. It was suggested by several Member States that WHO should have a more proactive role in this area (*8*).

[1] *Type I diseases* are incident in both rich and poor countries, with large numbers of vulnerable populations in each. *Type II diseases* are incident in both rich and poor countries, but with a substantial proportion of the cases in poor countries. *Type III diseases* are those that are overwhelmingly or exclusively incident in developing countries.

At the Health Assembly itself, most speakers from developing countries voiced these and other concerns about the report and suggested the need for a new expert group or an intergovernmental process to remedy its perceived deficiencies. Member States eventually agreed to the resolution setting up "a consultative expert working group on research and development: financing and coordination."(*9*)

Our approach

Therefore our task is:

> "to examine current financing and coordination of research and development, as well as proposals for new and innovative sources of financing to stimulate research and development related to Type II and Type III diseases and the specific research and development needs of developing countries in relation to Type I diseases"

In addition we are asked to "take forward the work of the Expert Working Group" and "deepen the analysis of the proposals in the Expert Working Group's report, and in particular:

> (i) examine the practical details of the four innovative sources of financing proposed by the Expert Working Group in its report;
>
> (ii) review the five promising proposals identified by the Expert Working Group in its report; and
>
> (iii) further explore the six proposals that did not meet the criteria applied by the Expert Working Group;"

These proposals are set out in Table 1.1.

Table 1.1 Proposals stemming from the work of the EWG and noted in resolution WHA63.28

Four innovative financing sources (section 5.3 of the EWG report)
A new indirect tax
Voluntary contributions from businesses and consumers
Taxation of repatriated pharmaceutical industry profits
New donor funds for health research and development
Five promising proposals (section 5.6)
Open source
Patent pools (UNITAID model)
Health impact fund
Priority review voucher
Orphan drug legislation
Six further proposals (Appendix 2)
Transferable intellectual property rights
Green intellectual property

Removal of data exclusivity
Biomedical research and development treaty
Large end-stage prizes (impact-based rewards)
Neglected disease tax breaks for companies.

Apart from the proposals that it specifically identifies, the resolution also asks us to consider additional submissions and proposals from Member States, from any regional and subregional consultations, and from other stakeholders. However, the resolution is silent about whether we should deal with five proposals in section 5.4 of the EWG report (described as "Approaches to funding allocation") and two proposals in section 5.5 of the report ("Proposals to improve efficiency") (see Table 1.2).

Table 1.2 Proposals stemming from the work of the EWG but not noted in resolution WHA63.28

Five proposals relating to funding allocation (section 5.4 of the EWG report)
Product development partnerships
Direct grants to small companies and for trials in developing countries
"Milestone" prizes
"End" prizes (cash)
Purchase or procurement agreements
Two proposals to improve efficiency (section 5.5 of the EWG report)
Regulatory harmonization
Precompetitive research and development platforms

At our first meeting in April 2011 (see Appendix 1) we decided it was appropriate to analyse all 22 proposals referred to in the EWG report (i.e. those in tables 1.1 and 1.2) together with any new or revised proposals submitted by Member States or other stakeholders. We also wanted Member States and other stakeholders, if they wished, to resubmit any proposals from among the 109 that had originally been compiled by the EWG, or any other proposals that they felt had not received proper consideration by the EWG. To make sure that we understood the landscape of proposals and mechanisms being considered by EWG, we did a mapping of the 109. This is described in Appendix 2.

That is why we decided to launch immediately after our first meeting an invitation to submit proposals so that stakeholders could make known to us new or revised proposals that related to the 22 EWG proposals, as well as any other proposals that the EWG, for one reason or another, had not addressed adequately. As a result of this call we received 22 proposals which we analyse, along with the 22 EWG proposals, in Chapter 3 and Appendix 3.

At the first meeting we decided that our focus should be the financing and coordination of research and development for health products and technologies (including, for example, medicines, vaccines, diagnostics, devices and delivery technologies) related to Type II and Type III diseases and the specific research and development needs of developing countries in relation to Type I diseases, and we define this as the scope of R&D in line with our mandate. However, we also acknowledge the importance of other relevant areas of health research which may require additional financing and/or improved coordination such as:

- better policies for research and development and innovation;
- improved public health, clinical and preventive interventions including, for example, diagnostic algorithms;
- health policy and health systems, to improve delivery and access to new and existing products.

In Chapters 2 and 4 we present some data both on total health R&D investments and on investments on R&D for Type II and Type III diseases. However, no aggregated data on investments exist for R&D in line with our mandate.

We were also keen to recognize the links between our specific mandate and the other elements of the GSPA-PHI. We decided that our core mandate centred on element 2 (Promoting research and development) and element 7 (Promoting sustainable financing mechanisms). However, it was also important to take account of research and development needs and priorities (element 1), improving innovative capacity (element 3), technology transfer (element 4) and intellectual property management (element 5). Moreover we recognized the central importance of ensuring that research and development policies took account of the need to improve availability, acceptability and affordability to contribute to improved delivery and access (element 6). And it also became increasingly clear to us that element 8 (Establishing monitoring and reporting systems) was critical.

Our terms of reference also asked us to consider the views of regions and sub-regions and to examine the appropriateness of different approaches to R&D financing and the feasibility of implementation of these approaches at that level. We felt it would be very challenging for us to analyse the regional appropriateness of different proposals within the time available to us, and that a full assessment should be carried out by local policy-makers who would be able to take regional and national issues into account in ways that we could not. However, we did our utmost within the limited resources available to us to organize regional consultations which we found most helpful. Appendix 4 provides details of the meetings we held in five of the six WHO regions. Unfortunately it proved impossible to arrange a consultation in the Eastern Mediterranean Region.

We were also very mindful, in light of the problems experienced by the EWG, of the requirement to "observe scientific integrity and be free from conflict of interest" in our work and to take account of the views expressed by Member States at the 128th session of the WHO Executive Board in 2010 (*10*). We discussed the determination by WHO legal officers that four members of the CEWG were judged to have relevant conflicts of interest (see Box 1.1). We were informed that it was WHO's policy to be transparent about conflicts of interest, and to seek to manage such conflicts while bearing in mind the contributions that individuals could make to public health in spite of a declared conflict of interest. After due consideration, it was agreed that any members of the CEWG would be free to raise the issue of the potential conflict of interest of any other members at any time during discussions if they considered it relevant, and that the CEWG would then agree how to address any perceived conflict of interest in relation to the topic being discussed. In the particular case of Professor Herrling, it was agreed that he should excuse himself from participating in the discussion of the proposal that he and his employer had sponsored (see Appendix 3).

Box 1.1 Declared conflicts of interest

Professor Rajae El Aouad (Morocco) holds a patent relating to the use of synthetic peptides of M.Tuberculosis for immunodiagnosis of tuberculosis and new vaccine design.

Mr Shozo Uemura (Japan), in his capacity as a patent attorney, works for a law firm that provides advice on a range of legal matters relating to patents held by a variety of pharmaceutical clients.

Professor Bongani Mayosi (South Africa) is Professor and Head, Department of Medicine, Groote Schuur Hospital and University of Cape Town, and his department has received funding from several pharmaceutical companies for a variety of institutional research projects.

Professor Paul Herrling (Switzerland) is currently Chair of the Board of Novartis Institute for Tropical Diseases. Furthermore, he was the sponsor of a proposal under review by the CEWG.

Outline of the report

In Chapter 2 we provide an overview of the issues relevant to our terms of reference. In Chapter 3 we analyse specifically the proposals of the EWG and those submitted to us. In Chapter 4 we address the issue of sustainable financing, including analysis of the EWG proposals on sources of financing. In Chapter 5 we review the need for coordination, while in Chapter 6 we propose how our recommendations can be implemented through a convention.

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CHAPTER 2. SETTING THE SCENE: THE ISSUES

In this chapter we provide a brief review of the wider issues relevant to our terms of reference.

The need for action

The fundamental premise of the World Health Assembly resolution that established the CEWG is that current incentive systems fail to generate enough research and development, in either the public or private sectors, to address the needs of developing countries. The GSPA-PHI states that "further funding on a sustainable basis is essential to support a long-term research and development effort for products to meet the health needs of developing countries."(*1*)

In developed countries, intellectual property rights are regarded by many as one of the most important incentives to invest in pharmaceutical R&D: these rights allow companies to temporarily exclude competition and recoup investment costs. In the absence of such rights, the private sector has less incentive to invest in R&D; economists call this an example of market failure. With intellectual property rights, supported by a reliable market for the products generated by R&D, the private sector has incentives to develop and market products to address health needs where commercial prospects exist.

But this is not always the case. For instance, a particular cause for concern currently is the low level of investment in R&D on antibiotics. Antibiotics, by controlling the spread of disease when appropriately taken, confer a positive health benefit on others. Moreover, the spread of resistance to antibiotics is detrimental to public health and necessitates further R&D which is insufficiently incentivised and scientifically challenging. Vaccines are another example where investment in R&D is considered low. In these circumstances, and with short treatment periods for antibiotics and vaccines compared to treatments for chronic diseases, it is argued that industry invests too little in antibiotics and vaccines (*2*). Ways are now being sought to overcome this serious market failure, some of which are similar to the proposals we analyse in Appendix 3. (*3*) (*4*) (*5*) (*6*)

The CIPIH noted in 2006 that in developed countries:

> "For conditions such as cancer and asthma, incremental improvements are commonplace, and companies have a reasonable assurance that health-care providers and patients will purchase their products. That provides the basic economic and financial incentive for innovation. Whatever the various problems encountered in the innovation cycle, either technical or in terms of the policy framework..., it broadly works for the developed world and sustains biomedical innovation directed at the improvement of public health."(*7*)

As we discuss below, much has changed in the last five years or so in developed countries. Health-care budgets are under increasing strain as the costs of new treatments rise, along with life expectancy, and as the R&D challenges of finding treatments for diseases which particularly affect older people are faced. Given the strains on the system, there are policy initiatives to align better commercial incentives and actions by the public sector with health needs, while also seeking to minimize costs.

However, the CIPIH said:

> "For developing countries, where the demand is weak – but not the need – there is little incentive to develop new or modified interventions appropriate to the disease burden and conditions of the country. This economic reality introduces an important gap in the innovation cycle: either no products exist in the first place, or if they do, then there is often disproportionately small effort, globally, to make them more effective and affordable in poorer

> communities. Broadly speaking, the innovation cycle does not work well, or even at all, for most developing countries**…**

Where the market has very limited purchasing power, as is the case for diseases affecting millions of poor people in developing countries, patents are not a relevant factor or effective in stimulating R&D and bringing new products to market". (*7*)

In the case of developing countries, the market failure which intellectual property rights try to correct is compounded by a lack of reliable demand for the products generated by R&D. So the incentive offered by intellectual property rights fails to be effective in correcting the market failure. This is the basic economic case for further action to develop diagnostics, medicines and vaccines that are needed in developing countries. It is the reason why the public sector needs to play a role either directly or through the provision of incentives for private sector investment. This applies not just to the so-called neglected diseases (Type II and Type III) but also to needs of developing countries to address Type I diseases in their particular economic, social and cultural circumstances.

The CIPIH also made a moral case:

> "While we have the technical capacity to provide access to lifesaving medicines, vaccines or other interventions, which are indeed widely available in the developed world, millions of people, including children, suffer and die in developing countries because such means are not available and accessible there. Governments around the world have recognized the force of this moral argument, but there is still a large gap between rhetoric and action." (*7*)

The moral case for making existing life-saving products available applies equally to products that are needed but have not yet been developed. Men, women and children are suffering because there are no appropriate treatments for the diseases they face. Control and elimination of many of the neglected tropical diseases require the development of new tools.[1] In spite of renewed efforts, no new tuberculosis drugs have been developed in nearly 50 years.[2] New formulations to treat children with AIDS are desperately needed.[3] The R&D needs related to addressing noncommunicable diseases in the circumstances of developing countries are potentially large but as yet unexplored.

The moral case is also an aspect of the commitments governments have entered into in relation to human rights. The International Covenant on Economic, Social and Cultural Rights recognizes "the right of everyone to the enjoyment of the highest attainable standard of physical and mental health"[4] which builds on the first article in WHO's Constitution that WHO's objective "shall be the attainment by all peoples of the highest possible level of health" and its declaration that "enjoyment of the highest attainable standard of health is one of the fundamental rights of every human being without distinction of race, religion, political belief, economic or social condition."(*8*)

The Special Rapporteur on the right of everyone to the enjoyment of the highest attainable standard of physical and mental health applied human rights principles to R&D in a report to the Human Rights Council in 2008 where he was asked "to identify and explore the key features of an effective,

[1] For more information see *Disease summaries* press release at: http://unitingtocombatntds.org/downloads/press/ntd_event_disease_summaries.pdf.

[2] See description of *Inadequate treatment* at http://www.tballiance.org/why/inadequate-treatment.php.

[3] For more information see DNDi press release on *DNDi launches new drug development programme to address treatment needs of children with HIV/AIDS* at http://www.dndi.org/press-releases/928-paediatric-hiv.html .

[4] For more information see the International Covenant on Economic, Social and Cultural Rights on the web site of the Office of the United Nations High Commissioner for Human Rights at http://www2.ohchr.org/english/law/cescr.htm.

integrated and accessible health system from the perspective of the right to health". Among other things he concluded:

> "The right to the highest attainable standard of health encompasses an obligation on the State to generate health research and development that addresses, for example, the health needs of disadvantaged individuals, communities and populations. Health research and development includes classical medical research into drugs, vaccines and diagnostics, as well as operational or implementation research into the social, economic, cultural, political and policy issues that determine access to medical care and the effectiveness of public health interventions."(*9*)

Thus we see a need to act based on economics and morality and the obligations of States to fulfil human rights.

Trends in R&D in the pharmaceutical industry

The global pharmaceutical industry is in a state of transition, or crisis according to some analysts. (*10*) The principal symptom of this state of affairs is the decline in the number of new medicines approved for use at a time when expenditures on research and development, until very recently, were expanding rapidly.

For example, the United States Food and Drug Administration (FDA) provides data on "original new drug approvals", including "new molecular entities" and new "biologics", approved for the first time in the United States market.[1] The latter have declined from an average of over 33 in 1995–2001 to under 19 in 2005–2011. The number of new molecular entities and new biologics that, prior to approval, appeared to the FDA to promise an advance over available therapies (which FDA classifies as "priority review") has fluctuated between a peak of 19 in 1999 and a trough of five in 2009. In 2011, 10 of the 24 approvals in this category were classified as "priority" and 14 as "standard review" – products appearing to the FDA to have therapeutic qualities similar to those of an already marketed drug, and often colloquially known as "me-too" drugs. Over the whole period 1990–2011, 42% of the new molecular entities and biologics were classified as "priority review".[2] The therapeutic impact of new patented medicines is assessed following marketing approval and reported in the annual reports of the Canadian Patented Medicine Prices Review Board on the basis of whether the new medicines represent "no, slight or moderate improvement" or are "breakthroughs".[3]

At the same time, R&D investments, as reported by member companies of the Pharmaceutical Research and Manufacturers of America (PhRMA), increased from US$ 15 billion per year in 1995 to US$ 49 billion in 2010.[4] Figure 2.1 plots R&D investments, as reported by PhRMA, against original new drug approvals for new molecular entities and biologics reported by the FDA.

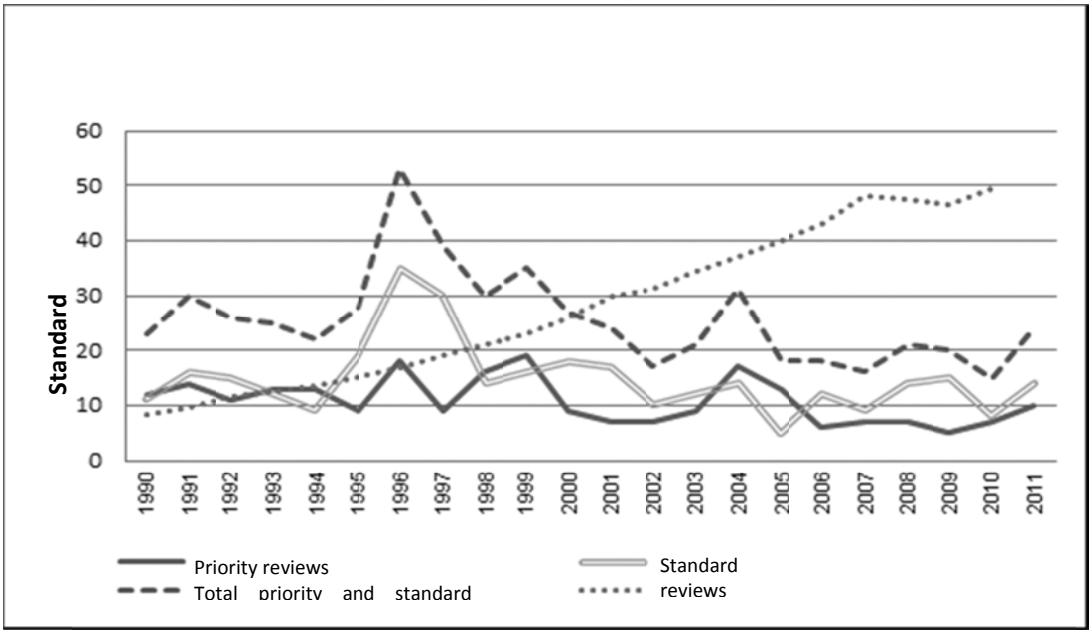
[1] See: http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?fuseaction=Reports.ReportsMenu .

[2] See: http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?fuseaction=Reports.ReportsMenu.

[3] For more information see: http://www.pmprb-cepmb.gc.ca/english/View.asp?x=91.

[4] See: *2011 Profile by* PhRMA http://www.phrma.org/sites/default/files/159/phrma_profile_2011_final.pdf. These figures are based on companies' data reported to PhRMA, and have not been independently checked particularly regarding what items are considered as a component of R&D.

Figure 2.1 Number of new drug approvals and R&D expenditures (as reported by PhRMA) (US$ billions) in the United States of America, 1990–2011



Source: FDA and PhRMA

As a direct result of the fall in new approvals, patents expiring on existing products are not being replaced by new patented products with comparable commercial prospects. In addition, the return from each new drug has declined. A recent study calculated that productivity in terms of sales generated per dollar of research and development spending had fallen by 70% between 1996–2004 and 2005–2010. (*11*) Similar conclusions were reached by, among others, an analysis by the Organisation for Economic Co-operation and Development (OECD) in 2008 (*12*) and a study by the United States Government Accounting Office in 2006. (*13*)

One reason for the change is that for many chronic conditions with very large markets there are now safe and effective therapies increasingly provided, as patents expire, by generic companies. Generic prescriptions now account for 78% of the United States market by volume, up from 49% in 2000.[1] There are also scientific challenges in addressing the most common diseases where good therapies do not currently exist (e.g. cancers and degenerative diseases).

Health-care budgets in developed countries are increasingly under scrutiny. On the one hand it is difficult to generate a return on so-called "me-too" drugs because purchasers increasingly relate willingness to pay to incremental health benefits. (*14*) On the other hand the new priority drugs, so-called "breakthroughs", in oncology or degenerative conditions are often highly-priced and encounter resistance from paying authorities if, for example, they extend life by only a few months. The sensitivity of regulatory authorities to risk appears to have increased, perhaps as a reflection of the lower incremental benefits against which risks are now more frequently assessed.

[1] See: *2011 Profile* by PhRMA http://www.phrma.org/sites/default/files/159/phrma_profile_2011_final.pdf.

Associated with this "crisis" in R&D has been a massive round of mergers and acquisitions in the industry. Out of the 42 members of PhRMA in 1988, only 11 remain today. Each merger results in the rationalization of the merged entities' research infrastructure in a search to realize "synergies" and cost savings sufficient to justify the costs of acquisition. As a result the number of traditional PhRMA companies researching any particular area has declined, although clearly the growth of biotechnology companies and start-ups has offset this to some extent. Thus, for many observers, the consolidation of the industry is as much a cause of the decline in R&D productivity as a solution to it. A former President of Research at Pfizer estimates that R&D expenditures by Pfizer in 2012 will be US$ 6.5–7 billion, compared with joint expenditures of US$ 11.3 billion in 2008 before Pfizer took over Wyeth. Bigger is not necessarily better – the merged pipeline of products in development often seems to be less than the sum of its parts. In addition, mergers can be hugely disruptive to ongoing research programmes and damaging to staff morale. (*15*.

Hard times and changed circumstances have also brought about new thinking. On the one hand, while developed country markets are now growing very slowly, the so-called emerging markets offer opportunities for rapid growth. Thus IMS Health estimates the share of the United States and European markets will decline from 68% to 50% in the period between 2005 and 2015.[1] By contrast, the global market share of 17 high-growth emerging markets will increase from 12% to 28% in the same period. But the growth in these markets will predominantly be of generic products, implying the need for repositioning by traditional brand-name pharmaceutical companies.

That is one reason these companies have been forming new alliances or even takeovers of companies in emerging markets, particularly India where the growth of the generic industry is most advanced. (16) This new market-driven orientation also offers a possible incentive to develop and adapt products suited to the health needs of people in emerging markets and developing countries, and to adopt new pricing and marketing strategies which reflect the realities of marketplaces characterized by a highly unequal distribution of incomes, where governments and health insurance schemes are responsible for a relatively small proportion of total purchases. A new generation of leaders in the pharmaceutical industry is seeking to solve the dilemma of how to deliver value to their shareholders while meeting expectations that they should promote "the public good". (*17*)

Another response of the pharmaceutical industry, along with some governments and funding bodies, has been to reconsider the way they conduct research and development. If the existing business model is not working, new approaches are required. One approach is that of "open innovation", a term coined by a United States academic, Henry Chesbrough. (*18*) In essence this means moving from a "closed" model where all phases of the R&D process are conducted in-house to one where the external environment (e.g. universities, research institutions, start-ups, biotech companies) is actively scanned for, and involved in, the development of promising technologies or compounds. This approach seeks to maximize the possibility of identifying the most promising technologies or compounds while spreading the costs of failure (which account for a large part of the costs of drug development) more widely. Greater openness and collaboration with external partners challenge the conventional management of intellectual property in the pharmaceutical industry, but "open innovation" does not depend on abandoning it. Rather, it involves the use of various licensing strategies that facilitate collaboration while preserving key rights of value to the licensor. Chesbrough provides an example of "open innovation" in the field of malaria (see Box 2.1). In 2011 Eli Lilly launched its Open Innovation Drug Discovery initiative[2] and in 2010 Pfizer started a partnership with academic institutions in its

[1] See: *Global Pharmaceutical Market Outlook: 2015, Express Pharma,* http://www.expresspharmaonline.com/20120115/market02.shtml.

[2] For more information see: https://openinnovation.lilly.com/dd/docs/oidd_executive_summary.pdf.

Global Centers for Therapeutic Innovation initiative[1]. The Innovative Medicines Initiative, a partnership between the European Commission and European industry, is another example of fostering collaboration between multiple partners in the public and private sectors. (*19*)

Box 2.1 Amyris: an example of "open innovation"

Amyris is a fascinating example of open innovation in practice. This company started up at Berkeley in California, USA, using synthetic biology research discoveries at the university to programme bacterial organisms to excrete useful chemical compounds. Amyris' initial compound was artemisinin, which is an active ingredient for treating malaria in developing countries. The Bill & Melinda Gates Foundation funded the work to create this drug at Amyris, and then helped Amyris license it to Sanofi-Aventis for international distribution. Thus open innovation changes pharmaceutical development from a marathon (where the pharmaceutical company does all the work internally) to a relay race (where different parties take the baton for different parts of the race, from university to start-up to large pharma, with multiple and different funding sources).

However, the story does not end there. Amyris licensed its technology to Sanofi-Aventis for malaria medicines, but reserved to itself the intellectual property rights using the synthetic biology processes it developed for other applications. The one that the company focused on was using bacteria to excrete precursors for biofuels (a much larger market than antimalarial drugs). Thanks to the malarial work, the company already had a proof-of-concept that they had scaled up into pilot production, and had licensing revenues from Sanofi-Aventis to offset part of their development costs. This reduced the capital required for the biofuels opportunity, as well as the time to market and the business risk. The company was able to raise venture capital because of these improved risk factors, and Amyris became a public company in the spring of 2010, earning a nice return for its venture capital investors.

Source: Chesbrough H. Pharmaceutical innovation hits the wall: how open innovation can help. Forbes, 25 April 2011 http://www.forbes.com/sites/henrychesbrough/2011/04/25/pharmaceutical-innovation-hits-the-wall-how-open-innovation-can-help

It is difficult to define "open innovation" since almost any form of collaboration with outside parties can be described as such; there is no defining methodology or use of intellectual property which clearly separates one type of collaboration from another. However, the open innovation approach described here is different from the approaches discussed in Appendix 3 which we see as conforming in general with the definition of "open knowledge".[2] These include open source drug discovery, open access publishing, precompetitive R&D platforms and equitable licensing. In policy discussions some of these terms are often used quite loosely and in some cases more or less interchangeably. (*20*) We would prefer to distinguish more clearly between the open innovation approach espoused by Chesbrough, which focuses on how individual companies can benefit by a more open approach to external collaboration, and open approaches where the problem or opportunity is the focus of attention and there is more open sharing of information between multiple partners, including the principle that research results should be in the public domain. (*21*)

It is notable that many of the initiatives of the last decade or so which have been aimed at promoting the development of new products to address diseases prevalent in developing countries involve new approaches to R&D (Box 2.2). Thus product development partnerships (PDPs), and other initiatives such as the Open Source Drug Discovery project in India, are regarded by some as leading the way "in exploring new business models for broader pharmaceutical R&D" (*22*).

[1] For more information see: http://www.imi.europa.eu/content/history.

[2] See: http://opendefinition.org

Box 2.2 Public–private partnerships for product development

These arose largely as a result of initiatives on the part of individuals in companies, foundations, nongovernmental organizations and WHO. The first of the recent wave of these public–private partnerships was the International AIDS Vaccine Initiative (IAVI), founded in 1996 on the initiative of the Rockefeller Foundation. These initiatives now include the following:

HIV/AIDS

International AIDS Vaccine Initiative (IAVI)
International Partnership for Microbicides (IPM)
South African AIDS Vaccine Initiative (SAAVI)

Malaria

European Malaria Vaccine Initiative (EMVI)
Malaria Vaccine Initiative (MVI)
Medicines for Malaria Venture (MMV)

Tuberculosis

Aeras Global Tuberculosis Vaccine Foundation (Aeras)
Foundation for Innovative New Diagnostics (FIND)
Global Alliance for TB Drug Development (TB Alliance)

Other "neglected infectious diseases"

Drugs for Neglected Diseases Initiative (DNDi)

In addition, the Institute for OneWorld Health, a nonprofit pharmaceutical company, develops new affordable medicines for infectious diseases that disproportionately affect people in developing countries, including visceral leishmaniasis, malaria, diarrhoea and Chagas disease.

Common characteristics of these public–private partnerships include:

- They contract work externally – by forging collaborations with others in the public and private sectors.
- They target one or more "neglected diseases".
- They use, or intend to use, variants of the multi-candidate/portfolio management approach.
- Their primary objective is public health and access rather than a commercial goal.
- Their principal funders to date have been foundations rather than governments.

Source: CIPIH report

Research and development relevant to developing countries

Expenditure estimates and sources of funding

In 1990 the Commission on Health Research and Development (CHRD) estimated, on the basis of its own survey, that in 1986 out of US$ 30 billion of health research worldwide, US$ 1.6 billion was oriented to the needs of developing countries. Of this, US$ 685 million was spent in and by developing country institutions, overwhelmingly funded by governments, and only eight countries accounted for three quarters of this spending. The balance of US$ 950 million was provided by developed countries, of which industry contributed an estimated US$ 300 million and governments (including through development assistance) contributed US$ 590 million. Foundations and NGOs contributed just US$ 60 million. The commission estimated that only 5%, or US$ 1.6 billion, of total spending was devoted to the health problems of developing countries. (*23)*

In 1996 the Ad Hoc Committee on Health Research Relating to Future Intervention Options published another careful study of spending on health R&D in 1992. (*24*) It calculated that total global investment had increased to US$ 55.8 billion. It estimated that governments accounted for US$ 28.1 billion of this expenditure, of which governments in developing countries provided US$ 1.2 billion. The pharmaceutical industry contributed US$ 24.7 billion, and the not-for profit sector US$ 3 billion. The report also sought to estimate the amount of this spending devoted to the health problems of developing countries. Using a variety of approaches, it concluded that the amount was US$ 2.4 billion (or 4.3% of global spending on health research). Of this amount, developing country governments spent US$ 1.2 billion, US$ 680 million came from developed country governments (of which US$ 380 million was through development assistance), US$ 400 million came from the pharmaceutical industry and US$ 80 million from nonprofit organizations.

The Global Forum for Health Research, set up in 1998 at the instigation of the 1996 Ad Hoc Committee, coined the phrase "the 10/90 Gap", indicating that 10% of research was devoted to 90% of the world's health problems. Ironically this appears to have been derived from the calculations of the CHRD, although the CHRD never referred to this ratio. Rather more dramatically, the CHRD said that an "estimated 93% of the world's burden of preventable mortality (measured as years of potential life lost) occurs in the developing world... [yet] only 5% [of research] was devoted specifically to health problems of developing countries...For each year of potential life lost in the industrialized world, more than 200 times as much is spent on health research as is spent for each year lost in the developing world". (*23*) The Global Forum for some years published intermittent reports on research spending. It is estimated that in 2005 total global health research spending was US$ 160 billion, of which the public sector accounted for US$ 66 billion and the private sector US$ 94 billion. The amount spent by the public sector in developing countries was estimated at US$ 3 billion, of which some US$ 0.6 billion was provided by development assistance. (*25*)

Since 2008 annual surveys, known as G-Finder and funded by the Bill & Melinda Gates Foundation,[1] have been undertaken to assess global R&D funding for neglected diseases. G-Finder quantifies investments that meet three criteria: 1) where the disease disproportionately affects people in developing countries, 2) where there is a need for new products and 3) where there is a market failure. Broadly this means Type II and Type III diseases, but not the needs of developing countries in relation to Type I diseases.

The latest G-Finder report finds that nearly US$ 3.2 billion was invested in such research in 2010. (*26*) Of this amount, it is estimated that 65% came from public sources, 18.5% from philanthropic sources and 16.4% from industry. Developing country governments in the relatively small G-Finder sample (just 12 countries, not including China or several other large developing countries with innovative capacity) provided less than $70 million. This amount seems implausibly low as an estimate of total developing country spending if the figures estimated by the CHRD and subsequently are correct. Thus a better measure of progress since 1986 might be to compare the other components of research. For instance, public funding for "neglected" diseases in developed countries has increased substantially from US$ 590 million in 1986 to US$ 1.925 billion in 2010, an increase of nearly 90% in real terms (Table 2.1)[2].

[1] See: http://www.policycures.org/projects.html

[2] For more information see: Implicit Price Deflator US Bureau of Economic Analysis http://www.bea.gov/national/index.htm.

Table 2.1 Top neglected disease funders, 2010 (2007 US$)

Funder	2010 (US$)	2010 (%)
United States National Institutes of Health (NIH)	1 211 704 054	39.6
Bill & Melinda Gates Foundation	455 832 350	14.9
Aggregate pharmaceutical and biotechnology companies*	503 525 794	16.4
European Commission	92 529 756	3.0
United States Department of Defence (DOD)	69 942 925	2.3
United States Agency for International Development (USAID)	85 975 465	2.8
United Kingdom Department for International Development (DFID)	97 229 720	3.2
Wellcome Trust	80 459 662	2.6
United Kingdom Medical Research Council (MRC)	60 857 019	2.0
Dutch Netherlands Ministry of Foreign Affairs	-	-
Inserm – Institute of Infectious Diseases	20 196 417	0.7
Institut Pasteur	45 158 519	1.5
Australian National Medical Health and Medical Research Council	19 464 047	0.6
Subtotal top 12 funders	2 742 875 728	89.6
Total R&D funding	**3 062 669 973**	**100**

* Includes new survey respondents in 2009 and 2010

Source: G-Finder Report 2011

However, the most striking feature has been the rapid increase in funding from foundations, which increased from just US$ 60 million in 1986 to US$ 568 million in 2010, amounting to perhaps a five-fold increase in real terms and nearly 19% of total funding monitored by G-Finder. Of this, philanthropic funding from the Bill & Melinda Gates Foundation accounted for 80%. Over half of its funding goes to product development partnerships and over half of funding of product development partnerships comes from the foundation. By contrast, industry funding, at just over US$ 500 million in 2010, appears to have stagnated or declined in real terms since 1986. However, it seems probable that the estimates for industry, as well as developing country expenditure, are probably the least accurate estimates in both 1986 and 2010, so these trends should be interpreted cautiously (Table 2.2).

Table 2.2 Top product development partnership funders, 2010 (reported in 2007 US$)

Funder	To PDPs 2010 (US$)	Proportion of total spending by funder (%)	Share of total PDP funding 2010 (%)
Bill & Melinda Gates Foundation	253 755 901	55.7	52.5
United Kingdom Department for International Development (DFID)	97 229 720	100.00	20.1
United States Agency for International Development (USAID)	40 243 034	46.8	8.3
Dutch Netherlands Ministry of Foreign Affairs	15 833 146	92.1	3.3
Royal Norwegian Ministry of Foreign Affairs	9 047 299	100.0	1.9
European Commission	7 914 688	8.6	1.6
Spanish Ministry of Foreign Affairs and Cooperation for Development (MAEC)	7 159 668	100.0	1.5

Funder	To PDPs 2010 (US$)	Proportion of total spending by funder (%)	Share of total PDP funding 2010 (%)
Irish Aid	6 508 789	99.7	1.3
Médecins Sans Frontières (MSF)	4 725 479	100.0	1.0
Swedish International Development Agency (SIDA)	4 231 695	31.9	0.9
Swiss Agency for Development and Cooperation	3 764 103	86.2	0.8
World Bank	2 757 154	100.0	0.6
Subtotal top 12 PDPs funder*	453 170 675	56.9	93.8
Total PDP funding	483 166 820		
% of total PDP funding (top 12)	**93.8**		

Source: G-Finder Report, 2011

Over 70% of recorded G-Finder expenditure goes to fund R&D on HIV/AIDS, malaria and tuberculosis (Table 3). Of this amount, 43% is provided by the US National Institutes of Health (NIH), accounting for 78% of total NIH funding. A further 14% each is provided by the Bill & Melinda Gates Foundation, accounting for 68% of its funding, and by industry, accounting for 63% of its expenditure. Thus total funding for R&D is quite concentrated in terms of its source, and in terms of its disease coverage.

Table 2.3 Total R&D funding by disease, 2010 (2007 US$)

Disease	2010 (US$)	2010 (%)
HIV/AIDS	1 073 033 520	35.0
Tuberculosis	575,361,902	18.8
Malaria	547 042 394	17.9
Dengue	177 643 516	5.8
Diarrhoeal diseases	158 918 128	5.2
Kinetoplastids	147 867 513	4.8
Bacterial pneumonia & meningitis	92 866 038	3.0
Helminth infections (worms & flukes)	73 685 406	2.4
Salmonella infections	43 982 149	1.4
Leprosy	8 840 532	0.3
Buruli ulcer	5 456 026	0.2
Trachoma	4 507 718	0.1
Rheumatic fever	1 736 877	0.1
Platform technologies	27 358 501	0.9
Core funding of a multi-disease R&D organization	76 884 279	2.5
Unspecified disease	47 485 474	1.6
Disease total	**3 062 669 973**	**100.0**

Source: G-Finder Report, 2011

Research outcomes

It may be asked what impact the renewed interest in R&D relevant to developing countries, particularly on the part of foundations and governments, has had in terms of new products developed. An influential article published in 2002 estimated that of 1393 new chemical entities (NCEs) marketed between 1975 and 1999, only 16 targeted ‘‘tropical diseases’’ and tuberculosis. (*27*) A recent review reassessed the original study and sought to evaluate progress since 2000. Using the same methodology as the original study, it concluded that 32 relevant entities had been marketed in 1975–1999 based on the original study definitions, and 46 on the wider G-Finder definition (which includes, inter alia, paediatric HIV research). Between 2000 and May 2009, it identified 26 new products that had been approved on the G-Finder definition. Of those, 10 were for HIV/AIDS and 11 for malaria. It also found that the proportion of approved products sponsored by private industry had declined from 83% to 46% over the same period while those sponsored by PDPs had increased from 15% to 46%. In addition, it identified 97 relevant products in development, of which 68 were for HIV/AIDS, tuberculosis and malaria. The study concluded that there had been progress in neglected product development, particularly in malaria, but that it was very uneven. For instance, there had been no new products for tuberculosis or vaccines or microbicides for HIV/AIDS, or for Buruli ulcer, dengue fever, trachoma, rheumatic fever, or typhoid. (*28*)

Table 2.4 Products developed by product development partnerships which are part funded by the Bill & Melinda Gates Foundation

Product	PDP	Type	Disease
1. ASAQ (artesunate/amodiaquine)	DNDi	Medicine	Malaria
2. ASMQ (artesunate/mefloquine)	DNDi	Medicine	Malaria
3. NECT (Nifurtimox Eflornithine combination therapy)	DNDi	Medicine	Human African trypanosomiasis
4. SSG&PM combination therapy	DNDi	Medicine	Visceral leishmaniasis
5. Xpert MTB/RIF	FIND	Diagnostic	Tuberculosis
6. Liquid culture	FIND	Diagnostic	Tuberculosis
7. Rapid speciation for MDR-TB	FIND	Diagnostic	Tuberculosis
8. LPA line probe assay	FIND	Diagnostic	Tuberculosis
9. Fluorescence microscopy	FIND	Diagnostic	Tuberculosis
10. KalazarDetect	IDRI	Diagnostic	Kalazar
11. Paromomycin	iOWH	Medicine	Visceral leishmaniasis
12. Killed whole-cell oral cholera vaccine	IVI	Vaccine	Cholera
13. Coartem dispersible	MMV	Medicine	Malaria
14. Injectable artesunate	MMV	Medicine	Malaria
15. MenAfriVac	MVP	Vaccine	Meningitis A
16. JE Vaccine India	PATH	Vaccine	Japanese encephalitis

Source: PDP Message Manual, 2011

The Bill & Melinda Gates Foundation estimates that, to date, 8 of the 15 product development partnerships it funds have developed in total 16 new products (see Table 2.4). In addition, these 15 are planning more than 100 active and new clinical studies in 2011–2012. They plan to conduct 142 total studies in 45 countries in 20 disease areas. Among these, 38% are Phase I trials, 25% are Phase II

trials and 20% are Phase III trials, with 53% of the studies on vaccines and 33% on drugs. These include:

- a malaria vaccine called RTS,S, the first–ever vaccine against a parasite, being developed by the PATH Malaria Vaccine Initiative (MVI) and GlaxoSmithKline (Phase III);
- two new tuberculosis vaccine candidates sponsored by Aeras (both in Phase IIb);
- two vaccines for rotavirus from PATH in advanced clinical trials (Phase I and II);
- several malaria drugs targeting different strains and patient groups, managed by the Medicines for Malaria Ventures (MMV) (Phase IIa and III);
- several projects led by the Drugs for Neglected Diseases *initiative* (DND*i*) for visceral leishmaniasis (Phase III) and sleeping sickness (entering in Phase I and II/III). (*32*)

Bio Ventures for Global Health estimates that there are in total 440 drugs, diagnostics and vaccines in development for neglected diseases (including tuberculosis and malaria) in research institutions in all sectors. (*30*)

Research and development and access

Our terms of reference recognized the need to further "explore and, where appropriate, promote a range of incentive schemes for R&D including addressing, where appropriate, the delinkage of the costs of R&D and the price of health products, for example through the award of prizes, with the objective of addressing diseases which disproportionately affect developing countries".

Delinkage is a powerful principle. The intellectual property system encourages a business model that allows developers of products to recoup the costs of R&D and to make profits through charging consumers on the basis of the exclusivity conferred by intellectual property rights. Depending on the pricing policies of the originator in developing countries, this can result in the patient, or those purchasing on behalf of a patient such as a government or a health insurer, being unable to afford a life-saving treatment. Delinking, which can happen in a number of different ways, is a means of divorcing the funding of R&D from product pricing. Once a patent has expired, delinking occurs naturally because generic competition should bring the price down to levels determined by market conditions and the cost of production rather than by R&D costs.

The controversy over access to treatments for HIV/AIDS a decade ago illustrated the issues well. While originator companies introduced schemes to provide these treatments at lower prices in certain countries, it was only when Indian companies, who were able to produce versions of drugs patented elsewhere because of Indian patent laws at that time, entered the market that prices began to drop dramatically as a result of competition. With the help of new international funding sources such as the Global Fund, these products became affordable to developing countries. Indian producers now account for over 80% of the donor-funded antiretroviral market. (*31*) (*32*) Moreover, annual treatment costs for a common first line treatment (stavudine, lamivudine, and nevirapine) have fallen from US$ 741 per patient for the lowest-cost originator brands in September 2001 to US$ 61 for the lowest-cost generic in June 2011. The equivalent lowest-cost originator was still US$ 347 in 2011. (*33*)

Thus, the price of treatment in developing countries has, de facto, been delinked from the cost of R&D borne by the originator companies as a result of generic competition. Originators are still able to charge much higher prices in developed countries that allow them to recover R&D costs and make profits (i.e. the concept of tiered or differential pricing). It is estimated that, in 2010, 745 000 HIV

patients in developed countries generated over US$ 14 billion in sales revenue while 6.6 million patients in developing countries generated about US$ 1 billion.[1] (*34*)

There are many ways that delinking can take place, a number of which we explore further in the next chapter and in Appendix 3. These include:

- open knowledge R&D and open innovation models where the R&D costs are covered by public or philanthropic sources and research results are made available in the public domain;
- licensing conditions imposed by funders or research organizations that permit non-exclusive licensing or prescribe a low target price for a product (for instance, where the public sector has funded most of the R&D;
- schemes such as the Advance Market Commitment (AMC), the proposed Health Impact Fund (HIF) or prize funds which involve separate payments to compensate for the costs of R&D and prescribe either predetermined product prices at a low level or permit competitive manufacture of developed products;
- more comprehensive schemes that envisage wholesale replacement of the intellectual property system by government-funded payments for R&D.

There are clearly other practices or policies that can contribute to improved access to medicines in different ways, including compulsory licensing and government use of patents for non-commercial purposes, price controls and product donations by companies.

Research and development financing

Over the years various bodies have recommended increasing the resources available for R&D relevant to developing countries. The CHRD recommended that governments should spend 2% of their health budgets on what it called essential national health research and that donor nations should spend 5% of their aid for health in developing countries on research and the strengthening of research capacity. In 2005, WHO Member States passed a resolution in the World Health Assembly which urged Member States to "consider implementing" these recommendations. (*35)*

In 2001 the Commission on Macroeconomics and Health called for the establishment of a new Global Health Research Fund of US$ 1.5 billion annually and for an equivalent increase in the amount of money going through existing channels to bodies such as WHO or public–private partnerships, making a total of US$ 3 billion. As noted above, total public funding from developed countries has increased significantly but currently amounts to less than US$ 2 billion annually.

The proposal for a Global Health Research Fund was not pursued when it was first proposed, but the Intergovernmental Working Group on Public Health, Innovation and Intellectual Property considered in its deliberations in 2007 and 2008 the possibility of establishing a similar fund. This proposal did not encounter sufficient support, and the compromise reached was to recommend establishing the Expert Working Group (as described in Chapter 1).

We recognize that R&D for new medicines and technologies, while the focus of our work, is not the only necessary type of R&D. As noted above by the Special Rapporteur, there are important research questions that need to be addressed to tackle the best means of improving health and improving the

[1] Sales estimates are based on company investor reports and internal analysis conducted by the Medicines Patent Pool in January 2011.

delivery of health services – often called operational research. Epidemiological research, for example, is central to identifying correctly the burden of disease. A recent study in the *Lancet* provided evidence that malaria mortality might be much larger than previously estimated and more prevalent in adults than previously thought. (*36*) There are many unanswered questions concerning the choice of interventions, alternative treatment practices and changes in clinical interventions. Research in ethics and health policy, such as cost implications, is also important. The concept of essential national health research formulated by the CHRD captured the need for wider research of this nature.

The context for our report is the critical situation affecting the global economy, particularly developed countries which have traditionally been the largest funders of biomedical research (in the private and public sectors). This threatens to bring to an end a decade in which the international commitment to development has resulted in large increases in development assistance for health, including for health-related R&D. (*37*)

That situation makes particularly relevant our mandate to consider further the four innovative sources of financing proposed by the Expert Working Group. It also highlights the danger of overreliance on one source of funding such as development assistance which is vulnerable to changes in economic or political circumstances.

Financial transactions taxes have been supported by a global movement consisting of academics and civil society groups that have spoken out in favour of a financial transactions tax (FTT) to finance global public goods. Derived from an idea for a foreign currency transaction tax first proposed by Nobel laureate James Tobin in 1972 with the objective of mitigating problems caused by volatile exchange rates (*38*), the idea has now gained momentum as a tax on all financial transactions. Advocates see it as a way of addressing the technical issues highlighted by the financial crisis in the way financial markets operate, and of obliging the financial sector to pay its fair share of taxes at a time when it is in receipt of vast sums paid or guaranteed by taxpayers. It is also a means of generating potentially large revenues which can be used to meet global development and environmental goals, including health, from a sector which has benefited from globalization and free trade. This idea has been supported by leading economists who have written a letter to the G20 asking for its support[1]; by the Leading Group on Innovative Financing for Development, a group of 63 countries and other organizations;[2] by a coalition of NGOs and other organizations;[3] and by leading politicians including President Sarkozy of France and Chancellor Merkel of Germany. (*39*)

There is currently a proposal to introduce an FTT in the European Union (EU). (*40*) As currently constructed, this is a proposal to finance the budget of the EU although its effect may be to liberate national tax resources in EU member states that could be used for development purposes. It is currently opposed by some countries in the EU, and by several other OECD member countries. Although it is widely recognized that a global approach to the implementation of such a tax is preferable (to avoid distortions and tax avoidance through relocating financial transactions), the European Commission believes that a tax in the EU only would be feasible. France has recently announced it will implement a modest tax on share trading in large firms headquartered in France, which is estimated to raise about €1 billion. The United Kingdom has had a longstanding tax on share sales that currently raises over US$ 4 billion annually.

[1] For more information see:http://robinhoodtax.org/latest/1000-economists-tell-g20-support-robin-hood-tax

[2] For more information see: http://www.leadinggroup.org

[3] For more information see: http://robinhoodtax.org

Box 2.3 Innovation with impact: financing 21st century development (Gates report to the G20, 2011)

The report by Bill Gates to the G20 in 2011 points out that developing countries are themselves by far the largest source of development financing. They should first seek to raise more revenue from their own resources by reforming their tax systems including, for instance, improving transparency and returns to their budgets from taxation arrangements for natural resources.

In Gates' view, investment in agriculture and health will have the greatest impacts on growth and poverty reduction. Apart from increasing the volume of investments, there is great scope for improving efficiency, including by devoting more resources to evaluating the impact of current spending.

At the same time, developed countries should not cut their development assistance because of the economic crisis. Gates urges developed countries to reach the targets set for development assistance in 2015. If countries meet their pledges by then it would generate an additional US$ 80 billion and, if all countries reached the target of 0.7% of gross national product (GNP), US$ 170 billion. Similarly more effort needs to be devoted to evaluating cost-effectiveness and finding out what works best.

Gates also believes that the private sector should play a bigger role, both through additional philanthropic contributions and through direct investments. A particular priority would be investments in infrastructure. He suggests that sovereign wealth funds should devote a small proportion of their capital to infrastructure investment in poor countries. For instance 1% of such funds would currently generate US$ 40 billion or more annually, a sum that is rapidly growing. And the diaspora community should also be provided with incentives to invest in their country's development.

While emphasizing the importance of development assistance and private sector investment, Gates recommends three tax proposals to keep countries investing in development assistance.

He endorses WHO's idea of a Solidarity Tobacco Contribution, (*41*) instituting a levy on tobacco taxes at differential rates for high-, middle- and low-income countries which would be allocated to global health. It is estimated this could generate US$ 10.8 billion annually in addition to the health benefits of reduced smoking.

Secondly he provides endorsement for a financial transactions tax which could yield between US$ 9 billion in Europe alone, US$ 48 billion in the G20, or very much more with wider scope and coverage.

Thirdly he advocates carbon taxes, including in the medium term higher taxes on shipping and aviation fuels, which could raise together over US$ 50 billion annually.

Source: Gates W. Innovation with impact: financing 21st century development

There are also many other proposals for generating funds for development, or for environmental purposes in general, of which a proportion could be devoted to health and health-related R&D. United Nations work in this area, and in particular processes under innovative financing for development, have provided a global forum for new initiatives.[1] Bill Gates was asked to report on these for the G20 in 2011 (see Box 2.3). (*42*) The G20 summit in Cannes in November 2011 concluded rather equivocally:

> "In order to meet the Millennium Development Goals, we stress the pivotal role of ODA. Aid commitments made by developed countries should be met. Emerging countries will engage or continue to extend their level of support to other developing countries. We also agree that, over time, new sources of funding need to be found to address development needs and climate change. We discussed a set of options for innovative financing highlighted by Mr Bill Gates. Some of us have implemented or are prepared to explore some of these options. We acknowledge the initiatives in some of our countries to tax the financial sector for various purposes, including a financial transaction tax, inter alia to support development."(*43*)

[1] For more information see: http://www.un.org/esa/ffd/overview.

We examine these issues in more detail in Chapter 4.

Research and development coordination

The landscape of R&D relevant to our mandate is quite complex. Key organizations conducting research, with many partnerships and alliances between them, include:

- government research organizations (e.g. national public health institutes, medical research councils);
- pharmaceutical companies in developed and developing countries;
- biotechnology companies in developed and developing countries
- universities in developed and developing countries;
- product development partnerships;
- foundations (e.g. Wellcome Trust, Institute of Cancer Research).

Funders of research are also very diverse and include:

- government health ministries;
- government research organizations;
- government development/foreign affairs ministries/agencies;
- other government ministries (e.g. defence);
- foundations;
- pharmaceutical companies in developed and developing countries;
- biotechnology companies in developed and developing countries.

For many years there have been calls for better coordination of these diverse efforts. The CHRD identified this problem in 1990, stating:

> "It is difficult to escape the conclusion that the current system of promoting research on developing country health problems is fragmented and lacks overall coherence. No mechanism exists currently to identify and promote research on problems that lack an advocacy group. There is no mechanism to deal with the normal, difficult questions of rationalizing global research efforts, for example: Which problems deserve more attention? Which less? When is a problem "solved"? There is no institutional memory for research. What lessons are being learned? How are these lessons informing other initiatives? ... And there is no independent, informal voice to speak frankly and critically on the policies and practices of agencies."

It recommended that "an international facilitation mechanism for health research, similar to the Consultative Group for International Agricultural Research, should be established. This would bring greater coherence to support for research on health problems of developing countries, and also would have the potential of mobilizing greater long-term funding in support of such research."(*23*)

The CIPIH similarly noted in 2006:

> "…there are few or no available mechanisms at present to advise on appropriate priorities for resource allocation between R&D on different diseases, the balance between resources needed for R&D and delivery for each disease or the means to monitor and evaluate the impact of resources devoted to treatment and delivery."

It recommended that "WHO should bring together academics, small and large companies in pharmaceuticals and biotechnology, governments in the form of aid donors or medical research councils, foundations, public–private partnerships and patient and civil society groups for a standing forum to enable more organized sharing of information and greater coordination between the various players."(*44*)

In 2011 the G-Finder report noted the following:

> "...there is currently no system to help funders identify which investments are likely to generate the highest health return, with the result that R&D funding is often poorly matched with disease needs and scientific and technical possibilities... In order to deliver the highest health return on investment, funders need tools to help them assess and compare disease burden, state of the science, and knowledge and product gaps, as the basis for deciding into which disease and product areas they can best invest. For some diseases, this may mean a stronger focus on basic science rather than product development. For other diseases, basic science is at the right stage to be translated into useable health technologies, and funding should preferentially be directed to product development."(*26*)

Thus there has been a longstanding recognition of an unmet need for better coordination – to exchange information between funders and researchers, to improve resource allocation by identifying gaps in funding or duplication of effort, and to learn lessons and act on them. The fact that the issue is still being raised over two decades after the CHRD met indicates both that it is still very much an identified deficiency in current arrangements and that, correspondingly, very little has been done to address it in the last 20 years. The absence of action is itself a reflection of the difficulty of improving coordination precisely because the field is so fragmented and the interests of funders and researchers are so diverse.

We examine issues related to improved coordination in more detail in Chapter 5.

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CHAPTER 3. REVIEW OF PROPOSALS

One of our principal tasks, as set out in resolution WHA63.28, is to deepen the analysis of the proposals reviewed or mentioned in the EWG's report. As described in Chapter 1, we decided to review all the 22 proposals mentioned in the EWG report, and not just those specifically identified in the resolution, as well as the 22 submissions received as a result of our own call for submissions.

Criteria and method of assessment

We set about this task by developing at our first meeting a number of criteria against which we would judge the value of each of the proposals. These are set out in our Inception Report (Appendix 1). We then used these criteria to do a first assessment of the 22 proposals and the submissions which we discussed at our second meeting. In the light of this first-round consideration, we revised the criteria and the assessments further. In Table 3.1 we show the first set of criteria derived from the Inception Report and the modified set of criteria on which we finally converged. Thus the assessments of each of the proposals in Appendix 3 contain a table assessing the proposals against the "final" criteria shown in the table below. The table also provides brief explanations of each of the criteria in the comment section.

Table 3.1 CEWG criteria

Inception Report	Final	Comment
Potential public health impact in developing countries	Public health impact	A judgement about the potential health impact in developing countries – generally speaking there is very little hard evidence relating to new proposals or even existing ones.
Rational and equitable use of resources/efficiency considerations	Efficiency/cost-effectiveness	An assessment of the cost of implementation in relation to potential benefits.
Cost-effectiveness		
Technical feasibility, scaling-up potential, replicability, speed of implementation	Technical feasibility	The ease with which the proposal can be implemented from a technical point of view – from relatively automatic rule-based systems to proposals that involve a degree of complexity in their start-up and in their operation.
Financial feasibility and sustainability	Financial feasibility	An assessment of the direct costs (normally to government) of the scheme, and also indirect costs or savings imposed on others such as patients (e.g. as a result of changing exclusivity arrangements).
Additionality	*Not used*	This was dropped as an explicit criterion because of the difficulty in determining additionality in proposals designed to allocate funds.
Intellectual property management issues	*Intellectual property*	How far the use of intellectual property in a proposal will promote innovation and enhance access.
Potential for delinking R&D costs and the price of products	*Delinking*	The extent to which product pricing and the financing of R&D are determined independently.
Equity/distributive effect, including on availability and affordability of products and impact on access and delivery	*Access*	Whether the proposal has an element which promotes access, including the potential for lower prices as well as measures to promote effective demand for needed products.

Inception Report	Final	Comment
Accountability/participation in governance and decision-making	*Governance and accountability*	The extent to which governance arrangements are adequately transparent and accountable, and their complexity. This is often difficult to assess because schemes vary widely in their governance arrangements or they are ill-defined in new proposals.
Impact on capacity-building in, and transfer of technology to, developing countries	*Capacity-building*	How far the proposal is aimed at promoting technology transfer and capacity-building in R&D in developing countries.
Potential synergy with other mechanisms/potential for combining with others	*Not used*	This was dropped as an explicit criterion because of difficulty in interpretation for many proposals, but was used when considering the sum of proposals.

In devising these criteria it was assumed that proposals should have as their central purpose the promotion of R&D, as provided for in our mandate.

Mechanisms assessed

Appendix 2 provides a detailed explanation of how we understood, as far as we could, the methodology used by the EWG and how they arrived at their final list of 22 grouped proposals. It also describes how we incorporated into our analysis the submissions we received. Table 3.2 below shows the relationship between the 22 EWG proposals and the 22 submissions we received. As shown, we mapped 13 of the submissions (or parts of them) on to the 22 EWG proposals.

Table 3.2 EWG grouped proposals and CEWG submissions

The 22 EWG grouped proposals	Related submissions
1. A new indirect tax 2. Voluntary contributions from businesses and consumers	*Financing & incentives for neglected disease R&D.* Drugs for Neglected Diseases initiative.
3. Taxation of repatriated pharmaceutical industry profits	
4. New donor funds for health research and development	
5. Open source	*1. Submission to the CEWG.* Universities Allied for Essential Medicines. *2. Open Source Drug Discovery initiative*. Council of Scientific and Industrial Research, India.
6. Patent pools (UNITAID model) 7. Health impact fund	*Health Impact Fund.* Incentives for Global Health.
8. Priority review voucher	
9. Orphan product legislation	
10. Transferable intellectual property rights	
11. Green intellectual property	*International Fund for Innovation (IFI) ("Green intellectual property").* Institut des Hautes Études Internationales et de Développement. Nitta I.
12. Removal of data exclusivity	

The 22 EWG grouped proposals	**Related submissions**
13. Biomedical research and development treaty	1. *Submission to the CEWG.* Health Action International. 2. *Consideration of an essential health and biomedical R&D treaty.* Health Action International Global, Initiative for Health & Equity in Society, Knowledge Ecology International, Médecins Sans Frontières, Third World Network. 3. *A global framework on health research and development.* All India Drug Action Network, Berne Declaration, CENTAD, Initiative for Health and Equity in Society, People's Health Movement, Third World Network.
14. Large end-stage prizes (impact-based rewards) 15. Neglected disease tax breaks for companies	*Innovation inducement prizes.* Knowledge Ecology International.
16. Product development partnerships (PDPs)	1. *Fund for research and development in neglected diseases.* Novartis International. 2. *A global framework on health research and development.* All India Drug Action Network, Berne Declaration, CENTAD, Initiative for Health and Equity in Society, People's Health Movement, Third World Network.
17. Direct grants to small companies and for trials in developing countries	1. *Investing in small- and medium-sized enterprises in innovative developing countries.* COHRED & Global Forum for Health Research. 2. *A new incentive system for technological innovation in developing countries(ISTI).* Maito M, Franciosi E.
18. "Milestone" prizes	1. *A milestone-based prize to stimulate R&D for point-of-care fever diagnostics*. BIO Ventures for Global Health. 2. *Financing & incentives for neglected disease R&D.* Drugs for Neglected Diseases initiative. 3. *Innovation inducement prizes*. Knowledge Ecology International
19. "End" prizes (cash) 20. Purchase or procurement agreements	*Innovation Inducement Prizes*. Knowledge Ecology International.
21. Regulatory harmonization	*Financing & incentives for neglected disease R&D.* Drugs for Neglected Diseases initiative.
22. Precompetitive research and development platforms	*Financing & incentives for neglected disease R&D.* Drugs for Neglected Diseases initiative.
Submissions related to the 22 EWG proposals	
1. *Innovation inducement prizes.* Knowledge Ecology International.	
2. *A global framework on health research and development.* All India Drug Action Network, Berne Declaration, CENTAD, Initiative for Health and Equity in Society, People's Health Movement, Third World Network.	
3. *Consideration of an essential health and biomedical R&D treaty.* Health Action International Global, Initiative for Health & Equity in Society, Knowledge Ecology International, Médecins Sans Frontières, Third World Network.	
4. *Submission to the CEWG.* Universities Allied for Essential Medicines.	
5. *Investing in Small- and Medium Sized Enterprises in Innovative Developing Countries.* COHRED & Global Forum for Health Research	
6. *International Fund for Innovation (IFI) ("Green intellectual property").* Institut des Hautes Études Internationales et de Développement. Nitta I.	

The 22 EWG grouped proposals	**Related submissions**
7. *Fund for research and development in neglected diseases.* Novartis International.	
8. *A milestone-based prize to stimulate R&D for point-of-care fever diagnostics.* BIO Ventures for Global Health.	
9. *Health Impact Fund.* Incentives for Global Health.	
10. *A new incentive system for technological innovation in developing countries (ISTI).* Maito M, Franciosi E.	
11. *Submission to the CEWG.* Health Action International.	
12. *Open Source Drug Discovery initiative.* Council of Scientific and Industrial Research, India.	
13. *Financing & incentives for neglected disease R&D.* Drugs for Neglected Diseases initiative.	
Submissions not directly related to the 22 EWG proposals	
14. Equitable licensing/med4all. BUKO Pharma-Kampagne. Charité Universitätsmedizin Berlin. Universität Oldenburg	
15. *The ANDI model. African Network for Drugs and Diagnostics Innovation (ANDI).* Special Programme for Research and Training in Tropical Diseases.	
16. *Open source software for improving maternal, neonatal and child health services in Pakistan.* Kazi GN. WHO Pakistan country office.	
17. *Neglected tropical diseases management portal – epidemiological watcher.* Health Insight Ltd.	
18. *Employees' food safety knowledge and practices in foodservice operations serving high risk populations.* University of Costa Rica. Paez P.	
19. *Limbal stem cell bioengineering.* Clinical Research, Dr Agarwal's Eye Hospital Ltd.	
20. *Maternal mortality reduction proposal.* Clinical Research, Dr Argarwal's Eye Hospital Ltd.	
21. *Optimal hedging against the premature obsolescence of available treatments.* Euromed Management, Centre National de la Recherche Scientifique, (GREQAM), (IDEP). Leoni P, Luchini S.	
22. *Reduction of patents' duration to prevent collusion at industry level.* Euromed Management. Kellogg School of Management, Northwestern University. Leoni P, Sandroni A.	

Taking account of the above, and after several iterations, we finally arrived at 15 of our own grouped proposals for assessment. A majority of these are more or less exactly the same as the EWG proposals. In other cases we have grouped EWG proposals (e.g. Milestone prizes and End prizes), combined EWG proposals with those from submissions or elsewhere (e.g. Open approaches to research and development and innovation) or added new material as a result of developments since the EWG report (e.g. Patent pools). These 15 assessments are presented in Appendix 3 and shown in Table 3.3. A full table showing which of the EWG proposals and which of the submissions are included in each of our assessments is contained at the end of Appendix 2. We deal separately with the four proposals relating to sources of financing in Chapter 4.

Of the remaining submissions not directly related to the EWG proposals, we have included number 14 on "Equitable licensing" in our assessment of open approaches to research and development and innovation. We discuss number 15 (ANDI – African Network for Drugs and Diagnostics Innovation) in Chapter 4. Of the remaining submissions we considered that five (numbers 16–20) were out of the scope of our terms of reference because they were requests for project funding rather than proposals for improving R&D financing and coordination. We considered that the two remaining proposals (20 and 21) were insufficiently supported by empirical evidence and we were not convinced by the theoretical arguments which were used by the sponsors to justify the proposals – essentially that companies failed to invest in innovation for particular products (vaccines rather than treatments for HIV/AIDS are provided as an example) because it might make the existing intellectual property or treatment infrastructure redundant. As regards "optimal hedging", there was insufficient information for us to judge exactly what was being proposed as an insurance mechanism. In the case of reducing patent duration, there was no indication of what reduction in patent terms was being sought or how

such a reduction would impact on R&D beyond the specific example on which the authors based their conclusions. There are certainly good arguments that vaccines, as preventive treatments, are inherently less commercially attractive than treatments for chronic illnesses, but it does not follow that reducing the incentive for investment in both treatments and vaccines is the correct solution. In addition, changing minimum patent length would require negotiations in the World Trade Organization with implications for all sectors. It was therefore not clear to us that either proposal, as currently presented, would materially improve R&D for diseases mainly affecting developing countries.

Table 3.3 CEWG assessments

15 Assessments made by the CEWG	
Global framework on research and development	Open approaches to research and development and innovation
Removal of data exclusivity	Milestone prizes and end prizes
Direct grants to companies	Purchase or procurement agreements
Green intellectual property	Priority review voucher
Health Impact Fund	Regulatory harmonization
Orphan drug legislation	Tax breaks for companies
Patent pools	Transferable intellectual property rights
Pooled funds	

Summary of assessments

In our assessments we make use of and record whatever evidence we can find which relates to the proposal in question, including that contained in the submissions. However, for the great majority of proposals there is no definitive evidence on which to base an objective judgement about costs and benefits. Therefore we do not pretend that this method of prioritization is scientific; rather we used it as a means by which we could come in a reasonably systematic manner to a collective judgement, informed by our own diverse experiences of what is likely to work better in practice and what is likely to work less well or not at all. The detailed summary of assessments is in Appendix 3. These contain a discussion of the strengths and weaknesses of the different proposals supported, wherever possible, by reference to existing literature. Each assessment is set out under the following headings:

- Public health impact;
- Technical feasibility;
- Financial feasibility;
- Implementation feasibility.

These headings incorporate the CEWG criteria (as finalized) and are based on the template we devised for the call for submissions.[1] Drawing on these assessments, and using our criteria, we reached the following conclusions on each of the 15 proposals.

Global framework on research and development

Based on the two submissions we received proposing a treaty and a global framework, we considered that the time had now come for considering a coherent and comprehensive international framework or

[1] The text of the CEWG invitation to submit proposals can be seen here: http://www.who.int/phi/news/cewg_call_for_proposals.pdf (accessed 7 March 2012).

convention[1] under the auspices of WHO for supporting priority medical R&D aimed at diseases that are prevalent in developing countries.

Although the proposals appeared ambitious, they were worthy of further consideration. They contained clearly defined purposes and objectives, including setting up a transparent, participative and effective governance structure for needs assessment of R&D gaps, priority-setting and allocation of funds for enhanced R&D efforts for conditions prevalent in developing countries, and raising of global-level funding with contributions from Member States and other earmarked sources of funding.

The proposals submitted to us address almost all of the criteria that we set ourselves. The proposals do not provide specific details on the operational modalities of the envisaged convention or framework, although general principles are set out. This is deliberate, since the proponents consider that it should be up to the WHO Member States to decide on the institutional mechanism and modus operandi under the suggested instrument. The basic strength of these proposals is that, if adopted, they would provide a comprehensive solution to the problem of underfunding and lack of a global coordination of pharmaceutical R&D, particularly to address the diseases prevailing in developing countries.

As regards key steps necessary to begin implementation and the financial feasibility of the proposals, it was emphasized that since the idea is to make a recommendation to the effect that Member States should agree to begin a process for formal negotiations on a global framework or convention, such aspects should be deliberated upon during the course of such negotiations. Although the goal was challenging, the time was right to initiate necessary negotiations for a convention.

The submitted proposals elaborate on the principles that should be enshrined in a treaty or framework, such as a fair arrangement for burden-sharing of the R&D costs, knowledge-sharing to promote scientific progress, and equitable access to the products arising from R&D activities. Basic concepts underpinning these proposals are the delinking of the prices of medicines from the costs of R&D and the involvement of all governments in setting priorities and coordinating and funding R&D efforts. We view the proposals not as a replacement for the existing intellectual property rights system, but as a supplementary instrument where the current system does not function to meet the R&D needs of developing countries.

The feasibility of these proposals will naturally depend on the willingness of WHO Member States to engage in the negotiation of an international instrument on the matter. The WHO Framework Convention on Tobacco Control and the Pandemic Influenza Preparedness Framework for the sharing of influenza viruses and access to vaccines and other benefits are the most immediate precedents for a negotiation of that kind. We discuss the ideas of a global framework and convention further in Chapter 6.

Removal of data exclusivity

We considered that there was no evidence that data exclusivity materially contributes to innovation related to Type II and Type III diseases and the specific R&D needs of developing countries in relation to Type I diseases, and therefore we concluded that its removal where it existed would not adversely affect innovation incentives for these diseases and also would contribute to reduced prices of affected medicines. While recognizing that removal of data exclusivity would not constitute a significant contribution to increased innovation, we noted that it might enable generic companies to innovate incrementally on products which otherwise would have been under exclusivity.

[1] We use the term “convention” in preference to “treaty”, although in legal terms there is little difference between the two.

Thus while the removal of data exclusivity might not strongly contribute to the principal objective relating to R&D, the proposal nevertheless scored well on our criteria. It has a potentially good public health impact as a result of a positive effect on access to medicines through better availability and affordability. Its removal would be technically and financially feasible, subject to the possible need to renegotiate existing multilateral or bilateral obligations, and could be cost-effective. It addresses intellectual property management issues by removing one form of exclusivity and promoting earlier generic competition. It is complementary to other existing incentives and mechanisms.

Direct grants to companies

We considered that schemes on these lines directed to small and medium companies in developing countries could meet many of our criteria. They were technically and financially feasible. The schemes could have a positive effect on capacity building and technology transfer particularly if, as suggested by the Global Forum for Health Research, they are combined with assistance in commercialization and technology management. The proposed Innovation Fund also contains measures to promote capacity-building and technology transfer, and links with universities and public research institutions. They are perfectly compatible with other existing and proposed mechanisms. On the other hand, the schemes do not directly address issues of availability, affordability, delivery and access. Complementary mechanisms would therefore be required to maximize their effectiveness. Accountability and governance criteria remain to be defined. Intellectual property management issues could be addressed as part of these schemes, as is the case with the New Innovation Fund proposal.

These schemes needed to be considered in the context of other proposals for pooled funds. It was not clear, however, that these particular proposals would address major funding gaps in drug development (e.g. for Phase III trials). Nor was there clarity on exactly what the unmet funding needs were throughout the development cycle.

Finally, their relevance is directly related to the source of funds, nature of schemes and ways in which intellectual property rights were considered as part of the scheme. Where resources could be drawn from industrial policy sources and support, this was considered more feasible. This type of scheme may also be combined with licensing requirements for access.

Green intellectual property

We considered that this proposal did not meet many of our criteria very well. The overall purpose of the proposal was not well defined, nor the import of "green" in the title. There were many unanswered questions that arose from the documentation. The proposal addresses to some extent intellectual property management and delinking issues but it fails to demonstrate that this is the best way of addressing them. There are no provisions that would specifically address capacity-building and transfer of technology to developing countries, beyond perhaps encouraging voluntary licensing of technologies. The link with the TRIPS Council would seem to guarantee high standards of governance and accountability but this is outside the council's mandate. In particular, we questioned the technical and financial feasibility of the proposal. It was considered heavy in terms of management and governance, and did not provide sufficient evidence for the necessity and purpose of engagement of all organizations and actors involved.

While contributions from patent holders for public purposes would, in principle, be welcome to enhance R&D for underfunded causes and promote access to medicines, patent holders typically press for reductions in the fees they are charged, and it was not clear that the proposed scheme offered sufficient benefits to encourage governments to impose increased patent fees or a significant tax on the overseas income of patent holders.

Health Impact Fund

We considered that the ideas underpinning the HIF were of interest and that, if successfully implemented, it would address many of our criteria. The proposal addresses directly intellectual property management issues in that it seeks to incentivize R&D relevant to the disease burden in developing countries, while also facilitating access to these products by making them more affordable. For the products it covers it delinks the cost of R&D from the price of products. Similarly, on the basis that it will be financed by developed country taxpayers, it could have a favourable equity/distributive effect and boost the availability and affordability of products in developing countries while also incentivizing firms to promote access and delivery on which the assessment of health impact will depend. The proposal was considered as complementary to the existing set of intellectual property incentives in that firms can choose whether to register their product with the HIF or use the patent system as they do now.

However, we considered that in practice implementation of the HIF would be problematic on a number of grounds – particularly uncertainties about whether a sufficiently reliable measurement of health impact could be achieved in the circumstances prevailing in developing countries, even with the very large assessment apparatus envisaged by the sponsors. In addition, the proposal has a very high cost. The governance proposals were also rather underdeveloped although they would be very important, particularly if there were disputes about the measurement of health impact. And it would have no direct impact on capacity-building or technology transfer to developing countries.

On the above grounds we question whether the HIF, as currently proposed, will achieve its objectives in practice. We note that the sponsors plan a pilot project to test out the feasibility of the methods of impact assessment being proposed.

Orphan drug legislation

We considered that orphan drug schemes did not meet many of our criteria very well. Orphan drug schemes address intellectual property management, but by offering a marketing exclusivity of 7–10 years as the principal incentive for R&D. As such, there is no delinking of the costs of R&D from product prices (unless this was provided for in the complementary "pull" mechanism). Similarly, the proposal may increase availability of products for some rare diseases but its equity and distributive impact is difficult to isolate. The price of products in developed countries may be very high during the exclusivity period, and may even result in some cases in large increases over previous prices of the same product. These schemes largely depend on the application of rules laid down in legislation and require no extensive governance and decision-making arrangements. There is no impact on capacity-building in developing countries or technology transfer to them. Furthermore, orphan drug regulations, which adjust registration requirements to the rarity of a disease, are inappropriate in settings where the disease is common. However, as previously noted, there is potential synergy with a complementary "pull" mechanism for developing countries.

It is not clear how orphan drug schemes could be adapted for use by developing countries to meet their own needs. Their main priority is likely to be for diseases that are not "orphan" in their own countries. Their feasibility would thus depend on the circumstances and needs of different developing countries. However, such schemes would not help to provide a "pull" factor – the distinguishing feature of which in developed countries is market exclusivity linked to a market with an ability to pay often very high prices.

Patent pools

We considered one "downstream" pool which is now operational, the Medicines Patent Pool (MPP) sponsored by UNITAID which sought to make newer HIV treatments more affordable and to facilitate the development of new fixed-dose combinations suited to treatment needs in developing countries. This met many of our criteria although it does not directly address the financing problem as regards R&D. The public health impact was potentially high and the technical and financial feasibility was in the process of being tested; its impact could be highly cost-effective and could contribute to the efficient use of public funds in respect of R&D and access. The approach to the use of intellectual property was innovative and, by promoting competition, could contribute to delinking. The licences were also designed to promote technology transfer to licensees. There were potential synergies with other mechanisms. Although licences had already been signed, it was not clear that there were sufficient incentives for companies to join the MPP on the best possible terms (e.g. by providing the widest geographical scope). In addition, there could be scope for incentives, such as a prize fund, for promoting R&D on new formulations, including for paediatric or other adapted drugs.

We noted also the potential of two similar "upstream" pools designed to facilitate R&D on neglected diseases – the Pool for Open Innovation and the new Re:Search of the World Intellectual Property Organization (WIPO). An evaluation of the former was not so positive with regard to its potential to overcome research barriers, and there were also similar issues about the limited geographic scope of both initiatives. We encourage exploration of ways in which their potential public health impact can be enhanced. The potential for patent pools in other disease areas and the use of complementary incentives to encourage participation and promote R&D should also be explored.

Pooled funds

We considered that the proposals on pooled funding were promising but needed to be further developed. We did not consider that they should provide privileged funding for PDPs but, rather, extra opportunities for research organizations of all kinds. Their potential strength rested on the extent to which they could mobilize new and additional donor funds and/or be the trigger for establishing innovative and sustainable sources of funding. The proposals are technically feasible and potentially financially feasible. All proposals involve subsidizing R&D costs and thus involve an element of delinking, but the proposals differ on how they will deal with intellectual property – from all rights accruing to the fundee, to various provisions on licensing back to the funder (e.g. exclusive licensing under FRIND) or completely open licensing. The Third World Network (TWN) proposes that the products should not be protected as intellectual property. Thus the extent to which they address the access issue for developed products varies considerably. Some of the proposals explicitly include provisions to promote capacity-building and technology transfer (TWN, ISTI, DNDi), while in others it is either implicit or absent (e.g. the EWG proposals). In none of the proposals is accountability and governance very well defined. The proposals also need to be considered in relation to proposals on coordination with which they are closely linked, like for TWN, how they might fit into a global framework for financing and coordination. We concluded that potential value of the proposals on pooled funding depended on their more specific conditions, including on how intellectual property management, capacity-building and technology transfer were organized and defined.

Open approaches to research and development and innovation

We considered that open approaches to R&D – including open innovation, open source and open access publishing, as well as precompetitive R&D platforms and equitable licensing – met many of our criteria in relation to stimulating R&D in innovative ways. Typically these involve innovative, or at the least more flexible, applications of intellectual property in order to minimize intellectual property barriers to innovation. Such approaches could help to reduce the costs of R&D and accelerate

product development, and we favoured open and collaborative approaches that could also help to reduce duplication in research and widen the pool of researchers applying their expertise to the development of products needed in developing countries. Thus these approaches could also contribute to capacity-building and technology transfer. On the other hand, these approaches did not directly address access issues, with the exception of equitable licensing in relation to final products, although they could facilitate it in the longer term. They needed to be complemented by other measures that would promote access to products that are developed. However, we felt that the approaches had great potential and that funders and researchers in the public and private sectors should consider ways to promote initiatives that would focus on the development of products needed in developing countries.

Milestone prizes and end prizes

We considered that a number of prize proposals, and particularly milestone prizes, could meet many of our criteria. It was noted that even large companies might not be incentivized by large end prizes. We also saw the potential for prizes which were essentially a non-financial incentive. In general, prizes had been demonstrated to be technically and financially feasible. We considered that they should have, as a central purpose, delinking the costs of R&D from product prices in order to promote access to products. In all proposals there is the possibility of using intellectual property to promote access in developing countries. Exactly how this is done must depend on what is most likely to work. Prize proposals varied in the obligations they put on prize-holders to promote availability and affordable access. Such obligations need to be balanced against the disincentive such obligations might constitute for potential respondents to prizes, and the size of the prize that is being offered which might be used to compensate for such perceived disincentives. Milestone prizes have the advantage of shifting some of the costs of failure to the prize-funder rather than the originator of a project.

Prize proposals differ in how they view governance and accountability. If they are to work then they must have credible governance institutions which involve relevant stakeholders, and they must have clear rules for the award of prizes against robust criteria. Since disputes are likely to arise, they also need a reputable scientific advisory committee. In many proposals the governance arrangements and hosting institutions have not yet been worked out.

The prize proposals may or may not contribute to capacity-building and technology transfer. One example is Innocentive where a large number of researchers (solvers) are based in developing countries. Indirectly it offers researchers in developing countries an opportunity they would not otherwise have. This similarly might apply to proposals, such as for diagnostic prizes, which may open up avenues for developing country researchers. Otherwise, as noted above, in some proposals there might be obligations on prize-winners to transfer technology and know-how to producers in developing countries.

Many prize proposals are entirely complementary with other existing and proposed incentive mechanisms. In some proposals the intention is partially or wholly to substitute for patents as a means of financing R&D.

A series of pilot projects may be a useful way to proceed. In other cases coordination would seem appropriate – for instance, to avoid simultaneous prizes for a tuberculosis diagnostic with different characteristics and obligations on the winner.

Purchase or procurement agreements

We considered that normal procurement agreements, although they might have some incentive effect in relation to R&D, were outside our mandate and, in any case, met few of our criteria. As regards

advance market commitments, we were not convinced that experience to date had demonstrated their effectiveness or replicability.

In agreements such as the pilot AMC on pneumococcal vaccine, there is an element of delinking to the extent that the supplement paid to manufacturers is regarded as lowering the unsubsidized price offered to purchasers to a level below what it otherwise would have been. These agreements can have a favourable effect on availability and affordability, as well as on access and delivery, although there is debate as to whether the right balance has been struck on pricing in the pilot AMC. In addition, they do not exclude the possibility of claiming and enforcing intellectual property rights. Furthermore, there is a risk that AMCs can hinder competition and discourage potential new suppliers from investing in technologies for the development and production of a cheaper product. They also generally require quite sophisticated arrangements to ensure that the legal basis is sound and that there are credible governance bodies to take decisions which can affect, for instance, the size of payments to companies. For instance, the AMC has an independent assessment committee which determines the specifications for product eligibility for the AMC and whether or not a product meets those specifications. As regards capacity-building and technology transfer, it was noted that there are no elements to promote these in the AMC. However, it should be noted that two Indian companies have indicated their interest by registering with the AMC, though it is not known when they might have a product that would meet AMC criteria. The agreement between GlaxoSmithKline and Brazil involving technology transfer is an exception to this. Generally, these agreements are complementary to, and potentially synergistic with, existing incentive mechanisms.

Priority review voucher

We did not consider that the priority review voucher met many of our criteria very well. Although the scheme is technically feasible it is not clear that, as currently structured, it will achieve its objectives. The experience with the one priority review voucher awarded to date casts some doubt on its likely effectiveness as a powerful incentive for companies to devote more resources to R&D to meet developing country needs. It does not address intellectual property management except inasmuch as priority review allows companies to extend the effective patent term (from product approval to patent expiry) beyond what it would have been. It does not delink prices from the cost of R&D nor have any impact on affordability, access and delivery. Potentially it would have an impact on the availability of products, but not in terms of availability in developing countries. As an automatic scheme built into current structures, it has no need for accountability and participation in governance or decision-making. It has no impact on capacity-building or technology transfer to developing countries. However, the scheme is clearly complementary and consistent with existing incentive mechanisms.

Regulatory harmonization

We were not convinced that regulatory harmonization as such was the key issue, or that it met many of our criteria. In particular, we did not see that regulatory harmonization would materially contribute to improved incentives for R&D relevant to developing countries. At the root of the problem was a lack of capacity in many regulatory authorities in developing countries. Strengthening this capacity was a priority but it was not clear that harmonization was necessarily the best way to approach capacity-building. Improved regulation and harmonization might improve access to quality-assured medicines and health technologies through quicker availability of new products needed by patients, but it was not clear that any cost-savings generated by companies through more efficient regulation would necessarily be passed on to patients. Furthermore, we also draw attention to the fact that relevance of regulatory harmonization was also related to where, how and on what basis this was done, drawing attention to the role of health policy considerations and the relevance of WHO's role in the area. Needs specific to country and region had to be taken into account, including different assessments that might be made in relation to risks and benefits.

Tax breaks for companies

This proposal does not meet many of our criteria. The proposal is technically feasible and, given the relatively small amount of private-sector R&D globally in the neglected disease areas, the financial cost on a global scale would not be huge. It is also perfectly compatible with other existing or proposed incentives. However, we did not consider that it addressed in any significant way our other criteria. The impact on public health would depend entirely on the extent to which the proposal would increase R&D and the development of new products which would then be made available and affordable and used in developing countries. Evidence, to date, was not encouraging. In that light, the efficiency and cost-effectiveness of the proposal could not be demonstrated. In particular, the lack of impact of the United Kingdom scheme was notable. We were conscious that a tax credit was equivalent to the expenditure of public money, and its costs and benefits needed to be compared with other uses of public money. There would be no additionality arising from the scheme. As a push mechanism, the scheme does not address intellectual property, delinking, availability, affordability and delivery and access issues in developing countries, nor capacity-building or technology transfer. We were aware that, even if schemes generated additional R&D and potential new products, which was not certain, they did nothing to create incentives on the demand side, or to promote access by patients in developing countries. The proposal could be combined with other mechanisms to provide better availability, affordability, delivery and access, but this would lead to further administrative and governance complexities.

The proposal was not considered appropriate as a global solution since tax-break schemes are national in nature and global harmonization would not be realistic. However, we also recognized that most developed countries and several developing countries did use general tax breaks for R&D and countries should consider the extent to which such schemes might fit their local needs, bearing in mind the available evidence on their impact and potential other uses for these public funds.

Transferable intellectual property rights

We did not consider that the proposal on transferable intellectual property rights (TIPR) met many of our criteria. It is a technically feasible proposal but with the defect that it is financed by extending exclusivity on a best-selling drug, thereby delaying generic entry. In some versions this could be mitigated by open licensing or relinquishing intellectual property rights on the neglected disease product. In the same vein it does not delink prices from the cost of R&D, but rather the opposite, although the opportunity exists to delink the cost of the R&D of the neglected disease product from its price. However, like the priority review voucher, the scheme provides no incentive to promote access to medicines in developing countries and the TIPR beneficiary has no limitation on acquiring and exercising intellectual property rights in developing countries. In its simplest form based on unambiguous rules, it has no need for accountability and participation in governance or decision-making. More complex forms, which might require judgements and adjudications as to whether the rules have been met, would necessitate more substantial governance and accountability requirements. TIPR has no direct impact on capacity-building or technology transfer to developing countries, except inasmuch as such conditions are built into the criteria for triggering the reward. The scheme is clearly complementary and consistent with existing incentive mechanisms.

Regional perspectives

We held meetings of various kinds in five of WHO's regions to solicit opinions on our proposals as they developed. A record of these meetings is in Appendix 4 and details are on the CEWG web site.

Issues raised in the regions were diverse, reflecting different national realities and the mix of people participating. We have taken account of these in reaching our conclusions. Generally speaking there

was support for the broad thrust of our tentative recommendations, particularly from developing countries. The proposal for a global framework or convention on R&D received support from these countries, but developed countries were more cautious about the implications of such a framework.

Conclusions

Surveying each of our assessments, we decided that the following proposals met our criteria less well:

- Tax breaks for companies;
- Orphan drug legislation;
- Green intellectual property;
- Priority review voucher;
- Transferable intellectual property rights;
- Health Impact Fund;
- Purchase or procurement agreements.

This does not necessarily mean, as we have indicated in a number of assessments, that countries or the international community should not adopt such measures, nor that it might not be in their interest to do so. Indeed, several of these proposals (e.g. orphan drug legislation, and procurement agreements) are already in existence and are regarded by many as successful in achieving their objectives. It simply means that, in relation to our terms of reference, we do not think they do, or will, perform well in stimulating R&D needed by developing countries on health-care products for Type I, II and III diseases.

A second category consists of proposals that, irrespective of their other merits or drawbacks, do not principally contribute to improved financing or coordination of R&D. In that category we place:

- Regulatory harmonization;
- Removal of data exclusivity.

The third category consists of proposals that we felt best met our criteria:

- Global framework on research and development;
- Open approaches to research and development and innovation;[1]
- Pooled funds;
- Direct grants to companies;
- Milestone prizes and end prizes;
- Patent pools.

It would be possible to pursue each of these proposals individually but we see them as part of a wider package of measures that will promote R&D in ways that can also help address access issues. Thus delinking should be a fundamental principle underpinning open approaches to R&D and innovation. An absolutely necessary condition for implementing these approaches will be a sustainable source of funding. We consider in Chapter 4 the options for achieving this objective. We will discuss a coherent and comprehensive approach to R&D in Chapter 6.

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

CHAPTER 4 STRENGTHENING GLOBAL FINANCING OF HEALTH RESEARCH AND DEVELOPMENT

Introduction

In this chapter we first review, in accordance with our terms of reference, the proposals made by the EWG on generating new funding and funding streams. We then consider the current status of R&D funding on health, before analysing and recommending the ways in which governments, in particular, should commit to enhanced spending on R&D to meet the public health needs of developing countries.

Sources of finance: proposals assessed by the EWG

Our terms of reference ask us to "examine the practical details of the four innovative sources of financing proposed by the Expert Working Group". We have therefore reviewed the EWG proposals and conducted an analysis of particular options that seem to offer potential.

The issue of securing sustainable financing for the health sector in general, and for the health R&D sector in particular, is central to achieving the goals that underlie our mandate. The EWG put forward four options, which it assessed in relation to fundraising capacity, additionality, likelihood of acceptability, and operational efficiency:

- **A new indirect tax.** This could be applied to any number of areas, such as tobacco, alcohol, the arms trade, airline travel, Internet traffic or financial transactions.
- **Voluntary contributions from businesses and consumers.** Again, a number of actual and potential models exist for soliciting such contributions through, for instance, airline ticket purchases, lotteries, project RED, mobile phone usage.
- **Taxation of repatriated pharmaceutical industry profits.** This is a proposal from Brazil to tax pharmaceutical industry profits.
- **New donor funds for health research and development.** This would simply involve the raising of additional funds from new or existing providers of development assistance.

The EWG concluded that the estimated revenue from an appropriate combination of these mechanisms could be US$ 4.6 billion per annum by 2015, but this figure was based more on assumptions and judgements about how much could be raised from different sources rather than on detailed analytical work. The level of revenue generation will of course depend on the tax level and the uptake of different financing mechanisms.

Implicitly the EWG appeared to conceive of these as mechanisms that could raise funds on a global basis for health R&D relevant to developing countries, while noting that decision-making rested ultimately with national governments. However, it did not address how such global fundraising could be made operational. Raising funds that would be used on a global basis implies an institutional mechanism at global level for receiving such funds and then allocating them to research organizations in different countries in the public or private sectors or public–private partnerships. The EWG did not identify the operational and institutional mechanisms as an issue, but we see it as central to building a sustainable mechanism at global level for enhancing R&D as determined in our mandate.

We now review the specific EWG proposals in more detail in reverse order.

New donor funds for health research and development

Sustainable global action on R&D to address the needs of developing countries cannot rely on voluntary contributions alone. However, the EWG examined the possibility of generating additional funding from non-traditional donors such as China, India and Venezuela; from additional contributions from existing donors, including, for example, earmarking a percentage of GDP for health R&D; or from philanthropic organizations. The EWG's very rough calculations suggested possible revenues of US$ 440 million annually, assuming that donors met their commitments to increase aid overall and allocated 10% of extra funding for health to R&D. However, the EWG recognized that this would depend on a convincing case being made and on the existence of political will for this to happen. What is clear is that in reality donors, with one or two exceptions, are unlikely to live up to commitments they made for reaching specified development assistance goals such as those made at the Gleneagles G8 summit in 2005. The OECD calculated that, while development assistance was at a historic high in 2010, there was a US$ 19 billion shortfall overall compared to the Gleneagles commitments, and a shortfall of US$ 14 billion in the commitments made to Africa.[1] The severity of the economic crisis now facing many traditional donors suggests there will be little or no growth in development assistance in the medium term. Moreover the EWG did not pursue in its recommendations the proposal for 10% earmarking of donor funding for health for R&D.

In our judgement it is unwise, in current economic conditions, to rely on possible additional development assistance being forthcoming from existing or potential new donors. Indeed, we are very aware that, according to G-Finder, only about 8% of total funding for R&D currently comes from development agencies. By far the larger amount comes from other government departments and medical research councils, as well as from industry and foundations. There is, therefore, a need to reframe the issue away from development assistance. It is not just a responsibility of development aid or indeed of donors; it is rather a challenge to countries, both developed and developing, to find ways to invest appropriately in health R&D relevant to developing countries in the various ways available to them. Thus, as regards commitments to this field of research, it is necessary to consider the contributions of government as one entity, and not just the actions of one part of government responsible for development assistance.

Taxation of repatriated pharmaceutical industry profits

Under this proposal, which was made to the EWG by Brazil, funds are raised by taxing the profits remitted by non-domestic pharmaceutical companies. The proceeds would then be recycled by a directing council, run somewhat on the lines of UNITAID. Pharmaceutical companies, along with other research entities, would be eligible for funding. The EWG estimated that if all low- and middle-income countries participated in such a venture, a 1% tax on relevant profits would generate US$ 160 million annually. If high-income countries participated also this number could increase significantly. The EWG thought this scheme "particularly attractive".

Appropriate assessment of the feasibility of this proposal would require further information and knowledge on, inter alia, specific matters related to transfer pricing, international corporate taxation, applicable tax agreements, relationships with national industry, as well as commitments made by individual countries as part of bilateral and multilateral trade and investment agreements. Views differ on the justification for specific taxes on the pharmaceutical industry but they exist in several countries. For example, France raises levies on the pharmaceutical industry in a number of different ways to finance its health-care system. (*1*) However, assessment of further practical implications and feasibility of the proposal would require more specific expertise and information than was available to

[1] Details are provided at: http://www.oecd.org/document/35/0,3746,en_2649_34447_47515235_1_1_1_1,00.html, accessed 7 March 2012.

the working group. Apart from the short submission by Brazil to the EWG outlining the proposal, (*2)* we also have not seen any further development of it.

Voluntary contributions from businesses and consumers

The EWG considered a number of voluntary contribution schemes. Noting various complications with the introduction of new taxes, it considered that voluntary consumer contributions were "the most innovative funding proposal and the most likely to be sustainable". From among the different options, the EWG considered that US$ 1 billion could be raised, principally from a voluntary airline solidarity contribution.

Since the EWG reported, the Millennium Foundation, established by UNITAID in 2008, has attempted to implement a voluntary airline contribution under the brand name MASSIVEGOOD. UNITAID committed up to US$ 22.4 million to the Millennium Foundation for this purpose in order to raise money for UNITAID operations. The intention was, after the development of an information technology platform, to install this technology with travel companies, online and offline. The original business plan forecasted revenues of US$ 590 million in 2010 and US$ 980 million in 2011. Former President of the United States Bill Clinton and United Nations Secretary-General Ban Ki-moon launched MASSIVEGOOD in March 2010. It soon became clear that these forecasts were grossly optimistic. In fact, the foundation generated voluntary contributions of only about US$ 200 000 in 2010 and even less in 2011. In 2011 the foundation discontinued the voluntary contribution project and reduced its staff to a minimum, and UNITAID is now considering its future. (*3*) The reasons for this failure included:

- The size of the market was smaller than originally thought.
- The market was more fragmented and more difficult to penetrate than originally envisaged.
- Travel industry partners were not adequately incentivized to collaborate enthusiastically.
- There was a deterioration in global economic conditions.
- Consumers were less willing to give than had been forecast.
- Building a fundraising brand was more costly and time-consuming than envisaged.
- UNITAID was not a well-known brand outside the global health community.

This experience clearly demonstrates that estimates of the amounts that can be raised by entirely new voluntary contribution schemes are quite possibly vastly overstated. In addition, a significant investment is required to generate funds. Of the initiatives already in existence and noted by the EWG, the actual revenues are much smaller. These include:

- **Product RED.** In this scheme, companies which partner with Product Red agree to contribute a portion of profits from the sale of a product to Global Fund-financed HIV/AIDS programmes in Africa. Between its founding in 2006 and 2012 it has generated about US$ 180 million for this purpose.[1]
- **Lotteries.** The EWG quoted a 2009 World Bank estimate that lotteries in Belgium and the United Kingdom transferred US$ 66 million to countries in 2007. The United Kingdom lottery's corporate plan for 2011–2012 provides for nearly £25 million (US$ 38 million) to be provided to international communities for overall development purposes.[2]

[1] For more information, see: http://www.joinred.com/red/#impact, accessed 7 March 2012.

[2] For more information, see: http://www.biglotteryfund.org.uk/pub_corp_plan11-12.pdf, accessed 7 March 2012.

- **Charity.** The EWG also highlighted charity as a major existing source of funding for development in general, including public health. For donations to health, good estimates exist only for the USA. These indicate that in 2011 an estimated US$ 2.7 billion was channelled through United States NGOs for health in developing countries, of which nearly US$ 1.3 billion was provided by the United States and other governments. This represented a decline from their peak of US$ 3.7 billion in 2008, of which US$ 1.4 billion was provided by governments. Thus private giving declined from about US$ 2.3 billion to about US$ 1.4 billion. At the same time, funding from United States foundations increased from US$ 600 million in 2001 to a peak of US$ 2 billion in 2010, declining slightly in 2011. (*4*)

On the basis of the above, we do not believe that it is realistic to expect voluntary contribution schemes to raise very large sums of money on a sustainable basis for health R&D relevant to developing countries. The experience of the Millennium Foundation suggests that "innovative" voluntary contribution schemes are quite difficult to develop into significant and sustainable flows of funds. Moreover the willingness of the public to contribute will be determined by the priority they assign to this particular use of funds as compared to the variety of other possible uses in the field of health or of development more generally. Our view is that "traditional" financing mechanisms based on direct or indirect taxation are more likely to succeed than a complex landscape of uncoordinated voluntary so-called "innovative funding mechanisms" of uncertain funding capacity and stability.

A new indirect tax

The EWG considered a variety of possible taxes, namely:

- a 10% tax on the arms trade which might raise US$ 5 billion annually;
- a tax on Internet traffic which could yield "tens of billions of US dollars";
- Brazil's tax on bank account transactions which was abolished in 2007;
- an airline tax which could raise totals in the "low billions of US dollars";
- a tobacco tax where a 5–10% increase in tax rates in low-income countries could raise "US$ 0.7–1.4 billion" and a similar increase in developed countries of "US$ 5.5–11 billion".

In the end the EWG favoured a digital Internet tax at a very low rate which it said "could be estimated conservatively to raise about US$ 3 billion per annum". The EWG noted a number of implementation issues with some or all of these taxes but did no detailed analytical work to identify how these issues could be addressed in practice. For instance, the EWG said that monitoring Internet traffic cost-effectively in order to tax consumers "might prove to be a challenge" and it might place a high burden on companies that send large amounts of data. Its conclusion was that the "problem could be overcome by appropriate scoping of the tax". The EWG did not point out that a tax on the Internet of the sort it proposed was currently banned in the USA under the Internet Tax Freedom Act.[1] The EWG did note that proposals for an Internet tax dated from the very early days of the Internet in the 1990s and the example it gave was based on a small tax on e-mail messages. (*5*) In terms of Internet usage today, this seems quaint. The EWG did not consider the practical details of its implementation and we are not aware of any serious work being done elsewhere considering the practical dimensions of its implementation. Nor are we aware of recent further proposals for a similar Internet tax.

Availability of small firearms is a public health issue and a public health concern. (*6*) The issue of taxing the arms trade has been part of international discussion since the Brandt report in 1980. It was

[1] Details can be seen here: http://www.govtrack.us/congress/billtext.xpd?bill=h110-3678, accessed 7 March 2012.

an issue at the G8 meeting in France in 2003, where Brazilian president Luiz Inacio Lula da Silva declared that an international arms sales tax was one of his favoured schemes to fund efforts to eliminate hunger. (*7*) However, it would be prudent to assume that prospects of imminent realization of this tax are currently not high. Further assessment and exploration on this type of broad initiative is likely to be best made through the United Nations Office for Disarmament Affairs.[1]

Brazil's tax on bank transactions is one particular form of financial transactions tax, a subject discussed in more detail below, as are also the tobacco and airline taxes.

It is our view that some form of taxation is the most fruitful avenue to explore in the search for new and sustainable sources of funding. However, it would be unrealistic, given the multifaceted nature of development needs, to think that one specific new source that would generate very significant amounts of money on a global scale would or should be devoted to the particular field of health R&D of relevance to developing countries. Rather we would argue that, from any new source of funding that might emerge, a portion should be related to the improvement of health as an acknowledged development priority and that another portion also should be devoted to currently underfunded R&D areas, including those within the CEWG mandate.

Having said this, we acknowledge the very significant contribution made to global health, including health R&D relevant to developing countries, as a result of charitable giving, notably in our field by organizations such as the Bill & Melinda Gates Foundation and the Wellcome Trust. That taxation is likely to be a more sustainable source of funding does not detract from the importance of charitable funding. As discussed in Chapter 5, it is also important to find better ways to integrate funding from different sources, including public, private and philanthropic.

Tax options

As we are appointed by WHO, and for the most part come from public health disciplines, our professional interest and inclination is towards taxes that not only generate revenue but also have a potentially positive impact on health by reducing consumption of products that harm health. The oldest and most common are taxes on alcohol and tobacco, imposed in the first instance because they are obvious sources of revenue. Sugar, rum and tobacco were found to be commodities which were not necessary but almost universally consumed and thus were considered extremely proper subjects of taxation already in 1776 by Adam Smith in *The wealth of nations*.

From a public health perspective, taxes are part of a broader package of fiscal policies for health promotion and disease prevention. (*8*) We recognize that, along with indirect taxation, progressive direct taxation has an important role in reducing poverty and inequality and in generating resources for the social infrastructure, services and benefits which will help to improve health. (*9*) As public health measures, the primary aim in the case of indirect taxes is health impact rather than revenue-raising only. Raising tobacco and alcohol taxes are included as "best buys" on action for prevention of noncommunicable diseases. (*10*) The WHO Global Strategy on Diet, Physical Activity and Health recommends using fiscal policies to influence consumption patterns, while taking into account potential unintentional impacts on vulnerable populations. (*11*)

In looking at the various tax options, we considered a number of criteria. The principle that taxes should be, if possible, progressive – bearing more proportionately on the rich than the poor – should be respected, particularly for sources unrelated to public health (e.g. an airline tax). On the other hand we recognized that particular forms of indirect taxation relevant to public health, such as "sin" taxes

[1] For more information, see: http://www.un.org/disarmament/convarms/ArmsTradeTreaty, accessed 7 March 2012.

related to reducing lifestyle risks, are regressive in nature and that in these cases the public health benefits, particularly for the poor, should outweigh the possible adverse impact on income distribution. At the same time, it was important that tax and benefit policies were looked at as a whole; regressive impacts could, in principle, be offset by changes in other taxes.

For instance, there is a clear-cut case for tobacco taxes on the grounds of public health. It has been well known for a long time that increasing tobacco taxes is one of the most effective ways of reducing smoking, (*12*) and that reducing smoking has a favourable impact on public health, even within a relatively short space of time. (*13*) Implementation of a tax is administratively relatively simple, including in developing countries, as it involves a narrow range of easily identifiable products. Although a tobacco tax is regressive, the evidence suggests that the less well-off are more sensitive to price increases than the better-off. Thus, while the effect on income inequalities may be negative for those who continue smoking, the impact on health inequalities is likely to be the opposite because poorer people, who in any case smoke more, will reduce smoking proportionately more than the rich.[1] The public health benefits of taxation of alcohol for reduction of harmful use of alcohol are also already established. (*14*)

The case for public health measures with respect to sugar and fats has increased as concerns about rapidly growing obesity rates in both developed and developing countries have come to the fore. Finland introduced a sweet tax in 2011 (*15*), and taxation of sugary drinks and foods on the basis of public health concerns has been increasingly discussed (*16*). Taxing of fat or foods with high saturated fat content – so-called "fat taxes" – has also come on the agenda. In 2011, Denmark introduced apparently the first such tax on butter, milk, cheese, pizza, meat, oil and processed food if they contain more than 2.3% saturated fat (*17*). As "fat taxes" are new measures, empirical evidence on impacts is scarce. However, on the basis of what is known it is important that governments considering this type of tax should take into account i) the potential shift of consumption to other unhealthy but less-taxed foods, and ii) regressivity (i.e. impacts on the consumption of poor and vulnerable populations). In addition, their implementation can be quite complex, particularly in the context of developing countries. A wide diversity of foods – many produced and sold informally – could be regarded as unhealthy and taxable. The literature suggests that both regressivity and public health benefits could be addressed by using the proceeds to subsidize "healthy" foods but this would, of course, reduce their net revenue-raising capacity (*18*).

National taxes

We reviewed various existing examples of countries that have used taxes to raise money for the purpose of improving health. These include the following:

- Ghana applies a 2.5% share of its Value Added Tax (VAT) to its National Health Insurance Scheme. (*19*)
- Thailand applies a 2% surcharge on excise duty on alcohol and tobacco which is used to fund health promotion. (*20*)
- Chile applies 1% of its VAT to fund health. (*21)*
- Gabon imposed a 1.5% levy on the post-tax profits of companies that handle remittances and a 10% tax on mobile phone operators to use for health care for low-income groups. Between them, the two taxes raised the equivalent of US$ 30 million for health in 2009. (*21*)

[1] For the evidence, see: http://www.saprp.org/KnowledgeAssets/knowledge_results.cfm?KAID=4, accessed 7 March 2012).

- In the Philippines, 2.5% of the incremental revenue from the excise tax on alcohol and tobacco products has, since 2005, been remitted directly to the Philippine Health Insurance Corporation for the purpose of meeting and sustaining the goal of universal coverage of the National Health Insurance Programme, and 2.5% of the incremental revenue is credited to the account of the Department of Health and constituted as a trust fund for its disease prevention programme. (*22*)

In 2009 WHO also identified 28 countries that allocated a proportion of tobacco-tax-related revenues for health-related purposes. (*23*)

We are also aware of at least one tax which is raised specifically to finance health R&D. The Italian Medicines Agency set up an ad hoc fund requiring pharmaceutical companies to contribute 5% of their yearly expenditure devoted to promotional initiatives (e.g. seminars, workshops) aimed at physicians. This raises about €40 million each year and it guarantees not only funding for research but also other activities as well. An independent scientific committee coordinates different aspects of the research programme. The R&D committee plays a fundamental role in proposing priority research areas, in conducting the first phase of the selection process, and in supervising the implementation of projects.[1] In Spain, industry is required to pay, inter alia, for R&D funds on a basis related to sales volume. (*24*)

Taxes for global purposes

We see the possibility that a truly international tax could be particularly suitable for earmarking for particular development purposes, including improving health and investing in health R&D relevant to developing countries.

There are in fact no existing international taxes (in the sense that the proceeds accrue directly to an international body rather than a national treasury). The nearest equivalent is the airline tax which France and other countries have used to provide a source of funding for health-related investments. (See Box 4.1)

Box 4.1 Airline tax

A group of countries led by France has implemented an additional airline tax, called the airline solidarity contribution, in order to generate resources for global health. The additional airline tax is not a global tax in the strict sense of a single agreed-upon tax with a global authority having the power to levy it and allocate proceeds. Rather, it is a domestic tax that participating countries have agreed to coordinate and allocate to support UNITAID, an International Drug Purchase Facility for AIDS, tuberculosis, and malaria.

In 2006 France introduced this levy on passengers departing from French airports, including domestic flights. A flat-rate tax is added to the price of a ticket, with the amount dependent on destination and class of service. Basing the rate on class of service is intended to impart a progressive aspect to the tax. A round-trip within France costs an extra €2 in economy class and €20 in first class. The new intra-Europe solidarity levy represented a 26% increase in the tax for economy class and a 255% increase for first class. For other destinations, the increases were 57% and 568%, respectively. Thus the increased tax is not trivial but it is small in relation to the total cost of a trip or a holiday. Total revenue from this new levy will approach €180 million per year, with 90% allocated to UNITAID and 10% going to the International Finance Facility for Immunization.

The solidarity contribution or "tax" on airline tickets represents 70% of UNITAID's financial base and is complemented by multi-year budgetary contributions from a number of member countries. As of September 2011, nine of UNITAID's 29 member countries were implementing the airline tax: Cameroun, Chile, Democratic Republic of Congo, France, Madagascar, Mali, Mauritius, Niger, and the Republic of Korea.

[1] For more information, see: http://www.agenziafarmaco.gov.it/en/content/independent-research-drugs, accessed 7 March 2012.

Norway allocates part of its tax on CO2 emissions from aviation fuel to UNITAID.

Source: Brookings Institution http://www.brookings.edu/~/media/Files/Projects/globalhealth/healthsnapshots/airline.pdf, UNITAID

It should be noted that this type of funding mechanism – a national tax hypothecated to an international body – is in principle little different from any other commitment by a national government to finance international activities (e.g. to fund the United Nations, the World Bank or the Global Fund). Money flows into the national treasury and then flows out again for a specified purpose – in the example cited to UNITAID. The essential difference may be that there is an implication of a long-term and sustained commitment by the funder, and of equivalence between the amount of tax raised and the money donated. On the other hand, the same objective could be achieved in different ways. For example, the government of the United Kingdom does not believe in hypothecating taxes but has made a 20-year commitment of £1.4 billion from its development assistance budget to UNITAID. In any event, there is no necessary automaticity in either form of commitment; ultimately, whether hypothecated or not, such commitments will be vulnerable to political changes and any financial or economic crises in nation states.

Financial transactions tax

As noted in Chapter 2, there is already support for the adoption of a financial transactions tax (FTT). On a technical level, bodies such as the World Bank and the International Monetary Fund (IMF) have reviewed these proposals. A World Bank study in 2009 concluded that attempts "to raise a significant percentage of gross domestic product in revenue from a broad-based financial transactions tax are likely to fail both by raising much less revenue than expected and by generating far-reaching changes in economic behaviour. Although the side-effects would include a sizable restructuring of financial sector activity, this would not occur in ways corrective of the particular forms of financial overtrading that were most conspicuous in contributing to the crisis."(*25*) An IMF study, although not quite so negative, reached broadly similar conclusions. The tax was called "an inefficient instrument for regulating financial markets and preventing bubbles" and more "efficient tax measures should therefore be considered before an [FTT]". Other studies are far more positive about its economic impact and ability to stabilize the financial sector. (*26*) In addition, because there are relatively few financial centres accounting for a majority of financial transactions, the yield from the tax would be highly uneven and measures might be needed to align relative national contributions more closely to relative GDP. (*27*) On the other hand, there were no insuperable administrative problems to be overcome in implementing such a tax. (*28*)

A recent overall review of the evidence available concluded:

> "Given the answers that we have been able to glean from the literature on our four questions, our overall conclusion is moderately positive. Although the literature is far from conclusive on many points, it seems clear that an FTT is implementable and could make a non-trivial contribution to revenue in the major financial economies. It seems unlikely to stabilise financial markets, but, if appropriate (sic) designed, unlikely to destabilise them either; and, although a multilateral agreement between the key economies is clearly preferable, it would not be impossible to implement unilaterally, at least for a major economy. The incidence of an FTT would not be as progressive as its proponents claim, but we have no reason to believe that it would be significantly worse than most alternatives, nor that it would be any more difficult to collect. In short, we conclude that, somewhat contrary to our initial instincts, a financial transaction tax may not be such a bad idea after all." (*29*)

We are not in a position to provide further analysis of the issues surrounding the implementation of a possible FTT; whether or not it will be implemented, and how, will be decided politically. Our position is that, if any international tax is agreed, then a proportion of that tax should go to provide

support to health services in developing countries and a proportion should be earmarked for health R&D that meets the needs of developing countries.

Solidarity tobacco contribution

As noted above, tobacco taxes in particular have been shown to be a particularly effective way of reducing smoking and improving public health. A WHO paper has proposed a "solidarity tobacco contribution" (STC) (see Box 4.2). The paper suggests that, with the agreement of governments, an international funding mechanism could be established which would be used to fund international health and would not be confined to addressing tobacco-related issues. Citing the example of other novel mechanisms, such as the air solidarity levy, the International Finance Facility for Immunization, and the advance market commitment for a pneumococcal vaccine, it notes that, "given today's challenging times for international health financing, the STC will require high-level political support from a group of interested path finding Member States that are prepared to launch a pilot." (*23*)

Box 4.2 The solidarity tobacco contribution

A WHO document has proposed a solidarity tobacco contribution (STC) in which participating countries would add a small "micro-levy" to existing national taxes on tobacco.

WHO assessed the potential revenue that could be generated from an additional micro-levy on a pack of cigarettes among the 43 "G20+" countries. These are the 19 G20 countries, 22 member states of the European Union that are not members of the G20 (data for Luxembourg were not available), as well as Chile and Norway. The results were that an STC could generate between US$ 5.5 billion and US$ 16.0 billion in extra excise tax revenues annually, depending on the chosen scenario. The exercise was purely hypothetical and the countries concerned were not consulted about their views on the proposal.

For illustrative purposes, WHO estimates that if all G20+ countries were to devote an additional small amount to existing or new tobacco taxation (US$ 0.05 for high-income countries, US$ 0.03 for upper middle-income countries and US$ 0.01 for lower middle-income countries) for each cigarette pack sold, **US$ 5.47 billion** could be generated each year. The proposed contributions are based on US$ 0.05 per pack in high-income countries, US$ 0.03 in upper middle-income countries and US$ 0.01 in lower middle-income countries. The 3.3% average increase on the price of cigarettes as a result of the STC is estimated to prevent 149 000 young people from starting smoking and to cause 223 000 adults to quit smoking.

WHO assessed additional scenarios to determine how much a higher-level STC micro-contribution could yield in revenue. If twice the amount were to be devoted – i.e. US$ 0.10 for high-income countries, US$ 0.06 for upper middle-income countries and US$ 0.02 for lower middle-income countries per pack of cigarettes sold – **US$ 10.8 billion** could be generated by the STC each year. If rates were further increased by 50% – i.e. US$ 0.15 for high-income countries, US$ 0.09 for upper middle-income countries and US$ 0.03 for lower middle-income countries per pack of cigarettes sold – **US$ 16 billion** could be generated by the STC each year.

The innovative feature of this proposed levy is that Member States would decide voluntarily whether to contribute STC funds for international purposes. Those expressing their intent to support a voluntary STC contribution for global health purposes will then decide upon the specific purposes for which the funds will be used and, on the basis of this decision, what mechanisms should be used to disburse them.

Source:(23)

The WHO paper usefully sets out a process which would need to be followed in the case of establishing an international mechanism to promote public health. From our point of view a similar process would be needed whatever the source of money generated (e.g. from a FTT or from another source). Countries would need to decide:

1. **The specific purpose and scope for using funds generated**. What are the broad objectives for the use of funds? Should a proportion be earmarked for health R&D?

2. **Whether to pool funds internationally**. Some form of pooled fund is often used for international health initiatives. This can permit, in principle, greater efficiency in fund management and greater predictability and sustainability, and it can minimize risks of substitution for other international aid and official development assistance commitments.

3. **Whether to use an existing fund management/disbursement mechanism or create a new one**. Are there existing mechanisms that could meet the purpose or purposes envisaged for the fund? If not should a new one be created?

4. Whether and what type of governance is required.

Beyond that stage would be many practical issues about how the new mechanism will work.

Conclusion: tax options

In summary, we believe that countries should first consider at **national level** what tax options might be appropriate to them as a means of raising revenue to devote to health and health R&D, and we have provided a few examples to indicate what countries are currently doing. Secondly we have highlighted, in particular, two possible taxes – the financial transactions tax and the solidarity tobacco contribution – that, in addition to the airline taxes implemented in some countries, could be used to generate funds to be channelled through an **international mechanism** to supplement national resources. It is our hope that such a tax could be agreed as part of an international commitment to finance global public goods, including for health and health R&D relevant to developing countries. We noted that our position is that if any international tax is agreed, then a proportion of that tax should go to provide support to health services in developing countries and a proportion should be earmarked for health R&D meeting the needs of developing countries. Thirdly, we think that it is important that WHO has the capacity to contribute to policy discussions on new and national and international financing initiatives as well as the use of fiscal measures in support of health policy priorities.

Global health research and development: goals and targets

In this section we review the current status of R&D and progress against various targets that have been proposed internationally. As noted in Chapter 1, we define our scope as R&D focused on health products and technologies (including medicines, vaccines, diagnostics and devices) related to Type II and Type III diseases and the specific R&D needs of developing countries in relation to Type I diseases. Therefore, when we define a quantitative target, this is the scope of R&D we would wish to be measured against the target. However, we also recognized in Chapter 1 and subsequently that other forms of health R&D are important, including those relating to improving health systems and delivery systems, epidemiology, and policy research aimed at improving the effectiveness of policy interventions. We therefore also present data on investments in total health R&D and suggest that countries may also aim for quantitative targets relating to general health research spending.

There is limited data on health R&D investments, particularly of a systematic nature. There is some selective data on total health R&D from OECD (see Table 4.1) and then data from G-Finder on biomedical R&D on type II and III diseases, which includes R&D on drugs, vaccines, diagnostics, microbicides, vector control products and platform technologies (including diagnostic and delivery devices). The exact definition of health research used by the Global Forum for Health Research is unclear. It is also the case that there is no existing data source encompassing the scope of the CEWG

mandate including the specific research and development needs of developing countries in relation to Type I diseases.

Table 4.1 R&D, health R&D, government health expenditures 2009 (%) in OECD countries

	1	2	3	4	5	6
Country	**Total R&D (GERD) (% of GDP)**	**GERD financed by government (GRD) (%GDP)**	**Government health R&D (GHRD) (% of GDP)**	**GHRD (% of GRD) (3/2)**	**Government health expenditures (GHE) (% of GDP)**	**GHRD (%GHE) (3/5)**
Australia	2.21[c]	0.76[c]	0.22[c]‡	28.84	5.94[c]	3.70
Austria	2.75	0.96	0.25[d]	26.03	8.58	2.91
Belgium	1.96	0.50	0.01 †	2.01	8.17	0.12
Canada	1.92	0.66[c]	0.10[c]†	15.25	8.06	1.24
Chile	0.39[c]	0.13[c]	0.02 [c] ‡	15.02	3.98	0.50
China	1.70	0.40	n/a	--	2.29	--
Czech Republic	1.53	0.67	0.10	14.92	6.92	1.44
Denmark	3.02	0.84	0.15[d]	17.85	9.81	1.53
Estonia	1.42	0.70	0.13	18.70	5.28	2.46
Finland	3.96	0.95	0.16	16.82	6.84	2.34
France	2.21	0.85	0.15[c]	17.59	9.18	1.63
Germany	2.78	0.83	0.15[d]	18.14	8.93	1.68
Greece	0.59[b]	n/a	0.04[b]	--	n/a	--
Hungary	1.15	0.48	0.07‡	14.52	5.19	1.35
Iceland	2.64[c]	1.02[c]	0.10 [c] ‡	9.76	7.91	1.26
Ireland	1.79	0.56	0.05	8.91	7.15	0.70
Israel	4.28	0.60[c]	0.01[d]†	1.67	4.60	0.22
Italy	1.27	0.53	0.08[d]	14.96	7.38	1.08
Japan	3.33	0.59	0.03[d]†	5.09	6.87[c]	0.44
Korea	3.36[c]	0.92	0.10‡	10.86	4.03	2.48
Luxembourg	1.68	0.41	0.09[d]†	22.10	6.53	1.38
Mexico	0.37[b]	0.19[b]	0.01[a]†	5.37	3.10	0.32
Netherlands	1.82	0.74	0.16[d]	21.50	9.50	1.68
New Zealand	1.17[b]	0.54	0.15‡	27.95	8.28	1.81
Norway	1.76	0.82	0.12[d]†	14.59	8.08	1.49
Poland	0.68	0.41	0.01[c]†	2.45	5.32	0.19
Portugal	1.66	0.75	0.12‡	16.00	6.54[c]	1.83
Russian Federation	1.24	0.83	0.01 [d]†	1.21	3.51	0.29
Slovak Republic	0.48	0.24	0.02‡	8.23	5.99	0.33
Slovenia	1.86	0.66	0.08	12.08	6.80	1.18
South Africa	0.93[c]	0.42[c]	n/a	--	3.41	--
Spain	1.38	0.65	0.16	24.55	7.00	2.28
Sweden	3.62	0.99	0.24	24.15	8.16	2.94
Switzerland	3.00[c]	0.68[c]	0.00[c]†	0.00	6.80	0.00
Turkey	0.85	0.29	n/a	--	4.44[c]	--
United Kingdom	1.85	0.60	0.14[c]	23.20	8.23	1.70

	1	2	3	4	5	6
Country	**Total R&D (GERD) (% of GDP)**	**GERD financed by government (GRD) (%GDP)**	**Government health R&D (GHRD) (% of GDP)**	**GHRD (% of GRD) (3/2)**	**Government health expenditures (GHE) (% of GDP)**	**GHRD (%GHE) (3/5)**
United States	2.79[c]	0.87	0.33	37.90	8.29	3.98
OECD Average	2.33[c]	0.71	0.18[c]	25.31	6.9	2.61

[a] 2006 data; [b] 2007 data; [c] 2008 data; [d] 2010 data; † and ‡ see source number 3 below

Sources

(1) OECD. Gross domestic expenditure on R&D, 1999 and 2009 (GERD). http://www.oecd-ilibrary.org/sites/sti_scoreboard-2011-en/02/05/index.html?contentType=/ns/Chapter,/ns/StatisticalPublication&itemId=/content/chapter/sti_scoreboard-2011-16-en&containerItemId=/content/serial/20725345&accessItemIds=&mimeType=text/html

(2) OECD. R&D expenditure by performing sectors, 2009 (GRD). http://www.oecd-ilibrary.org/sites/sti_scoreboard-2011-en/02/05/index.html?contentType=/ns/Chapter,/ns/StatisticalPublication&itemId=/content/chapter/sti_scoreboard-2011-16-en&containerItemId=/content/serial/20725345&accessItemIds=&mimeType=text/html

(3) OECD. Public funding of health-related R&D, 2010 (GHRD). (For those marked with †, Health R&D in government budget appropriations or outlays for R&D, 2010.) http://www.oecd-ilibrary.org/sites/sti_scoreboard-2011-en/04/02/index.html?contentType=/ns/Chapter,/ns/StatisticalPublication&itemId=/content/chapter/sti_scoreboard-2011-35-en&containerItemId=/content/serial/20725345&accessItemIds=&mimeType=text/html For those marked with ‡, Gross domestic expenditure on R-D by sector of performance and socio-economic objective http://www.oecd-ilibrary.org/science-and-technology/data/oecd-science-technology-and-r-d-statistics/gross-domestic-expenditure-on-r-d-by-sector-of-performance-and-socio-economic-objective_data-00188-en GDP in US dollars at current prices and current PPPs http://www.oecd-ilibrary.org/economics/gross-domestic-product-in-us-dollars_2074384x-table3 . See also footnote 9 below.

(4) No source – calculation of Government Health R&D divided by Government and Higher Education R&D

(5) OECD. Public and private expenditure on health. http://www.oecd-ilibrary.org/sites/factbook-2011-en/12/03/03/index.html?contentType=/ns/StatisticalPublication,/ns/Chapter&itemId=/content/chapter/factbook-2011-112-en&containerItemId=/content/serial/18147364&accessItemIds=&mimeType=text/html

(6) No source – calculation of Government Health R&D divided by Government Health Expenditures

It is estimated by the Global Forum on Health Research that total global health research spending in 2005 was US$ 160 billion, of which the public sector accounted for US$ 66 billion and the private sector US$ 94 billion. The amount spent by the public sector in developing countries was estimated at US$ 3 billion, of which some US$ 0.6 billion was provided by development assistance. (*30*)

In 2008, OECD figures suggested that OECD countries spent on average about 2.3% of GDP on R&D in the public and private sectors but, as Table 4.1 shows, there is a wide variation around this figure, from under 1% to over 4%. Of total R&D, approximately one third is publicly funded; such research accounts for about 0.7% of GDP for the OECD as a whole but again there is wide variability. Several countries have set themselves targets for overall R&D and public investment in R&D. For instance, the European Union agreed in 2002, as part of its competitiveness agenda, to an overall target of 3% of GDP in 2010, of which two thirds of new investment should be in the private sector.[1] Although there are significant difficulties relating to the quality and consistency of data on public spending on health R&D,[2] our best estimate is that in the OECD approximately 0.18% of GDP is spent on publicly-funded health R&D, which is about 25% of total publicly-funded R&D, but some countries invest relatively more in health R&D (e.g. the USA at about 0.33% of GDP or 38% of total publicly-funded R&D). High income countries generally invest on average about 7% of GDP on health care and delivery.

Most of these figures relate to developed countries precisely because there is a serious lack of good data relating to R&D expenditures in the majority of developing countries. As we noted in Chapter 2, even the best current source of data in this field – G-Finder – has very limited coverage of developing countries and is also limited to examining research on Type II and Type III diseases. We understand that there is no long-term secured funding for G-Finder. Similarly the Global Forum for Health Research (now part of the Council for Health Research and Development), quoted above, used to provide regular reports on global R&D spending but these ceased in 2009. This lack of data is important because in its absence it is very difficult to measure progress in relation to goals and targets. We return to this important issue in the next chapter.

Target: 15% of government expenditure to health in Africa

African heads of state pledged in 2001 "to set a target of allocating at least 15 per cent of our annual budget to the improvement of the health sector." (*31*) This commitment is relevant to our mandate although it does not include a specific commitment to health R&D.

Table 4.2 Government expenditures on health

Country group	General government expenditure on health as % of total government expenditure		General government expenditure on health as % of GDP	
	2000	2008	2000	2008
WHO REGION				
African Region	8.2	9.6	2.4	3.0
Region of the Americas	14.5	16.1	5.2	6.2
South-East Asia Region	4.7	5.6	1.3	1.6
European Region	13.9	14.2	5.9	6.3
Eastern Mediterranean Region	7.0	6.9	2.0	2.2

[1] See: http://www.easac.eu/fileadmin/PDF_s/reports_statements/The.pdf, accessed 7 March 2012.

[2] We are using data from three sources in this column because the OECD has Public Funding of Health-Related R&D figures (the best source) for only 16 countries. Public health-related R&D is not fully included in the Health R&D in Government Budget Appropriations or Outlays for R&D data, meaning that the figures marked with a † do not include general university funds (from government block grants to universities) or general support for R&D in hospitals. Gathering the data from three different sources may be problematic if there is significant cross-funding (i.e. a large share of government-funded health R&D being carried out by the business sector or vice-versa).

Western Pacific Region	13.8	13.7	3.8	3.9
INCOME GROUP				
Low-income	7.7	8.9	1.7	2.2
Lower middle-income	7.1	7.8	1.6	2.0
Upper middle-income	9.0	9.9	3.2	3.6
High-income	15.3	16.7	5.9	6.9
GLOBAL	13.3	13.9	4.7	5.1

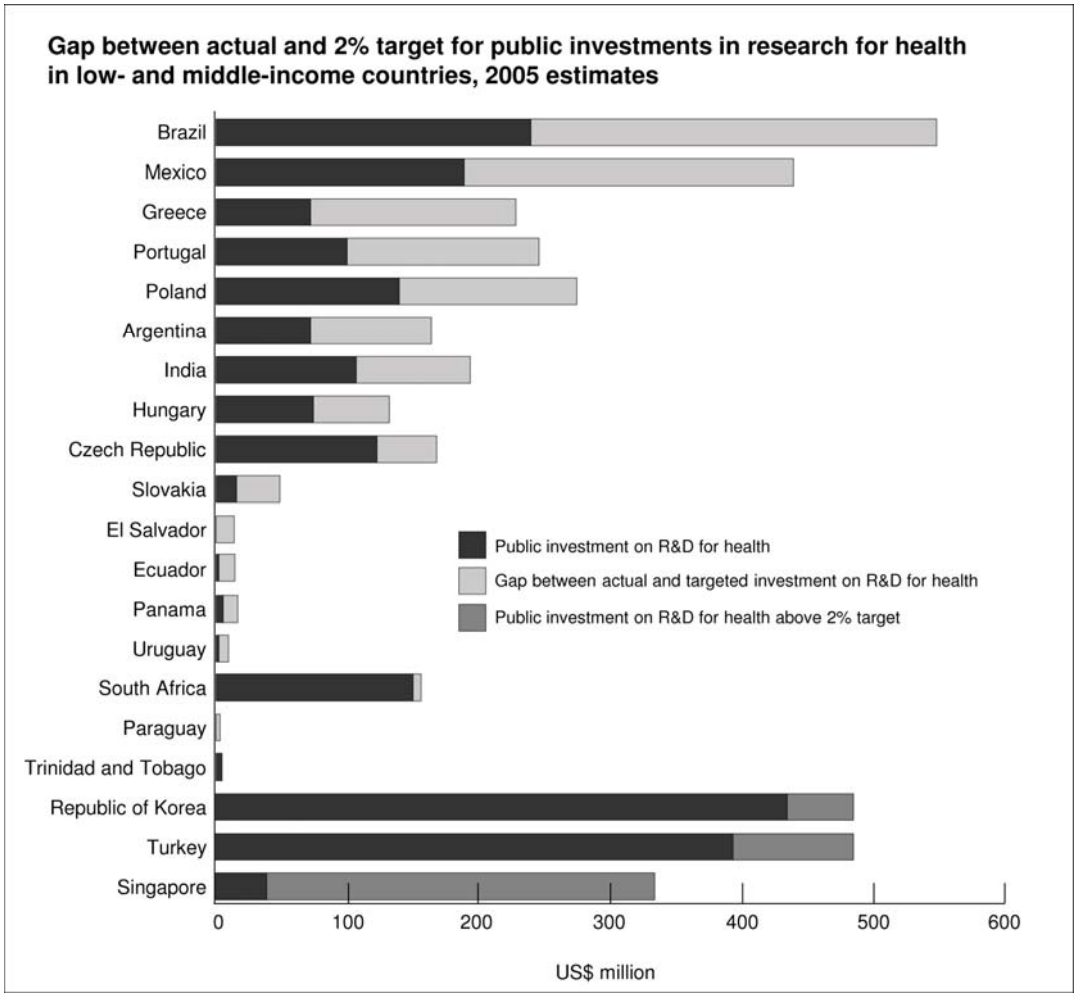
Source: WHO. *World health statistics 2011.*

The latest figures available for 2008 (see Table 4.2) suggest that, on average, African countries are a long way from reaching the Abuja targets. Health expenditure is less than 10% of total government expenditure, although this is a significant increase on 8.2% in 2000. According to WHO, only Rwanda and South Africa had reached the Abuja target a decade later. (*32*) In proportion to GDP, the increase has been slightly larger proportionately. It can also be seen that Africa's performance is considerably superior to that of the South-East Asia Region and the Eastern Mediterranean Region, which includes also North African countries. By contrast high-income countries, on average, more than exceed the Abuja target.

Target: 2% of national health expenditure on research and development

This target was originally proposed by the Commission on Health Research and Development in 1990, and in 2005 the World Health Assembly urged Member States to "consider implementing" the CHRD recommendations on this and development assistance (see below). According to the Global Forum on Health's estimates for 2005, no low- and middle-income countries met this target (see Figure 4.1 for available data). (*30*) Based on the data in Table 4.1 we estimate that OECD countries exceed this target.

Figure 4.1 Performance against 2% target



Sources: Global Forum for Health Research estimates of investments in R&D for health based on OECD, RICYT, and national surveys for countries reporting public investments in R&D for health in 2005; public investment in health estimates from WHO

Target: 5% of development assistance for health to health research

The Commission on Health Research and Development also proposed that donors should devote 5% of their total development assistance for health to health research. Table 4.3 indicates that in 2009 approximately 2.5% of development assistance for health channelled by bilateral agencies was devoted to health R&D for type II and III diseases as defined by G-Finder, but only 1.5% if one also includes development assistance provided through the United Nations and other multilateral agencies (such as the World Bank and Global Fund). However, as already noted, health R&D from development agencies is only about 15% of all such R&D funded by governments. Thus, meeting the 5% target for bilateral development agencies would add less than US$ 300 million to annual R&D relevant to developing countries.

Table 4.3 Research and development expenditures on Type II and III diseases from development assistance for health (DAH) by development agencies (DAs) and expenditures by other government departments (OGDs) in 2009, and as % of GDP in 2010

	1	2	3	4	5	6
Country	**Bilateral DAH 2009 (2009 US$ million)**	**Health R&D on Type II & III from DAs (2007 US$ million)**	**Health R&D on Type II & III From OGDs (2007 US$ million)**	**Health R&D on Type II & III (total) (2007 US$ million)**	**R&D on Type II & III from DAH as % of DAH**	**Health R&D on Type II & III as % of GDP (2010)**
United States	8372(5876)	84.5	1376.5	1461.0	1.0(1.4)	0.0100
United Kingdom	1946(1203)	84.4	58.2	142.6	4.3(7.0)	0.0061
Sweden	491(203)	23.5	9.6	33.1	4.8(11.5)	0.0041
Norway	708	11.7	5.6	17.3	1.7	0.0035
Luxembourg	75	0.1	1.7	1.8	0.1	0.0033
Ireland	166	5.2		5.2	3.1	0.0028
Denmark	220	6.7	10.2	16.9	3.0	0.0025
Switzerland	145	2.6	4.3	7.0	1.8	0.0025
Australia	331	0.1	22.7	22.8	0.0	0.0024
Netherlands	577	27.3	1.5	28.7	4.7	0.0023
France	969(373)	3.5	44.7	48.2	0.4(0.9)	0.0016
Germany	1026(517)	2.3	31.8	34.1	0.2(0.4)	0.0012
New Zealand	37	0.0	0.4	0.4	0.0	0.0010
Spain	770	14.3	5.3	19.7	1.9	0.0010
Belgium	304	2.9	2.0	4.8	1.0	0.0010
Canada	741	5.4	11.5	16.9	0.7	0.0007
Japan	738(283)	0.0	5.6	5.6	0.0(0.0)	0.0002
Italy	279	0.7	1.6	2.2	0.3	0.0001
Total of above	17897(8455)	275.5	1593.2	1868.4	1.5(2.3)	0.0049
Total bilateral DAH (through development agencies)	10842	275.5			2.5	
European Commission	364	0.0	118.3		0.0	
Other multilaterals	9481			13.2	0.1	

Source: Institute for Health Metrics, G- Finder.

Notes:

Column 1: Total development assistance in 2009 provided bilaterally and multilaterally in 2009 constant dollars, as defined by the Institute for Health Metrics and Evaluation (IHME). Figures in brackets are sums channelled bilaterally through development agencies (where available). Source: IHME *Statistical annex to financing global health*, 2011 (http://www.healthmetricsandevaluation.org/sites/default/files/policy_report/2011/FGH_2011_statistical_annex_IHME.pdf, accessed 8 March 2012).

Column 2: Health R&D provided by development agencies in 2009 as defined by G-Finder in 2007 constant dollars (as defined by G-Finder). Source: G-Finder.

Column 3: Health R&D provided by other government departments in 2009 in 2007 constant dollars (as defined by G-Finder). Source: G-Finder.

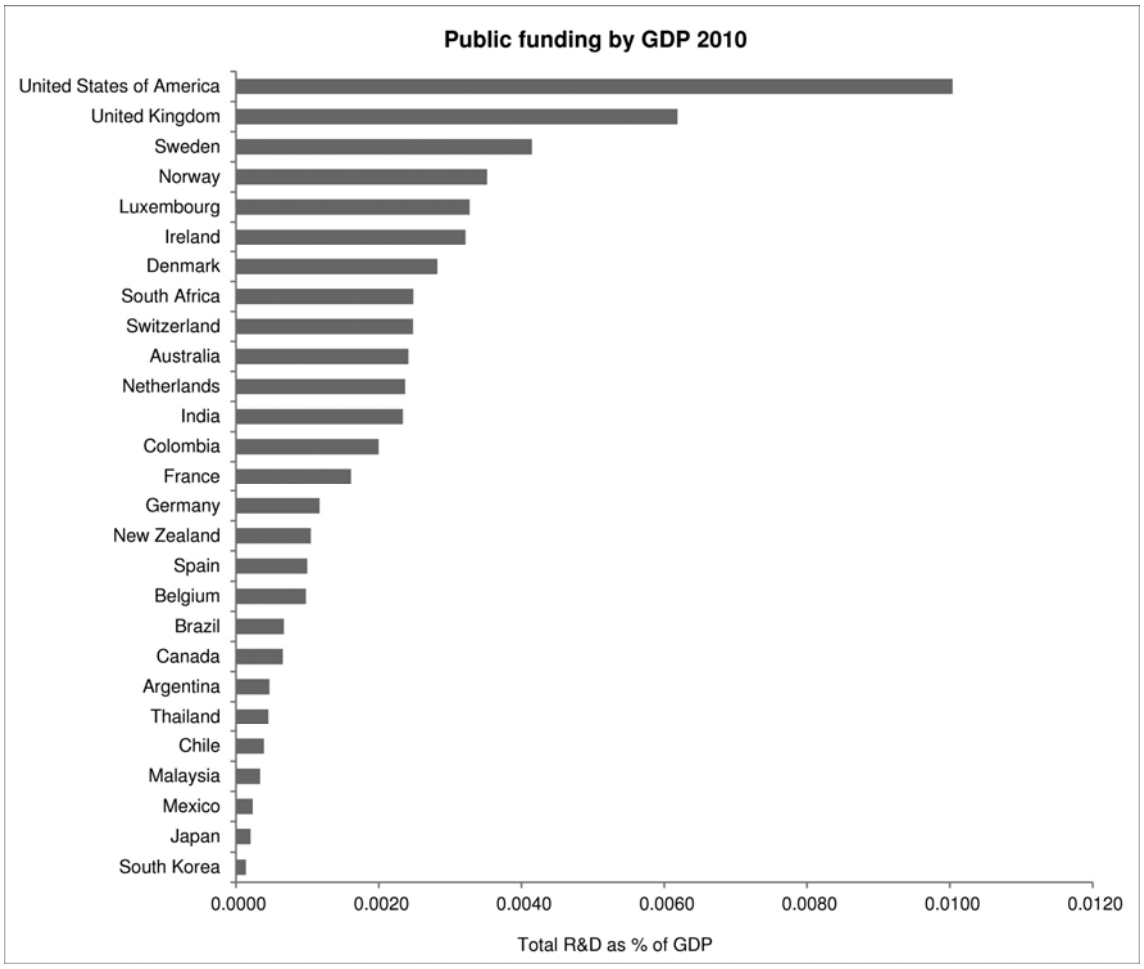
Column 4: Total publicly funded R&D in 2009 in 2007 constant dollars (as defined by G-Finder). Source:G-Finder.

Column 5: Column 2 as a percentage of Column 1.

Column 6: Publicly funded health R&D, as defined by G-Finder, as a percentage of GDP in 2010. Source: G-Finder.

For this reason we favour targets which relate the R&D effort to GDP, which is the best available measure of ability to pay. Thus the last column shows the effort of developed countries to fund R&D on Type II and III diseases, which is the best estimate of the current level of investments on R&D relevant to the health needs of developing countries, as defined by the scope of CEWG in relation to GDP. By far the largest funder, both absolutely and relatively, is the USA which spent about 0.01% of GDP on such R&D in 2010. Figure 4.2 shows the comparative performance on this measure in 2010. It can be seen that there is a large spread. Notably South Africa, India, Colombia, Brazil, Argentina, Thailand, Chile and Malaysia (part of G-Finder's sample of developing countries) also feature.

Figure 4.2 Public funding of health R&D on neglected diseases as a proportion of GDP in 2010 (%)



Source: G-Finder.

Meeting funding needs for R&D

From our perspective, this discussion illustrates that a measure of effort relative to GDP can be applied equally to donors and partner developing countries. Unlike a system such as that used to fund United Nations bodies or to determine burden-sharing in other financial institutions, the financial input to the production of an international public good is not necessarily the best measure of a country's contribution. R&D conducted by developing countries not only contributes to meeting their own needs for new products to address diseases they face, but also to meeting the needs of other developing countries and the greater public good. Thus we believe that the appropriate metric for determining "fair" contributions is, for developing countries, the proportion of GDP directed at health R&D. Similarly, for developed countries, the metric is not funds allocated through development assistance but the scale of their overall investment in R&D relevant to developing countries in relation to GDP. In other words, we propose to use the same measure for both developed and developing countries.

Since current funding is not sufficient because of market failures, an important question is: what level of public funding would be desirable to fund the kind of R&D currently insufficiently funded? There is no easy answer to this question and there are no published studies that directly address it. The Bill & Melinda Gates Foundation tell us that they estimate a total funding need for the PDPs they fund of about US$ 10 billion in the next 10 years. Out of about 100 products in the pipeline, they estimate the successful launch of 17 in the next decade. Financing needs may rise in the later part of the period because of an increasing proportion of Phase III trials. Since current annual funding of PDPs is about US$ 0.5 billion, this suggests there is a potential unmet need for this group of PDPs alone of up to US$ 0.5 billion annually.[1] Of course, this depends on an assumption that future funding by current donors will be maintained at current levels. However, our concern is with more than PDPs, and includes the needs of public-sector funders, of research organizations in developed and developing countries, and incentives that might be necessary to promote relevant private-sector research. Data from BIO Ventures for Global Health, funded by the biotechnology industry and foundations, suggests that their list of PDPs (which is considerably larger than the PDPs in the Bill & Melinda Gates Foundation portfolio) accounts for about 40% of the current global pipeline for drugs and vaccines for neglected diseases in development (and this excludes HIV/AIDS).[2]

Moreover our mandate – "proposals for new and innovative sources of funding to stimulate research and development related to Type II and Type III diseases and the specific research and development needs of developing countries in relation to Type I diseases" – is much wider than "neglected" diseases or the scope covered by G-Finder. It includes, for instance, the variety of health-care products relevant to their circumstances that developing countries might need to address the burgeoning scale of noncommunicable diseases. We are not aware of any studies that have systematically reviewed developing country needs in this area.

The G-Finder report concludes that the current level of funding of R&D for neglected diseases is just over US$ 3 billion annually, of which US$ 2 billion is provided by the public sector – mainly in developed countries. However, we know that G-Finder estimates of just US$ 65 million funding by developing country governments are very partial, based on returns from only 12 developing countries and on the G-Finder definition of qualifying neglected disease research. (*33*) The latest estimate we have of total spending by developing country governments on total health R&D is that of US$ 2.3 billion in 2005. (*30*) Some of this large difference may be definitional but it suggests that total

[1] Personal communication, Saara Romu, Bill & Melinda Gates Foundation.

[2] See: http://www.bvgh.org/GlobalHealthPrimer.aspx, accessed 7 March 2012.

developing country spending is higher than the G-Finder estimates, particularly as our mandate is much wider than neglected diseases which G-Finder covers.

Based on the above, we think that a conservative target for total public sector R&D spending annually relevant to our mandate would be US$ 6 billion. This is up to double current spending, depending on the actual amount spent by developing countries on R&D relevant to our mandate. This amounts in total to considerably less than 10% of the current level of health R&D funding from public sources globally. It is a target which is hard to see as overambitious given the discussions on the gross disparity in the allocation of R&D resources devoted to the needs of developing countries which we have had for over 20 years. This funding target for governments would be just 0.01% of global GDP which is now in excess of US$ 60 trillion.

Conclusion: health research and development: goals and targets

We have reviewed the current status of R&D and performance against proposed targets for health spending and R&D spending. Our review suggests that such targets have generally not been met by developing or developed countries but, on the other hand, there has been considerable movement towards meeting them. It is our contention, however, that proportionate targets related to health-related public expenditure or development assistance are not the best means of achieving the objective, principally because the denominator is itself not necessarily at its target level. We therefore propose an approach which sets targets that relate a country's effort in R&D spending, relevant to our mandate, to its GDP. This is a concept that is applicable both to developed and developing countries and takes account of the international public good that can be generated by each country's own R&D spending.

Our principal conclusion is that:

- *All countries should commit to spend at least 0.01% of GDP on government-funded R&D devoted to meeting the health needs of developing countries in relation to the types of R&D defined in our mandate.*

In addition we propose that countries should consider these targets:

- *Developing countries with a potential research capacity should aim to commit 0.05–0.1% of GDP to government-funded health research of all kinds.*
- *Developed countries should aim to commit 0.15–0.2% of GDP to government-funded health research of all kinds.*

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CHAPTER 5. STRENGTHENING GLOBAL COORDINATION IN HEALTH RESEARCH AND DEVELOPMENT

In this chapter we consider proposals for improving the coordination of R&D, the need for which we highlighted in Chapter 2.

The current landscape of coordination

As noted in Chapter 2, there have been successive calls for better coordination of health research relevant to developing countries, not least arising from the sheer diversity of different players in both research and its funding and a consciousness of the desirability of allocating scarce funds as effectively as possible, in particular given the fact that late-stage clinical research is costly.

The GSPA-PHI proposed the following actions for improving cooperation, participation and coordination of health and biomedical research and development:

"(a) stimulate and improve global cooperation and coordination in research and development, in order to optimize resources;

(b) enhance existing forums and examine the need for new mechanisms in order to improve the coordination and sharing of information on research and development activities;

(c) encourage further exploratory discussions on the utility of possible instruments or mechanisms for essential health and biomedical research and development, including, inter alia, an essential health and biomedical research and development treaty;

(d) support active participation of developing countries in building technological capacity;

(e) promote the active participation of developing countries in the innovation process." (*1*)

The EWG conducted an extensive review of current coordination arrangements both globally and by disease, health area and product in Chapter 4 of its report (*2*) and in a background paper (*3*). It noted that the field is highly fragmented and coordination occurs selectively in particular areas. It cites, for instance, coordination efforts in the area of vaccines and human reproduction, in relation to capacity-building, and between donors and international research organizations. We will not repeat this analysis here but focus on particular aspects of the landscape relevant to our argument before presenting our recommendations.

It is necessary to define what we mean by coordination. Coordination is not an end in itself – it is a means to an end. In our context, the end is that health R&D resources should be used as effectively as possible to produce technologies that will have the largest impact on health outcomes, particularly for poor people whose needs are not adequately met under current arrangements. However, this is not simple in practice. There is a tension between coordination and healthy competition: R&D can be more effective if several groups are working simultaneously on addressing the same high-priority goal, particularly if there is uncertainty about the correct research strategy to achieve a particular goal. Even then, the exchange of information and other forms of collaboration would be important. This is often the case for more upstream research. On the other hand, if several groups are addressing the same low-priority objective or following the same research paths in isolation from each other, this could be regarded as wasteful duplication. It is also clear that, because the science may be challenging and complex and the health problem can be addressed in several different ways (e.g. are better diagnostics or better medicines the higher priority for a particular disease?), there is often no consensus on how best to address a priority need. Moreover, there are the different interests of the parties involved –

which may be political, bureaucratic, religious, financial, economic or scientific. It is this very complexity of challenges and potentially diverging interests which emphasizes the importance of collecting and analysing evidence on research conducted, in order to learn and share lessons derived from current and past experience, and to promote coordination among various research groups where it does not exist.

History of coordination efforts

Each of the successive commissions or committees and conferences on health research has espoused the need for coordination and made suggestions for achieving it. Thus the CHRD recommended establishing a facilitation unit to strengthen country-specific research and help developing countries build capacity. This unit was eventually established in 1993 as the Council on Health Research and Development (COHRED). COHRED currently specializes in supporting countries in areas such as health research system assessment and development, policy development, priority-setting and research communication. COHRED was never intended to be a coordination mechanism. However the CHRD also recognized the need:

> "…for a mechanism to monitor the progress of research on developing-country needs and to identify unmet needs…to carry out regular, systematic reviews of research…responsible for monitoring, assessment, convening, and advocacy…credibility to attract participation of the relevant parties…sufficient resources to produce information of high quality…independent of particular interests – geographical, bureaucratic or scientific…" (*4*)

This particular recommendation was not followed up. The Ad Hoc Committee on Health Research Relating to Future Intervention Options in 1996 made a very similar recommendation:

> "...for a mechanism to enable the review of global health needs, the assessment of R&D opportunities and the monitoring of resource flows...for advocacy for health research to convince governments and investors, including non-traditional sources of its benefits...could be created out of existing health research structures...could bring governments, other investors and scientists together...identify existing effort and fill important gaps in global health research...and help reduce overlap and waste...would need access to high-quality analytic capacity to supply it with data on disease burden, measurements of the cost-effectiveness of potential interventions, current patterns of spending on R&D..." (*5*)

This recommendation led to the creation of the Global Forum for Heath Research (GFHR) in 1998. The GFHR centred its mission on the so-called 10/90 Gap – i.e. that only 10% of all health research is devoted to the health problems of 90% of the world's population (*6*). As noted in Chapter 2, however, the CHRD calculations would suggest a 5/93 gap.

The activities of the GFHR were intended to be concentrated on:

- an annual forum;
- analytical work for priority-setting, including:
  - burden of disease and health determinants,
  - cost-effectiveness analyses and methods to assist resource allocation,
  - analysis of resource flows and monitoring progress in correcting the 10/90 Gap,
  - analytical work on specific conditions in the forum priority areas;
- initiatives in key health research areas including, for instance, the Alliance for Health Policy and Systems Research;

- communication and information;
- evaluation and monitoring.

There was always a school of thought that there was insufficient distinction between the mandates of COHRED and the GFHR even if the former had a country focus and the latter had more of a global and international emphasis. In 2010 GFHR merged with COHRED, but largely because of GFHR's organizational and financial difficulties rather than any grand plan. In fact the division of labour between the two organizations was reasonably clear: COHRED concentrated on support to countries and capacity-building in research, while the GFHR, after an initial stage of developing and channelling funds to new initiatives, focused on its annual forum, which attracted several hundred people from across the globe each year, on monitoring financial flows on health research in an annual publication, and on various pieces of analytical work.

Thus the GFHR ended up carrying out a number of useful activities particularly, from our point of view, the annual publications on monitoring financial flows which have now ceased– but never really matched up in scope, scale, funding or normative legitimacy to the ambitions held for it by the Ad Hoc Committee as a global coordinating mechanism which would set priorities and influence resource allocation. A World Bank evaluation in 2009 noted:

> "...but it is not clear that the GFHR has substantially influenced the level and allocation of total global health research expenditure. Its core advocacy expenditures of US$ 3.5 million a year could hardly be expected to have a substantial impact on the level and allocation of the current world total of US$ 160 billion in annual spending on health research...The Forum does not appear to have had a significant impact on research priority setting within given allocations. This is especially the case at the global level which is the core of its mission." (*7*)

Thus neither of these mechanisms really fulfilled the ambitions of the CHRD and the Ad Hoc Committee on Health Research regarding coordination of health R&D.

The role of WHO

WHO's Constitution requires it "to act as the directing and co-ordinating authority on international health work". As might be expected, WHO has played a role in health research from the beginning. In 1949, the Second World Health Assembly resolved that "research and coordination of research are essential functions of the World Health Organization". Thus, from the beginning, a coordination function was accepted by the organization. On the other hand the same resolution noted that the "first priority should be given to research directly related to the programmes of the World Health Organization". (*8*) Thus there was an assumption from an early stage that, while WHO had a global role, its first priority would be research undertaken by it or related to its own activities, which in any case it saw as of global importance.

In the 1970s the Special Programme for Research and Training in Tropical Diseases (TDR) and the Special Programme of Research, Development and Research Training in Human Reproduction (HRP) were established and supported by WHO, other United Nations agencies and the World Bank. Then in 1999 the Initiative for Vaccine Research brought together WHO's vaccine research activities. There are many other research activities undertaken by different WHO departments (*9*). A review of WHO research activities in 2005 suggested a need for better coordination of research activities within the Organization, and a need for that research to be assigned a much increased role in WHO's policy, administrative and management procedures and to be given a commensurate proportion of funding. (*10*)

However, it is important to note that the GSPA-PHI has had an influence on the approach taken to the organization of research in WHO and is being used to frame research strategies in each of the regional offices. (*11)* With regard to priority-setting, WHO has been involved in more than 200 strategy-setting activities since 2005, with 60 of these setting research priorities in specified areas of public health. (*12*) This work informed the creation of a research priority-setting checklist of good practice – indicative of the global standards which are non-disease specific that are needed. (*13*) However, this also indicates that work on priority-setting not linked to downstream decision-making processes regarding funding may have too little impact in achieving coordination, and that WHO may need to take a stronger convening and coordinating role in line with its normative mandate.

Advisory Committee on Health Research

WHO's main advisory body on research is the Advisory Committee on Health Research (ACHR), which started life in 1959 as the Advisory Committee on Medical Research. Each regional office has, at times, had a regional version of the ACHR. The terms of reference of the ACHR, which reflect a similar tension between global priorities and WHO's own programmes, are:

- "to advise the Director-General on the general orientation of *WHO's research*;
- to advise on the formulation of *global priorities for health research* in the light of the policies set by the World Health Assembly and the Executive Board and on the basis of regional priorities evolved in response to the health problems of the countries;
- to review research activities, monitor their execution and evaluate their results, from the standpoint of scientific and technical policy;
- to formulate ethical criteria applicable to these research activities;
- to take a prominent part in the *harmonization of WHO's research efforts* as between the country, regional and interregional levels, and in their effective global synthesis." (italics added).[1]

In reality the ACHR has neither attempted to play a coordinating role or determine priorities, as its mandate and terms of reference imply that it might, nor has it had appropriate mechanisms for doing so. It has produced reports aimed at setting global strategies but there was little implementation beyond the publication of the reports themselves (*14,15,16)*. It does not initiate analytical work related to coordination or prioritization in any systematic manner. It tends to make quite wide-ranging recommendations and covers a large number of different topics, many of global significance, but over the years has tended to focus, as its terms of reference also suggest it should, on research-related activities associated with WHO programmes.

An internal review of the ACHR was undertaken in 2011. The new terms of reference seek to combine the function of oversight of the role of research within WHO and of the role of WHO globally in research. The intention is to collect more data of a global nature and act as a focal point to convene and engage major stakeholders on global health research issues. The ACHR is also intended to act as the committee responsible for reviewing the implementation of the WHO research strategy (see below) and elements 1, 2 and 3 of the GSPA-PHI – i.e. prioritizing R&D, promoting R&D and building innovation capacity.

[1] See the ACHR website at: http://www.who.int/rpc/advisory_committee/en/index.html, accessed 7 March 2012.

Special Programme for Research and Training in Tropical Diseases (TDR)

The activities of this WHO programme are of particular relevance to our agenda. TDR is a global programme of scientific collaboration that helps coordinate, support and influence global efforts to combat a portfolio of major diseases of the poor and disadvantaged. Established in 1975, TDR is based at and executed by WHO. It is cosponsored (i.e. financed and governed) by the United Nations Children's Fund (UNICEF), the United Nations Development Programme (UNDP) the World Bank and WHO. TDR is governed by three bodies: the Joint Coordinating Board (JCB), the Standing Committee, and the Scientific and Technical Advisory Committee (STAC).

In its current Ten Year Vision and Strategy, TDR notes the recent increase in funding for neglected disease research:

> "This increase in actors and resources is a very positive development for infectious diseases research, but it has also resulted in a fragmentation of efforts and resources. Multilateral and bilateral donors, philanthropies and governments would therefore welcome greater coordination in agenda setting, harmonization in research funding, and more reliable information on investments in infectious disease research. This would facilitate a better alignment of funding with priority research needs in disease endemic countries, and make donor actions more collectively effective in line with the Paris Declaration on Aid Effectiveness."(*17*)

TDR is involved in a number of initiatives which relate to coordination and/or capacity-building. It submitted to us the African Network for Drugs and Diagnostics Innovation (ANDI) as a model for better financing and coordination of research in other regions of the world and globally (*18*). It is described as an integrated regional and global coordination and financing mechanism of R&D for diseases that disproportionately affect developing countries. The ANDI model includes:

- focus on public health through enhanced local R&D capacity, linkage of R&D to local manufacturing that stimulates potential for sustainable production and access to health products;
- technical feasibility through the establishment of global or high level, regional, and sub-regional networks;
- financial feasibility through the potential of accessing local, regional, and international funding;
- cross-cutting issues such as intellectual property, delinking R&D from cost of products, accountability/participation in governance and decision-making, capacity-building, equitable access, and partnerships.

The model encompasses the establishment of regional and subregional networks, linking these into a global "network of networks" supported by a small central secretariat. The networks are proposed to be established with funds, staff and autonomy to enable decentralized decision-making to address local needs. The model can also provide multiple options for financing as the networks can access global, regional, subregional and nationally available resources. The coherent network approach can also stimulate enhanced intra-regional collaboration, public–private partnerships or PDPs, and even development of local public–private partnership projects. The ANDI business plan outlines the establishment and management of an innovation fund or global health R&D fund to support operations and R&D projects. This funding challenge needs to be overcome before the ANDI model can be implemented more widely.

Another initiative is ESSENCE, or Enhancing Support for Strengthening the Effectiveness of National Capacity Efforts (on health research).[1] This is a collaborative framework between funding agencies to scale up research capacity. It aims to improve the impact of investments in institutions and people, and provides enabling mechanisms that address needs and priorities within national strategies on research for health. It seeks to harmonize donor funding practices to prevent the development of complex unmanageable funding systems in countries. The ultimate beneficiary and user of this approach is the disease-endemic country policy-makers and researchers who have a stronger voice in determining the priorities of internationally-funded global health programmes. ESSENCE has developed a framework document that is designed to harmonize the planning, monitoring and evaluation of international health research programmes (*19*). This is designed to create a common methodology and common indicators that donors can use to assess their research capacity-building programmes. It is also sponsoring an ongoing review of funding practices, which aims to identify disparities, redundancies and overlaps between agencies. An ESSENCE country-based pilot project in Tanzania aims to facilitate a dialogue between international donors and representatives from all Tanzanian health research institutes on ways to harmonize international research funding to the country.

TDR also sponsors the Initiative to Strengthen Health Research Capacity in Africa (ISHReCA) which is to promote the creation of self-sustaining pools of excellence capable of initiating and carrying out high-quality health research in Africa. The initiative provides not only a platform for discussion of health research needs but a powerful voice capable of advocating for the government and societal support that many health research communities currently lack.[2]

All these seem to be useful initiatives which aim to strengthen research capacity, build research networks, harmonize donor practices and, to some extent, promote coordination. On the other hand, it is apparent that they very much have overlapping objectives but separate governance arrangements and there would be benefit in considering the scope for rationalizing these efforts

WHO International Clinical Trials Registry

An essential element for coordination is to ensure adequate, unbiased and relevant information. The WHO International Clinical Trials Registry can be seen as one element for coordination through better availability and more structured information on clinical trials. The mission of the WHO International Clinical Trials Registry Platform is to ensure that a complete view of research is accessible to all those involved in health-care decision-making. This will improve research transparency and will ultimately strengthen the validity and value of the scientific evidence base. WHO regards trial registration as the publication of an internationally-agreed set of information about the design, conduct and administration of clinical trials. These details are published on a publicly accessible web site managed by a registry conforming to WHO standards.[3] There are also others working in a similar way to make the results from trials publicly available.[4] This will further increase efficiency of the innovation process through knowledge-sharing.

[1] For more information on ESSENCE, see: http://www.who.int/tdr/partnerships/initiatives/essence/en/index.html, accessed 7 March 2012.

[2] For more information on ISHReCA, see: http://www.who.int/tdr/partnerships/initiatives/ishreca/en/, accessed 7 March 2012.

[3] See http://www.who.int/ictrp/en, accessed 7 March 2012.

[4] For example, see http://ottawagroup.ohri.ca, accessed 7 March 2012.

WHO research strategy

WHO has recently finalized a research strategy. The resolution adopting this strategy, adopted at the Sixty-third World Health Assembly in 2010, revealed the same ambivalence as between global priorities and those of WHO. The Director-General was requested "to provide leadership in identifying global priorities for research for health" but the succeeding requests revert to the needs of WHO itself, including: "to implement the strategy *within the Organization* at all levels and with partners"; "to improve the quality of research *within the Organization*"; and "to ensure that the highest norms and standards of good research are upheld *within WHO*" (italics added) (*20*). The accompanying draft WHO research strategy noted that it arose from a request from the World Health Assembly for the Director-General to produce a strategy for "the management and organization of research activities within WHO" – i.e. also principally an inward-looking perspective.

Nevertheless, the research strategy does propose the following:

> "Working with Member States and partners, the Secretariat will:
>
> (a) ensure that mechanisms are in place for synthesizing data on gaps in research relating to current health- and health system-related challenges at national and global levels;
>
> (b) convene high-level consultations to identify, and build consensus on, the priorities to include in global agendas for research for health and the financing necessary for implementing the relevant activities;
>
> (c) produce a report every four years on global priorities for research with an assessment of the alignment of financial and human resources with research agendas;
>
> (d) develop comprehensive research agendas for specific priority areas and develop plans for mobilizing the necessary resources;
>
> (e) advocate support for research areas, research groups and institutions that are working to close critical gaps in research agendas in support of global research priorities; and
>
> (f) improve the coherence of WHO's research activities by establishing mechanisms for the periodic review of the portfolio of research agendas, including decision criteria to guide decision-making concerning the initiation, adjustment and winding down of programmes."(*21*)

Thus a global coordinating role is possible but, in view of WHO's current financial situation, further resources would need to be made available. WHO's assessment of the financial and administrative implications of the research strategy suggests the need for nine professional staff to implement the strategy – three in Geneva and one in each of the six WHO regions and that nearly US$ 4 million annually will be required for implementation (*22*).

Other initiatives

There have been a variety of initiatives to enhance coordination.

There was for some time, from 2000 to 2005, an Initiative on Public–Private Partnerships for Health (IPPPH) sponsored by the GFHR which sought to bring together PDPs and funders to maximize the impact of PDPs on health. The initiative never really found its niche, being neither an organization of PDPs nor an organization of PDP funders. It was closed down in 2005. Since then there has been a PDP funders' group which is meant to allow funders of PDPs to coordinate their activities, but its

current status in unclear. As the principal funder of PDPs, the Bill & Melinda Gates Foundation holds an annual PDP forum which brings together PDPs and funders. There is no published output from these meetings.

The Heads of International Research Organizations is a body which meets periodically and brings together about 17 of the major governmental and philanthropic funders of biomedical research worldwide to share information about new developments in the field and coordinate policy responses where appropriate. However, there is hardly any information available on what topics are discussed at their meetings or of the outcomes (*23*).

The International Forum of Research Donors (IFORD) is an informal network of aid agencies, private foundations and multilateral organizations that provide significant funds for research, research capacity-building, and innovation related to international development. IFORD provides its members with a platform for sharing information about their organizations' strategies, funding priorities and programmes; learning from each other; discussing issues of mutual interest; and also for exploring opportunities for joint activities. It meets annually to discuss and reflect on issues related to research for development. It conducts no analytical work and is, in any case, not focused specifically on health research.[1]

The European and Developing Countries Clinical Trials Partnership (EDCTP), created in 2003 as a European response to the global health crisis caused by poverty-related diseases, aims to accelerate the development of new or improved drugs, vaccines, microbicides and diagnostics against HIV/AIDS, tuberculosis and malaria, with a focus on Phase II and III clinical trials in sub-Saharan Africa. It supports multicentre projects that combine clinical trials, capacity-building and networking. The aim of integrating these three activities is to ensure that the developed capacity is optimally utilized to conduct successfully the clinical trials in a sustainable way.[2]

Towards better coordination

Coordination also requires as its foundation the gathering of reliable information. However, standard mechanisms to record, classify and compare health research funding accurately on a global basis do not exist, although some initiatives such as the United Kingdom Health Research Classification System (HRCS) could be developed for global applications. The aim of the HRCS is to help in developing a coordinated approach to health research funding in the United Kingdom. The HRCS builds on WHO's *International statistical classification of diseases and related health problems* but its breadth of coverage across all types of research and areas of health and disease is unique.[3]

Access to, and availability of information on, financing flows is a challenge. While R&D on specific diseases or health concerns may be gathered, this needs to be assessed in relation to health needs. Estimates such as those GFHR used to produce, or those currently produced by G-Finder, were or are incomplete in various respects. For instance, we have already noted the sketchy coverage of developing country research in G-Finder. Steps towards coordination need to focus on identifying best practice – in building capacity, setting priorities, creating good practice and translating evidence into policy - where common approaches would improve the situation

[1] See: http://www.iford.org/en/Home, accessed 7 March 2012.

[2] For more information, see: http://www.edctp.org, accessed 7 March 2012.

[3] For more information, see: http://www.hrcsonline.net, accessed 7 March 2012.

Objectives of coordination

The objectives of coordination should therefore include:

- **Identifying research priorities.** Information on the global burden of disease is a guide to this, but needs to be supplemented by knowledge of existing tools and where they are inadequate. For example, we have good vaccines for a number of very common (or previously very common) diseases, but we have none or inadequate ones for other common diseases. Very little work has been done on the R&D priorities for developing countries in relation to Type 1 diseases.
- **Mapping priorities against current allocation of R&D resources.** Funding needs to be monitored, as do the purposes to which it is put. The current pipeline needs to be monitored. Gaps or duplications need to be identified. Funders and researchers need to be involved in a dialogue on research priorities. The classification of research itself needs to be improved in order to facilitate this mapping exercise (*24*).
- **Learning and sharing lessons.** A capacity for the collection of relevant information and a capacity for analysing it is essential to inform researchers and funders.
- **Providing advice and setting standards**. Advisory and normative functions are required to serve the needs of funders and researchers.
- **A mechanism for decision-making.** Better information, analysis and sharing may have limited impact unless there is some mechanism for collective decision-making, and a willingness of funders and researchers to act collectively, at least to a degree, to address problems faced in common.

Coordination and funding

The way research is funded is integral to the perceived need for better coordination. At one extreme the most effective form of coordination is likely to occur where funders of research agree to pool their funds which are then allocated and managed by an organization which they trust to do a better job, and do it more cost-effectively, than if each funder takes its own decisions on allocation and management and duplicates the capacity needed to make those decisions effectively. The willingness of funders to undertake pooling will be determined by their own governance and accountability arrangements, but governments do pool funds on a large scale for development purposes. Typically about 30% of development assistance is channelled multilaterally, and bilateral funding is also often done in collaboration with other donors (*25*).

At the other extreme is the situation where there are many funders and many research organizations, each taking decisions independently. In the absence of an adequately functioning market for the products of R&D, which is particularly the case for diseases mainly affecting developing countries, this is likely to result in uncoordinated decisions which do not produce the best outcomes in terms of the composition of the R&D portfolio.

The case of health R&D is more towards the latter extreme. There are many funders in both the public and private sectors, and many research organizations in the public and private sectors, and in partnerships between them. On the other hand, there are some dominant funders. Thus the United States National Institutes of Health and the Bill & Melinda Gates Foundation together account between them for 54% of all R&D funding targeted for neglected diseases as monitored by G-Finder. Industry funders, who are many, account for a further 16%. The remaining 30% of funding is shared mainly between many different kinds of government funders – development agencies, medical research councils and other government departments.

Box 5.1 The Consultative Group on International Agricultural Research (CGIAR)

In the apparently analogous field of agricultural research directed at the needs of developing countries, the central funding mechanism is the Consultative Group on International Agricultural Research (CGIAR), with a secretariat based in the World Bank. This has been in existence now for over 40 years. In 2010, CGIAR disbursed over US$ 670 million to a network of 15 agricultural research institutes. The biggest contributors are the USA, the World Bank, the European Commission, other OECD governments and, more recently, the Bill & Melinda Gates Foundation, but several developing countries also contribute relatively small amounts. Members include both developed and developing countries, as well as international organizations and foundations.

Apart from providing a single channel for donors to fund a multiplicity of research institutions in developing country agricultural research, CGIAR also provides strategic inputs in priority-setting, monitoring and evaluation, coordination and advocacy, and impact assessment. An independent expert panel, the Independent Science and Partnership Council, has the overarching purpose of providing independent expert advice to the funders of CGIAR and serves as an intellectual bridge between the funders and the Consortium (i.e. research centres).

The idea that a similar arrangement might be appropriate to health research is not new. The CHRD thought:

"…the CGIAR…mechanisms as highly relevant to the needs of the health field. The functions of maintaining a global overview across many specific health problems backed by independent technical assessments and the capacity to mobilize resources in support of larger research efforts are sorely missing. Provided there is ample developing country representation in the decision-making process, analogues to the CGIAR…could be extremely constructive for the health field….". (*4*)

The World Bank's World *development report 1993: investing in health* made a similar suggestion (*26*). The 1996 Ad Hoc Committee devoted an annex to it. The Commission on Macroeconomics and Health in 2001 recommended a global health research fund which "would act in health and biomedical research akin to the Consultative Group for International Agricultural Research (CGIAR)" (*27*).

Source: CGIAR or as cited.

One potential model, which could contain elements relevant to health R&D, is the Consultative Group on International Agricultural Research (CGIAR) described in Box 5.1. The CHRD recognized that the key structural difference in agricultural research is that CGIAR exists principally to fund the (now) 15 international agricultural research institutions predominantly located in developing countries.

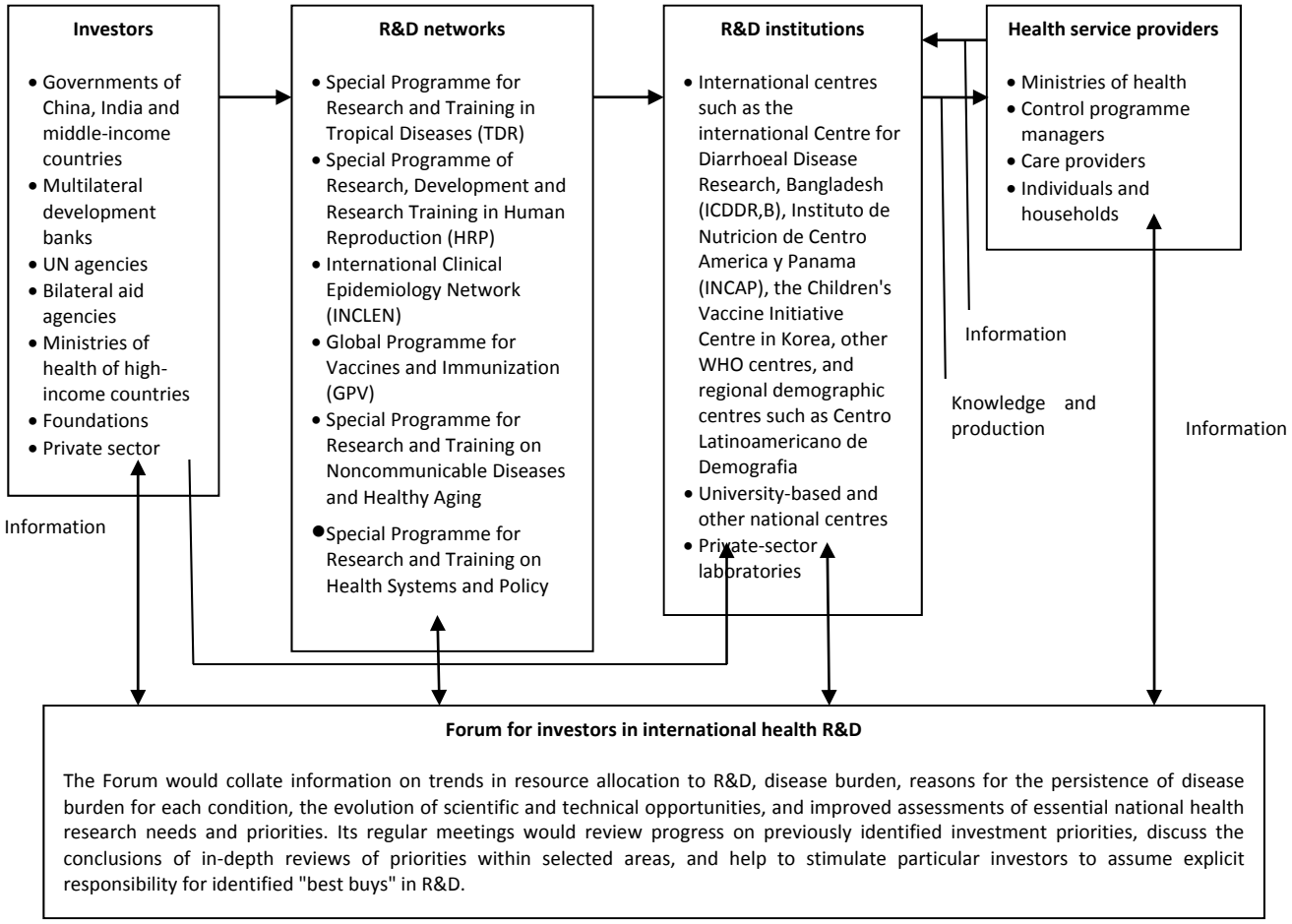
Such a network of publicly-funded international research centres does not exist in health R&D and the whole landscape is far more complex, in particular with far more private-sector entities than in the agricultural sector. The CHRD did not therefore recommend that particular aspect as a model for the health sector: establishing new publicly-funded international health research centres would not generally be an effective or economical way to proceed. Now, the development of PDPs as new R&D entities with an international reach, would probably have reinforced this view – and there are plenty of research institutions in developing countries in the public and private sectors with growing international reputations. Indeed, the CHRD recommended strengthening existing and new national research centres in developing countries and building them into networks that would address national as well as international needs. However, as noted in Box 5.1, it saw great value in the oversight mechanisms of CGIAR and its independent technical assessment capacity, and the possibility of mobilizing additional resources.

Interestingly, the World Bank, the main funder of the GFHR and secretariat of CGIAR, initially perceived the GFHR as the equivalent in the health sector to CGIAR. The 2009 World Bank evaluation of the GFHR noted this:

> "In 2000 Bank staff thought that the Global Forum would increasingly assume the role of raising money, channelling funding to high priority activities, and coordinating health research generally. While this may not have been a very realistic vision, the HNP Sector Board expected that the Bank would exit from separate international health R&D grants over time and channel its health R&D funding through an arrangement analogous to the CGIAR" (*7*).

This was similar to the vision of the 1996 Ad Hoc Committee for the GFHR, as set out in Figure 5.1, with the forum as the fulcrum of the international research effort on health. However, it is dissimilar in the sense that the Ad Hoc Committee did not associate the coordination functions with the funding mechanism.

Figure 5.1 Ad Hoc Committee framework



Source: Ad Hoc Committee, Chapter 7

Conclusions

We consider that coordination is likely to be most effective where it is associated with a funding mechanism which constitutes a significant part of total R&D funding for the disease areas of concern to us. In Chapter 3 we concluded that pooling of research funding was one of the set of proposals which we recommended, and in Chapter 4 we outlined the funding requirements and the need for increased public funding in particular. In Chapter 6 we present our recommendation for a convention as a binding instrument, which could incorporate, subject to the outcome of negotiations, elements along the lines we have suggested in previous chapters. Such an instrument will inherently have its own coordination mechanisms which could be developed on the lines we suggest below. However, we believe that in any case the mechanisms proposed below for monitoring, shared learning and decision-making would be a significant improvement on the status quo. We believe there is much that could and should be done to improve coordination within the existing structures and framework. We also think any proposed coordination, and indeed funding, mechanism should, wherever possible, build on existing institutional structures.

As our review of the landscape reveals, there are major challenges for WHO to address the conclusion of the Second World Health Assembly that "research and coordination of research are essential

functions of the World Health Organization". In spite of these challenges, it is our belief that WHO should play a central and stronger role in improving coordination of R&D directed at the health needs of developing countries in line with the first mandate in WHO's Constitution "to act as the directing and co-ordinating authority on international health work". The current WHO reform programme means that this is an opportune time for reviewing WHO's activities in research and its appropriate role in relation to the coordination of global R&D. We strongly emphasize the need to consider this task as part of WHO's reform process and consequent action and allocation of resources.

Our review suggests that, to be effective, coordination must:

- have a legitimate institutional basis for gathering information on health R&D and how this responds to global health needs;
- ensure that collection of information is transparent, sufficiently comprehensive and objective;
- provide services that are important for global health and for guiding decisions of funders and researchers;
- create the standards necessary to enable common approaches and improve the collection and sharing of data;
- collect data and analyse it in ways that are relevant to decision-makers, researchers and funders on health research;
- seek to improve the way resources for R&D are allocated so as to respond to health needs and improve health outcomes in developing countries.

A key message, perhaps reflected in the GFHR experience, is that to do this properly requires a critical mass of people and resources and therefore costs money. If that critical mass is not reached then the objectives will not be achieved. In addition, coordination policies (e.g. avoiding unnecessary duplication, addressing priorities) need to be effectively implemented through appropriate incentives and other measures. If these conditions are not fulfilled, useful things may be done but they will not amount to coordination as we define it. *The key elements of this coordination function under the auspices of WHO would include:*

(1) ***A Global Health R&D Observatory.*** *This would need to collect and analyse data, including in the following areas:*

- **Financial flows to R&D**, on the lines previously done by the GFHR and currently, in a different way, by G-Finder. We understand that G-Finder at present has no secured funding after the forthcoming 2012 report. We also noted that there is remarkably little data since the end of the GFHR on the extent of R&D funding globally, even when we include OECD as a source for developed countries, and particularly on R&D being undertaken in developing countries.
- **The R&D pipeline.** Monitoring the current composition of R&D and the progress of R&D. Identifying gaps and unnecessary duplication.
- **Learning lessons.** A capacity for analytical and advisory work on key issues in R&D responding to the needs of funders and researchers and monitoring and evaluation.

(2) ***Advisory mechanisms****. The arrangements for this would need to be decided by WHO Member States in the first instance, and later by Parties to a convention if negotiated. The mechanisms, although driven by governments, both developing and developed, should take into account the need to*

develop a shared vision and shared priorities with the diverse organizations involved in the funding and execution of health R&D. We see the role for elements like:

- **A network of research institutions and funders** that may include specialized sections according to the subject of research (e.g. type of disease), based on an electronic platform supported by WHO and which may provide inputs to the advisory committee.
- **An advisory committee**. This could be based on the current ACHR and also the ACHRs of the WHO regions, with suitably revised terms of reference and ways of operation. Subcommittees could be established to tackle specific topics and facilitate regional inputs.

We have looked at CGIAR as one example of how coordination can be attempted to produce public goods. However, we are very aware that the circumstances of health research are very different. We are also aware that the CGIAR system has longstanding problems which successive reviews have sought to address. In particular, over time donor funding has increasingly been restricted to particular purposes rather than core funding. It is therefore necessary to learn from the challenges in financing, governance and donor requirements identified, for instance, in the latest CGIAR independent review (*28*). A related review of CGIAR in 2008 identified three of its outputs which could be regarded as global public goods:

- knowledge – making freely available the results of its research to be applied and adapted by countries (e.g. new crop technologies);
- a series of services made available to countries (e.g. gene banks);
- the institutional capacity for conducting and coordinating international agricultural research (i.e. the coordinating, priority-setting and advisory functions that enhance the effectiveness of internationally funded agricultural research) (*29)*.

As the health research system is far larger and more diversified than that of agricultural research, we would argue that the coordinating function is more important than in agriculture and also, we recognize, correspondingly more difficult. Nevertheless, we believe that seeking further means to strengthen coordination of R&D for health research relevant to developing countries under the existing institutional structures of WHO is essential and an effort worth making with capacity to benefit all Member States in the long term.

Assessing the costs of what we propose would require more detailed work, but would mean only modest allocations with a potentially high impact if R&D coordination is improved. In 2006 the governance and secretariat costs of CGIAR were estimated at US$ 13.8 million (*28*). This was then about 2% of CGIAR spending on R&D. As a proportion of G-Finder estimated health R&D, it would be less than 0.05%. For comparison, the costs of G-Finder itself are about US$ 1.5 million annually and, as noted above, the estimated costs of the WHO research strategy are US$ 4 million.

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CHAPTER 6: IMPLEMENTATION: A BINDING INSTRUMENT

Introduction

Our terms of reference asked us to "deepen the analysis of the proposals in the Expert Working Group's report", with particular reference to 15 of its proposals. We have reviewed these proposals in some detail in earlier chapters. In this chapter, we summarize our conclusions and recommendations on this part of our work. In addition, we were asked to "take forward the work of the Expert Working Group" and in this chapter we also make proposals on how we think this could best be done.

Proposals assessed by the EWG: sources of finance

In Chapter 4 we reviewed the EWG's proposals on sources of finance. These were:

- **A new indirect tax.** This could be applied to any number of areas – tobacco, alcohol, the arms trade, airline travel, Internet traffic or financial transactions.
- **Voluntary contributions from businesses and consumers.** Again there are a number of actual and potential models for soliciting such contributions through, for example, airline ticket purchases, lotteries, project RED, and mobile phone usage.
- **Taxation of repatriated pharmaceutical industry profits.** This is a proposal from Brazil to tax pharmaceutical industry profits.
- **New donor funds for health research and development.** This would simply involve the raising of additional funds from new or existing providers of development assistance.

Only about 8% of total funding for R&D for neglected diseases currently comes from development agencies. By far the larger amount comes from other government departments and medical research councils, as well as from industry and foundations. There is therefore a need to reframe the issue of R&D for meeting the health needs of developing countries as being about more than development assistance. It is not just a responsibility of development aid or indeed of donors, but a common interest. It is rather a challenge to countries, both developed and developing, to find ways to invest appropriately in health R&D relevant to health needs in developing countries in the various ways available to them.

We found it difficult to evaluate the proposal for **taxation of repatriated pharmaceutical industry profits.** The proposal has not been elaborated since it was submitted to the EWG. Assessing its feasibility raises a number of potentially complex issues which would require more expertise and information than was available to us.

Nor did we think that it was realistic to expect **voluntary contribution schemes**, although they were to be encouraged, to raise very large sums of additional money on a sustainable basis for health R&D relevant to developing countries. The experience of the Millennium Foundation suggests that "innovative" voluntary contribution schemes are quite difficult to develop into significant and sustainable flows of funds. Moreover the willingness of the public to contribute will be determined by the priority they assign to this particular use of funds as compared to the variety of other possible uses in the field of health, of development or of other global challenges more generally.

Our view is that "traditional" financing mechanisms based on **direct or indirect taxation** are more likely to succeed than a complex landscape of uncoordinated voluntary or so-called innovative initiatives.

We concluded that countries should consider at national level what tax options might be appropriate to them as a means of raising revenue to devote to health and health R&D. These could include taxes on activities harmful to health – including those on alcohol, tobacco and sweet or fatty foods, as outlined in chapter 4. We highlighted also two possible taxes – the financial transactions tax and the tobacco solidarity contribution – that could be used *to generate funds to be channelled through an international mechanism to supplement national resources***.** We also considered a number of other options and there are no doubt others we have not considered. It is our hope that such an international tax could be agreed as part of a commitment by all countries to finance global public goods, including for health and health R&D relevant to developing countries. We noted that *our position is that if any international tax is agreed, then a proportion of that tax should go to provide support to health services in developing countries and that a proportion should be earmarked for health research and development meeting the needs of developing countries.*

Other proposals assessed by the EWG

In Chapter 2 we noted, in the context of the ongoing changes in the pharmaceutical industry, the tentative moves to develop new innovation models involving more open collaboration between different partners as a means of improving the effectiveness and efficiency of the R&D process. We emphasized our preference for open approaches where the problem or opportunity is the focus of attention, where there is more open sharing of information between multiple partners and with others, and where there is the principle that research results should be in the public domain. We distinguished this from the open innovation approach, espoused by Henry Chesbrough, which focuses on how individual companies can benefit from a more open approach to external collaboration with other companies and academic or public research institutions. Together with the appropriate targeting of

funding – including, for instance, milestone prizes – open approaches would also help to promote the delinkage of the costs of R&D from product prices.

In Chapter 3 we analysed all the allocation proposals in the EWG report (excluding the four proposals on sources of financing), including those highlighted in our terms of reference. We reviewed each of these proposals, and others submitted to us, and formed an assessment of each one on the basis of the evidence available and judged according to the criteria we devised.

Of the **five promising proposals** for financing and coordination in the EWG report, "Open source" was rated highly against our criteria. "Patent pools", which do not involve financing, also rated well. For the reasons given in Chapter 3 and Appendix 3, we were not convinced that the "Health Impact Fund", as currently structured, would be feasible because of its high cost and practical difficulties in implementation. However, we agreed that a pilot to test its practicability would be a good idea. We did not think that "Orphan drug legislation" as currently in place in many developed countries could be easily adapted to provide a greater incentive for R&D on diseases that mainly affect developing countries. One central problem is the lack of a reliable market (or "pull" mechanism) for products for these diseases, either in developed or developing countries. There can be a good or even large market in terms of revenues for medicines that are the focus of this legislation in developed countries, even though the diseases are, by definition, rare. On the other hand, the price of products may be very high during the exclusivity period, or may even result in some cases in large increases over previously available prices. Furthermore, we recognized that legislation which adjusts regulatory requirements for rare diseases is problematic for diseases which are common. Nor is it clear how developing countries could adopt similar schemes of their own for diseases that are more common than rare. The "Priority review voucher" scheme suffers from a similar defect in respect of the market and, in addition, experience to date does not suggest that the value of a voucher provides a sufficient incentive for companies to invest more in neglected disease R&D.

Of the **six proposals that did not meet the criteria applied by the EWG**, we saw merit in developing further the proposal for a "biomedical research and development treaty", which we discuss further below when considering the way forward. Although we favour the concept of prizes as a way to advance R&D, we were not persuaded that "large end-stage prizes" were a promising way to do so. However, milestone prizes have more merit, and prizes as a mechanism are also discussed below. The proposal for "transferrable intellectual property rights" has similarities to the "priority review voucher" although its potential value as an incentive is higher. However, like that scheme, it does not overcome the problem of the absence of a market and it has the disadvantage that it can be used to extend exclusivity of a best-selling drug in developed countries with potentially high cost to patients. The proposal on "green intellectual property" was not well-defined and we questioned the technical and financial feasibility of the proposal. We thought that the proposal on "removal of data exclusivity" would not constitute a significant contribution to increased innovation but we recognized that against many of our criteria, including access, it scored well. As regards "neglected disease tax breaks for companies", the evidence on the limited experience to date suggested that tax breaks to promote R&D on neglected diseases had not had any significant impact. However, we also recognized that most developed countries and several developing countries did use general tax breaks for R&D and countries should consider the extent to which such schemes might fit their local needs, bearing in mind the available evidence on their impact and potential other uses for these public funds.

CEWG recommendations

Approaches to research and development

On the basis of our assessments of all proposals, we came to a conclusion about those proposals we thought could best promote health R&D relevant to the needs of developing countries. We

characterize these as "open knowledge innovation", and define this as research and innovation that generate knowledge which is free to use without legal or contractual restrictions. They include the following particular mechanisms:

- **open approaches to research and development and innovation** (as described in Chapter 3 and Appendix 3) which include precompetitive research and development platforms, open source and open access schemes;
- **prizes**, in particular milestone prizes.

Two other approaches, **equitable licensing** and **patent pools**, may facilitate access to research results on equitable terms and/or with low transaction costs.

We believe that these approaches offer together the most effective ways, many of them at relatively low cost, to overcome the difficulties in early-stage research and in translating promising ideas into health technologies and products, and in facilitating access to research outcomes that meet the needs of developing countries. These approaches can also help to secure delinkage, inter alia, by encouraging competitive pricing of end-products.

Funding mechanisms

In Chapter 4 we concluded that substantial additional funding was required to fund the provision of global public goods through research which addresses the needs of developing countries for R&D "related to Type II and Type III diseases and the specific research and development needs of developing countries in relation to Type I diseases". *We concluded that all countries should commit to spend at least 0.01% of GDP on government-funded R&D devoted to meeting the health needs of developing countries in relation to product development for those types of diseases. In addition, we suggested that developing countries with a potential research capacity should aim to commit 0.05–0.1% of GDP to government-funded total health research and that developed countries should aim similarly to commit 0.15–0.2% of GDP to government-funded health research in general.*

The additional funding generated through fulfilling the 0.01% commitment should be used in particular with the following objectives:

- to fund R&D in all sectors (public, private and public–private partnerships) to address identified health needs of developing countries in relation to the types of R&D defined in our mandate;
- to fund all phases of R&D, in particular utilizing open approaches to R&D and prize funds, as well as the costs of late-stage development, including clinical trials;
- to help build R&D capacity in developing countries and promote technology transfer.

Pooling resources

In Chapter 5 we noted that the way research is funded is integral to the perceived need for better coordination. Coordination is likely to be most effective where it is associated with a funding mechanism which constitutes a significant part of total R&D funding for the disease areas of concern to us. That is why, in particular, we regard pooled funding as a desirable mechanism for improving coordination and for promoting the objectives outlined above. In that context, we consider that 20–50% of funds raised for health R&D addressing the needs of developing countries should be channelled through a pooled mechanism which would also have a coordination function. Our preference would be that such a mechanism should build on existing financing and/or coordination institutions.

Strengthening research and development capacity and technology transfer

In Chapter 5 we reviewed a number of initiatives whose principal objective is building research capacity in health in developing countries. These include TDR, COHRED, ANDI, ESSENCE and ISHReCA. There are many other organizations, associated with multilateral or bilateral agencies, that are too numerous to mention individually, which have similar capacity-building objectives. The Bamako Call to Action following the Ministerial Forum on Health Research in 2008, laid particular emphasis on the need for countries and funding agencies to strengthen work on capacity-building and technology transfer (*1*). We see a particular need for funding agencies to address the capacity needs of academic and public research organizations in developing countries and to promote technology transfer to them. There is scope for this, for example, through equitable licensing options. In addition there is an important role for schemes, such as **direct grants to companies** in developing countries**,** designed to build capacity in, and aid transfer of technology to, small and medium companies combined with licensing requirements to promote access.

We see the need for support to:

- capacity-building and technology transfer to developing countries;
- the promotion of partnerships and collaborations based on joint agendas and priority setting related to developing country health needs and national plans for essential health research;
- the development and retention of human resources and expertise;
- institutional and infrastructure development;
- sustainable medium/long-term collaborations.

The Bamako Call to Action asked funders and development agencies to "better align and harmonize their funding and programmes to country research and innovation for health plans and strategies, in line with the Paris Declaration on Aid Effectiveness" and to "better align, coordinate, and harmonize the global health research architecture and its governance through the rationalization of existing organizations, to improve coherence and impact, and to increase efficiencies and equity" (*1*). In view of their number, *there is a need to review research capacity-building initiatives for coherence and effectiveness*. We propose such an assessment before concluding how best to promote capacity-building using the approaches and resources described above.

Coordination

In Chapter 5 we concluded that, even in the absence of a pooled funding mechanism, or before it comes into existence, there was much that could be done to improve coordination within the existing structures and framework. In essence *our conclusion was that there was a need for a Global Health R&D Observatory and relevant advisory mechanisms under the auspices of WHO.* The observatory would monitor financial flows to R&D and the state of the R&D pipeline, identify gaps and unnecessary duplication and, through analytical work, learn lessons and propose policy options. The advisory mechanisms involving governments – both developing and developed – would take into account the need to develop a shared vision and shared priorities with the diverse organizations involved in the funding and execution of health R&D, paying due attention to managing conflicts of interest. This could include an enhanced role for the ACHR and the regional ACHRs and could form the basis of a coordination mechanism to be implemented as part of a convention on R&D, as elaborated below.

Implementation: a new way forward

We are aware that our report follows a number of other initiatives launched by WHO, described in Chapter 1, which have had essentially the same objectives. This began in 2003 with the establishment of the CIPIH. The central question asked of this commission was that "of appropriate funding and incentive mechanisms for the creation of new medicines and other products against diseases that disproportionately affect developing countries" (*2*). This is essentially the same question as was asked of the Intergovernmental Working Group on Public Health, Innovation and Intellectual Property, the Expert Working Group on Research and Development: Coordination and Financing and, now, the Consultative Expert Working Group on Research and Development: Financing and Coordination. That being so, we consider there is a need to consider new ways forward to achieve the objectives that WHO Member States have been grappling with for so long. There is a need for a coherent global framework that combines the different elements and recommendations in a concerted mechanism.

We are not alone in this. In May 2010 the European Council, in relation to the European Union's role in global health, called on:

> "...the EU and its Member States 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. This should be achieved by the EU and its Member States through:
>
> (a) working towards a global framework for research and development that addresses the priority health needs of developing countries and prioritises pertinent research actions to tackle global health challenges in accordance with the WHO Global Research Strategy.
>
> (b) increasing research capacities in public health and health systems in partner countries and strengthening cooperation between the EU and partner countries in this respect.
>
> (c) exploring models that dissociate the cost of Research and Development and the prices of medicines in relation to the Global Strategy and Plan of Action on Public Health, innovation and intellectual property, including the opportunities for EU technology transfer to developing countries.
>
> (d) ensuring that EU public investments in health research secure access to the knowledge and tools generated as a global public good and help generate socially essential medical products at affordable prices, to be used through rational use.
>
> (e) strengthening and balancing the complete health research process of innovation, implementation, access, monitoring and evaluation. International cooperation, common platforms of knowledge sharing and exchange of good practices are essential in this field.
>
> (f) improving health information systems of partner countries and the collection of quality and comparable data and statistics to enable benchmarking and inform on the impacts of global and national policies on social determinants in health including the adoption of equity indicators.
>
> (g) respecting the principle of evidence-based approach when setting normative action of food, feed, products, pharmaceuticals and medical devices, while taking into account the precautionary principle considered on a case by case basis" (*3*).

General use of conventions

Conventions are a means by which countries enter into agreements with legal force to achieve common goals. They have been used in a wide variety of fields – for example in human rights and in relation to the environment. Research has indicated that conventions are effective in promoting human rights (*4*). They have hardly been used in relation to health, except inasmuch as the "right to health" is incorporated in human rights treaties. The one example is the WHO Framework Convention on Tobacco Control (WHO FCTC) discussed below (see Box 6.1).

Box 6.1 Framework Convention on Tobacco Control

The WHO Framework Convention on Tobacco Control (WHO FCTC) is the first treaty negotiated under the auspices of the World Health Organization. The WHO FCTC is an evidence-based treaty that reaffirms the right of all people to the highest standard of health. The WHO FCTC represents a paradigm shift in developing a regulatory strategy to address addictive substances. In contrast to previous drug control treaties, the WHO FCTC asserts the importance of demand reduction strategies as well as supply issues.

The WHO FCTC was developed in response to the globalization of the tobacco epidemic. The spread of the tobacco epidemic is facilitated through a variety of complex factors with cross-border effects, including trade liberalization and direct foreign investment. Other factors – such as global marketing, transnational tobacco advertising, promotion and sponsorship, and the international movement of contraband and counterfeit cigarettes – have also contributed to the explosive increase in tobacco use.

The core demand reduction provisions in the WHO FCTC are contained in articles 6–14, namely:

- Price and tax measures to reduce the demand for tobacco, and
- Non-price measures to reduce the demand for tobacco, namely:

- Protection from exposure to tobacco smoke;
- Regulation of the contents of tobacco products;
- Regulation of tobacco product disclosures;
- Packaging and labelling of tobacco products;
- Education, communication, training and public awareness;
- Tobacco advertising, promotion and sponsorship; and,
- Demand reduction measures concerning tobacco dependence and cessation.

The core supply reduction provisions in the WHO FCTC are contained in articles 15–17:

- Illicit trade in tobacco products;
- Sales to and by minors; and,
- Provision of support for economically viable alternative activities.

The WHO FCTC opened for signature on 16 June to 22 June 2003 in Geneva. The treaty, which is now closed for signature, has 168 signatories, including the European Community, which makes it one of the most widely embraced treaties in United Nations history. Member States that have signed the Convention indicate that they will strive in good faith to ratify, accept, or approve it, and show political commitment not to undermine the objectives set out in it. Countries wishing to become a Party, but that did not sign the Convention by 29 June 2004, may do so by means of accession, which is a one-step process equivalent to ratification.

The Convention entered into force on 27 February 2005 – 90 days after it had been acceded to, ratified, accepted, or approved by 40 states.

Source: FCTC web site at: http://www.who.int/fctc/text_download/en/index.html.

The particular benefit of a convention is that it is the strongest form of international agreement because of its legally binding nature. Conventions have to be ratified by states, and a minimum number of ratifications have to occur before they come into force. Governments agree to make

commitments, and conventions should also include mechanisms for compliance. In reality, the provisions for compliance vary widely between conventions depending on the nature of the commitments, the extent to which progress towards them can be measured or assessed, and the mechanisms built into them for compliance. Thus the General Agreement on Tariffs and Trade (1994) incorporates a dispute settlement mechanism which allows countries to challenge other countries' adherence to the rules and, if there is a finding in their favour, impose trade sanctions on the offending country until the country complies with the finding of the settlement mechanism.[1] For instance, the Kyoto Protocol (Box 6.2) contains provisions which oblige countries to measure and assess their progress in relation to greenhouse gas emissions. The human rights treaties typically establish committees responsible for monitoring their implementation supported by the Office of the United Nations High Commissioner for Human Rights.[2]

Box 6.2 The Kyoto Protocol

United Nations Framework Convention on Climate Change (UNFCCC) is an international agreement reached in 1997 that sets binding targets for 37 industrialized countries and the European Community to reduce greenhouse gas emissions. In all, 189 countries have ratified the protocol. Although there is some controversy as to whether the Kyoto Protocol was successful at reducing emissions or not, there is also some evidence to suggest that the protocol, as a binding instrument, has had an impact.

In terms of the enforceability of the Kyoto Protocol, scholars have noticed positive elements of its monitoring and compliance mechanisms. The monitoring system requires countries to develop a national system of estimating emissions, annual submission of greenhouse gas inventories, and expert reviews.

Sources: UNFCCC web site at: http://unfccc.int/kyoto_protocol/items/2830.php.

Some conventions, particularly those in the environmental field, have funding provisions attached to them. The Global Environment Facility (GEF) is now the financing mechanism for four international treaties, including the UNFCCC. Since 1991 the GEF has allocated US$ 10 billion, supplemented by more than US$ 47 billion in co-financing, for more than 2800 projects in more than 168 developing countries.[3] The Adaptation Fund was established to finance adaptation projects in developing countries that are parties to the Kyoto Protocol. The fund is financed with 2% of the sales proceeds on "certified emission reduction units" issued under the Clean Development Mechanism which can be used under the Kyoto Protocol to meet emissions reduction targets. The fund can also accept other sources of funding, including donations. Eligible donors to the Adaptation Fund include sovereign governments, foundations, NGOs, private corporations and individuals.[4] The Green Climate Fund (see Box 6.3), also linked to the UNFCCC, has been agreed upon and is in the process of being established. In Cancun in 2010 developed countries committed themselves "in the context of meaningful mitigation actions and transparency on implementation, to a goal of mobilizing jointly US$ 100 billion per year by 2020" (*4*). However, there are many issues to resolve regarding how the fund will operate, and in particular how it will mobilize resources, and from whom, to meet the goal.

[1] For further information on dispute settlement in the World Trade Organization, see: http://www.wto.org/english/thewto_e/whatis_e/tif_e/disp1_e.htm, accessed 6 March 2012.

[2] For further information on human rights monitoring, see: http://www.ohchr.org/EN/HRBodies/Pages/HumanRightsBodies.aspx, accessed 6 March 2012.

[3] For further information on the GEF, see: http://www.thegef.org/gef/whatisgef, accessed 6 March 2012.

[4] For further information on the Adaptation Fund, see: http://www.adaptation-fund.org, accessed 6 March 2012.

In most of the above funds the obligations of the relevant treaty do not in themselves commit countries to provide financing at specified levels. For instance, the GEF operates on the basis of voluntary replenishments of the fund every four years. The Multilateral Fund, related to the Montreal Protocol, also operates on a replenishment cycle of three years but the proportionate contribution of each contributor is determined by the same formula as used for assessed contributions to the United Nations and its agencies. The overall scale of contribution is collectively determined by members and has, in fact, declined in nominal terms after peaking in 2003–2005 (see Box 6.3). The only fund that incorporates an element of automatic funding is the Adaptation Fund which, in the period 2009–2011, received US$ 168 million as the proceeds from the levy on sales of certified emission reduction units. However the revenue from this source is uncertain as the price of certified emission reduction units can rise or fall significantly (5).

Box 6.3 The Green Climate Fund and the Multilateral Fund

The Green Climate Fund

In Copenhagen in 2009 the Conference of the Parties of the UNFCCC decided that scaled-up, new and additional, predictable and adequate funding, as well as improved access, should be provided to developing countries to enable and support enhanced action on mitigation, adaptation, technology development and transfer, and capacity-building for enhanced implementation of the convention. The collective commitment by developed countries was to provide new and additional resources through international institutions, approaching US$ 30 billion for the period 2010–2012. Developed countries also committed to a goal of mobilizing jointly US$ 100 billion a year by 2020 to address the needs of developing countries. This funding would come from a wide variety of sources, public and private, bilateral and multilateral, including alternative sources of finance. New multilateral funding for adaptation would be delivered through effective and efficient fund arrangements, with a governance structure providing for equal representation of developed and developing countries. A significant portion of such funding should flow through the Copenhagen Green Climate Fund.

At its next meeting in Cancun in 2010, the Conference of the Parties of the UNFCCC decided to establish the Green Climate Fund, to be designated as an operating entity of the financial mechanism of the convention under Article 11. The fund would be governed by the Green Climate Board comprising 24 members, as well as alternate members, with equal numbers of members from developing and developed country Parties.

The Multilateral Fund

The Montreal Protocol on Substances that Deplete the Ozone Layer is a protocol to the Vienna Convention for the Protection of the Ozone Layer. The Multilateral Fund was established in 1991 to assist developing countries meet their Montreal Protocol commitments. Its main objective is to assist developing countries to comply with the control measures of the protocol. It is managed by an Executive Committee with equal membership from developed and developing countries. Since 1991, the Multilateral Fund has approved activities – including industrial conversion, technical assistance, training and capacity-building – worth over US$ 2.8 billion.

Contributions to the Multilateral Fund from the industrialized countries are assessed according to the United Nations scale of assessments. In essence, this relates the scale of contribution proportionate to gross national income for industrialized countries.

The Multilateral Fund has been replenished eight times: US$ 240 million (1991–1993), US$ 455 million (1994–1996), US$ 466 million (1997–1999), US$ 440 million (2000–2002), US$ 474 million (2003–2005), US$ 400.4 million (2006–2008), US$ 400 million (2009–2011) and US$ 400 million (2012–2014). As of November 2011, the contributions made to the Multilateral Fund by some 45 countries totalled over US$ 2.89 billion. Projects and activities supported by the fund are implemented by four international implementing agencies.

Sources: UNFCCC web site at: http://unfccc.int/2860.php and Multilateral Fund website at: www.multilateralfund.org, accessed 6 March 2012.

Hard and soft law

We assessed the advantages and disadvantages of a convention approach (so-called "hard law" which also encompasses treaties, covenants and some other regulations) and other forms of international agreements (so-called "soft law"). It is often thought that the main advantage of "soft law" approaches is that, precisely because they lack legal force and enforcement mechanisms, it may be easier to reach agreement and to achieve more bold or ambitious outcomes. However, this is not necessarily the case. For example, it took 12 years for the United Nations to adopt the non-binding "Declaration on the Rights of Indigenous Peoples". In addition, governments can make pledges in non-binding instruments and easily fail to meet them. For instance, the target for industrialized countries to provide development assistance of 0.7% of GDP was first set in 1970 with countries making "best efforts" to reach the target by "the middle of the decade" (*6*). In 2010, 40 years later, only five relatively small countries have met the target and the average for all aid donors is just over 0.3% (*7*). On the other hand, such "soft law" agreements may carry moral force. The International Code of Marketing of Breast-milk Substitutes was adopted by the World Health Assembly in 1981 as a recommendation under Article 23 of the WHO Constitution rather than a "harder" regulation (under Article 21). In forwarding the draft code to the World Health Assembly, the WHO Executive Board agreed "that the moral force of a unanimous recommendation could be such that it would be more persuasive than a regulation that had gained less than unanimous support from Member States" (*8*). UNICEF estimates that, since 1981, 84 countries have enacted legislation implementing all or many of the provisions of the code.[1] However, as illustrated by the negotiation of this code, a soft law agreement may just represent a final compromise when the parties fail to agree on a binding instrument which ultimately may not satisfy any of the sides in the negotiation (*9*).

By contrast while hard law has both legal and moral force, conventions can take a long time to negotiate and can involve quite complex governance arrangements and enforcement mechanisms. On the other hand, they provide a framework for future policy innovation and for future protocols to address particular issues in the scope of the convention (of which the Kyoto Protocol is but one of many in the environmental field alone) and the greater possibility of ensuring compliance by nation states with the agreement.

A background paper prepared for the negotiation of the FCTC set out the potential benefits of a binding agreement (see Box 6.4).

[1] See the International Code of Marketing of Breast-milk Substitutes at: http://www.unicef.org/nutrition/index_24805.html, accessed 6 March 2012.

Box 6.4 What Makes International Agreements Effective?

The empirical evidence suggests that international agreements can play a significant role in addressing international problems. For example:

- Arms control agreements limited the proliferation of nuclear weapons and led to a substantial reduction in the arsenals of the United States and the former Soviet Union.
- The General Agreement on Tariffs and Trade has brought down trade barriers and promoted the expansion of international trade.
- Production and consumption of substances that deplete the ozone layer have declined dramatically as a result of the Montreal Protocol.

International agreements are rarely successful in coercing a truly bad offender to change behaviour, and few even attempt to establish strong enforcement mechanisms. But they are often effective in facilitating cooperation among states to achieve mutually desired ends:

- by providing assurance that costly actions will be reciprocated by other states;
- by promoting a process of social learning;
- by giving supporters within national governments additional leverage to pursue the treaty's objectives;
- by establishing mechanisms to help to build the capacity of developing countries.

In order to encourage compliance, an international agreement can:

- articulate precise rules, adherence to which is easily verifiable;
- require states to submit national reports, and establish international review mechanisms that hold states up to public scrutiny;
- provide assistance to developing states in order to help them comply;
- encourage participation by a wide variety of stakeholders.

In the longer term international agreements can produce significant shifts in behaviour both because they change states' calculation of costs and benefits and because most states feel they ought to comply.

An evaluation of progress in the implementation of the WHO FCTC concluded, inter alia, that after five years of implementation a positive trend in global progress is visible. More than half of the substantive articles of the convention attracted high implementation rates, with more than two thirds of Parties that reported twice indicating that they implemented key obligations. Half of the Parties that reported twice implemented more than 80% of measures contained in all substantive articles. Overall, Parties have reported high implementation rates for measures on protection from exposure to tobacco smoke (Article 8), packaging and labelling (Article 11), sales to and by minors (Article 16), and education, communication, training and public awareness (Article 12). Rates remained low in other areas such as regulation of the contents of tobacco products (Article 9), tobacco advertising, promotion and sponsorship (Article 13), provision of support for economically viable alternative activities (Article 17), protection of the environment and the health of persons (Article 18), and the use of litigation as a tool for tobacco control (Article 19).

Sources: *What makes international. agreements effective? Some pointers for the WHO Framework Convention on Tobacco Control*. Document WHO/NCD/TFI/99.4. Geneva, World Health Organization, 1999 (http://whqlibdoc.who.int/hq/1999/WHO_NCD_TFI_99.4.pdf, accessed 10 March 2012).
2010 global progress report on the implementation of the WHO Framework Convention on Tobacco Control. Geneva, World Health Organization, 2010 (www.who.int/entity/fctc/reporting/progress_report_final.pdf, accessed 10 March 2012)

On balance we consider that the time has come for 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. This

would also be in order to put on a secure footing the implementation of the GSPA-PHI which Member States agreed in 2008, and in particular the sustainable financing of R&D.

Having said this, the landscape of international health law should also be considered. In recent times suggestions have been made for the adoption of international legal instruments on health-related issues. These include, for instance, alcohol (*10,11*), obesity control (*12*), counterfeit drugs (*13*), impact evaluation (*14*), and a framework convention for global health (*15*). Such calls need to be balanced against the very substantial costs of negotiating a series of agreements each with their own governance structure. We acknowledge that there are costs related to international health laws which should be taken into account when considering the available options, and that there would also be benefits from harmonizing new legal instruments in a common framework (*16*).

Nevertheless, and having considered these concerns, we believe a binding instrument on R&D is necessary to secure appropriate funding and coordination to promote R&D needed to address the diseases that disproportionately affect developing countries and which constitute a common global responsibility. Our mandate relates, as previously stated, to product-related research but we would repeat that we recognize the value also of greater investment in other kinds of health-related research.

A binding instrument on health research and development

In our second meeting in July 2011 we made two preliminary recommendations which were made public, namely:

- to strengthen global financing and coordination mechanisms for R&D for health needs of developing countries under the auspices of WHO; and
- that formal intergovernmental negotiations should begin for a binding global instrument for R&D and innovation for health.

As a result, at the third meeting we invited presentations on the negotiations for the WHO FCTC and on the provisions in the WHO Constitution for making agreements of different kinds between WHO member states.

Relevant WHO provisions

Under the WHO Constitution there are three different routes that Member States can use to make agreements, adopt regulations or produce recommendations. Under Article 19:

"The Health Assembly shall have authority to adopt conventions or agreements with respect to any matter within the competence of the Organization. A two-thirds vote of the Health Assembly shall be required for the adoption of such conventions or agreements, which shall come into force for each Member when accepted by it in accordance with its constitutional processes."

These require a two thirds majority in the World Health Assembly. Countries must then opt into the agreements and then accept them through mechanisms appropriate to their own constitutional processes. The only agreement made to date under Article 19 is the FCTC.

Under Article 21:

"The Health Assembly shall have authority to adopt regulations concerning:

(a) sanitary and quarantine requirements and other procedures designed to prevent the international spread of disease;

(*b*) nomenclatures with respect to diseases, causes of death and public health practices;

(*c*) standards with respect to diagnostic procedures for international use;

(*d*) standards with respect to the safety, purity and potency of biological,pharmaceutical and similar products moving in international commerce;

(*e*) advertising and labelling of biological, pharmaceutical and similar products moving in international commerce."

These can be passed by a simple majority in the World Health Assembly. Member States need to opt out of the agreement if they wish to, rather than opt in. Ratification by states is not necessary. These agreements are legally binding but, as can be seen from the Article, are confined to a particular set of topics of a technical nature or involving standard-setting unrelated to the objective of the convention we propose here. The only example under Article 21 is that of the International Health Regulations, last agreed in 2005.

Under Article 23:

"The Health Assembly shall have authority to make recommendations to Members with respect to any matter within the competence of the Organization."

Resolutions passed under Article 23 are the most frequent way the World Health Assembly makes recommendations. They include, for instance, the GSPA-PHI, the recently negotiated Pandemic Influenza Preparedness Framework and, as we have seen, the International Code of Marketing of Breast-milk Substitutes.

As indicated above, we believe that a recommendation under Article 23 is not sufficient due to the collective action problem of providing global public goods and since stronger commitments and monitoring and enforcement mechanisms are needed, and that 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.

Elements of a binding agreement

The content of an agreement would, of course, be determined by the outcome of the proposed negotiations between Member States, but we set out here the principles and objectives which we believe should inform the negotiation process and some ideas about the next steps.

The framework for a possible convention has in many ways already been agreed between member states in the GSPA-PHI in the framework utilized there, namely:

"(a) provide an assessment of the public health needs of developing countries with respect to diseases that disproportionately affect developing countries and identify their R&D priorities at the national, regional and international levels

(b) promote R&D focusing on Type II and Type III diseases and the specific R&D needs of developing countries in relation to Type I diseases

(c) build and improve innovative capacity for research and development, particularly in developing countries

(d) improve, promote and accelerate transfer of technology between developed and developing countries as well as among developing countries

(e) encourage and support the application and management of intellectual property in a manner that maximizes health-related innovation, especially to meet the R&D needs of developing countries, protects public health and promotes access to medicines for all, as well as explore and implement, where appropriate, possible incentive schemes for R&D

(f) improve delivery of and access to all health products and medical devices by effectively overcoming barriers to access

(g) secure and enhance sustainable financing mechanisms for R&D and to develop and deliver health products and medical devices to address the health needs of developing countries

(h) develop mechanisms to monitor and evaluate the implementation of the strategy and plan of action, including reporting systems". (*17*)

The proposed convention aims at providing effective financing and coordination mechanisms to promote R&D. As we noted in our third meeting, we see a convention not as a replacement for the existing intellectual property rights system but as a supplementary instrument where the current system does not function. R&D under the convention should focus on the development of health technologies for Type II and Type III diseases as well as the specific needs of developing countries related to Type I diseases.

We take as granted that our suggestions are set in the context of a broader framework for health research and that the proposed financing mechanisms and the convention should: i) be supportive of health research in general, including on public health and health systems, ii) not imply resource shifts from other important areas of health research or iii) limit scope for financing of R&D on health needs in developing countries only to particular technologies or options.

Within that broad framework we would suggest, on the basis of our own analysis, that the following proposals be considered as part of the framework for a negotiation process for a convention:

Objectives

- Implementing states' obligations and commitments arising under applicable international human rights instruments with provisions relevant to health.
- Promoting R&D for developing new health technologies addressing the global challenges constituted by the health needs of developing countries by means which secure access and affordability through delinking R&D costs and the prices of the products.
- Securing sustainable funding to address identified R&D priorities in developing countries.
- Improving the coordination of public and private R&D.
- Enhancing the innovative capacity in developing countries and technology transfer to these countries.
- Generating R&D outcomes as public goods, freely available for further research and production

- Improving priority-setting based on the public health needs of developing countries and decision-making relying on governance structures which are transparent and give developing countries a strong voice.
- Core elements under the convention should focus on development of health technologies for Type II and Type III diseases as well as the specific needs of developing countries related to Type I diseases.

Financing

- All countries should aim to achieve specified levels of public funding on health R&D relevant to the needs of developing countries.
- Countries could fulfil their financial commitment through contributions to a financing mechanism established under the convention, in combination with domestic spending on R&D undertaken to attain the convention's objectives, or through development assistance where applicable.
- A financing mechanism should be established on the basis of contributions by governments. The convention may determine a level of contribution, taking account of countries' own investments in relevant R&D, either domestically or in other countries. We have suggested a contribution of 20–50% of their total funding obligation to a pooled funding mechanism.
- Such financing may be generated from existing taxpayer resources, from new national revenue-raising measures, or by channelling a portion of the resources raised from any new international mechanism to this purpose. Voluntary additional public, private and philanthropic contributions to a pooled funding mechanism can also be envisaged.
- The convention and its financing mechanisms for the more defined objectives of R&D need to be supportive to the broader context of overall allocation of public financing to health research and the sustainability of financing in other areas of health research.
- The convention should define which research entities in the public and private sectors, in public–private partnerships, and in developed or developing countries, should be eligible for funding.
- Funding should be directed so as to promote cost-effective R&D in ways that will also promote subsequent access to technologies in developing countries, in particular using the tools identified in our report which best meet these criteria, such as open knowledge innovation.
- Funding should also be directed in ways that promote capacity-building and technology transfer to the public and private sectors in developing countries.

Coordination

- A coordination mechanism will be needed which would help to promote, in particular, the objectives in Element 2.3 of the GSPA-PHI ("improving cooperation, participation and coordination of health and biomedical research and development"). This could be based on the ideas we put forward in Chapter 5.
- The coordination mechanism would need to improve the measurement of the volume, type and distribution of relevant R&D and the evaluation of R&D outcomes, particularly so that progress against commitments and compliance could be measured. This will depend in part on data and reports provided by parties to the convention.

Compliance mechanisms also need to be devised, including through cooperation between the parties to the convention.

Next steps

As is evident from our report, the issues that will need to be addressed in a negotiation of a binding agreement are many and complex. One of the reasons why the negotiations on the GSPA-PHI took so long was that there was very little preparatory work done to generate a draft text for consideration by the Intergovernmental Working Group that was established to draft the GSPA-PHI. We suggest therefore a process on the following lines:

- When dealing with our report the World Health Assembly should consider, first, establishing a working group or technical committee composed of two Member States from each WHO region to undertake preparatory work on the elements of a draft agreement, soliciting inputs as necessary from other Member States, relevant intergovernmental organizations, funders, researchers, the private sector, civil society and academics as necessary. Alternatively, as was done with the FCTC, an open-ended intergovernmental working group could be established with appropriate technical support.
- It should also provide for the establishment of an intergovernmental negotiating body open to all Member States, to be established under Rule 42 of the World Health Assembly's Rules and Procedure, to draft and negotiate the proposed R&D agreement following on from the report of the proposed working group.
- WHO would need to provide appropriate resources to support the working group or technical committee.

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Appendix 1

INCEPTION REPORT

Report of the first meeting of the Consultative Expert Working Group on Research and Development: Financing and Coordination

1. The Consultative Expert Working Group on Research and Development: Financing and Coordination held its first meeting from 5 to 7 April 2011 in Geneva, attended by 19 of its 21 members. The Consultative Expert Working Group elected Professor John-Arne Røttingen (Norway) as Chair and Professor Claudia Inês Chamas (Brazil) as Vice-Chair. In addition, it elected rapporteurs from each of the other four WHO regions:

- Professor Bongani Mawethu Mayosi (South Africa)
- Dr Leizel Lagrada (Philippines)
- Mr L C Goyal (India)
- Ms Hilda Harb (Lebanon)

2. The meeting was open to observers on the first two days, except for the final sessions on each day. On 6 April, the Consultative Expert Working Group held an open forum at which 14 presentations were made by a variety of stakeholders. The audiovisual records of these open sessions, and presentations made, are available on the WHO web site. The final day was a closed session, ending with a briefing by the Chair on the outcomes in an open session.[1]

Summary of outcomes

Conflict of interest

3. The Consultative Expert Working Group discussed the issue of conflict of interest in the light of the determination by WHO that four members had relevant conflicts of interest.[2] The Secretariat noted that it was WHO's policy to be transparent about conflicts of interest, and to seek to manage such conflicts bearing in mind the contributions that individuals could make to public health in spite of a declared conflict of interest. The working group was fully mindful of issues raised with regard to the work of its predecessor, the earlier Expert Working Group on Research and Development Financing, the request in resolution WHA63.28 that the Consultative Expert Working Group should "observe scientific integrity and be free from conflict of interest in its work", and the views of Member States expressed at the 128th session of the Executive Board.[3]

4. After due consideration, it was agreed that it would be open to any member of the Consultative Expert Working Group to raise the issue of potential conflict of interest of any other member at any time during their discussions if they considered it relevant, and that the working group would then agree how to address any perceived conflict in relation to the topic being discussed. It was also agreed that, in the particular case of Professor Herrling, he should excuse himself from participating in the discussion of the proposal he had sponsored.

[1] See http://www.who.int/phi/news/cewg_2011/en/index.html (accessed 28 April 2011).

[2] See presentation at http://www.who.int/phi/news/cewg_2011/en/index.html

[3] See document EB128/2011/REC/2, summary records of the second meeting, section 2 and the ninth meeting, section 1.

Mandate/scope of work

5. The Consultative Expert Working Group considered how to interpret its mandate as set out in resolution WHA63.28, including taking forward the work of the Expert Working Group on Research and Development Financing, deepening its analysis, considering additional submissions and proposals, and the feasibility of regional approaches to implementation. The Consultative Expert Working Group noted also that its core mandate remained the one set out for the establishment of the earlier Expert Working Group in resolution WHA61.21 and in the global strategy and the agreed parts of the plan of action on public health, innovation and intellectual property as adopted by that resolution.

6. In light of the above, the Consultative Expert Working Group decided that its focus should be on the financing and coordination of research and development for health products and technologies (including, for example, medicines, vaccines, diagnostics, devices and delivery technologies) related to Type II and Type III diseases and the specific research and development needs of developing countries in relation to Type I diseases. However, it acknowledged the importance of other relevant areas of research and development which may require additional financing and/or improved coordination, such as:

- better policies for research and development and innovation
- improved public health, clinical and preventive interventions including, for example, diagnostic algorithms
- health policy and health systems, to improve delivery and access to new and existing products.

7. The Consultative Expert Working Group also emphasized the links between its specific mandate and the other elements of the global strategy and plan of action on public health, innovation and intellectual property. Its core mandate was centred on Element 2 (Promoting research and development) and Element 7 (Promoting sustainable financing mechanisms). However, it was important also to take account of research and development needs and priorities (Element 1), improving innovative capacity (Element 3), technology transfer (Element 4) and intellectual property management (Element 5). Moreover it recognized the central importance of ensuring that research and development policies took account of the need to improve availability, acceptability and affordability to contribute to improved delivery and access (Element 6).

8. The Consultative Expert Working Group recognized that resolution WHA63.28 had requested it to examine, in particular, the practical details of four innovative sources of financing,[1] to review five promising proposals,[2] and to further explore the six proposals that did not meet the criteria applied by the earlier Expert Working Group.[3] However, the working group decided to analyse all 22 proposals referred to in that Expert Working Group's report (including those in Chapters 5.4 and 5.5) together with any new or improved proposals submitted by Member States or other stakeholders. Furthermore, the Consultative Expert Working Group considered that Member States or other stakeholders should, if they wished, resubmit any proposals from among the 109 that had originally been compiled by the

[1] Report of the Expert Working Group on Research and Development Financing. Geneva, World Health Organization, 2010, Chapter 5.3.

[2] Report of the Expert Working Group on Research and Development Financing. Geneva, World Health Organization, 2010, Chapter 5.6.

[3] Report of the Expert Working Group on Research and Development Financing. Geneva, World Health Organization, 2010, Annex 2.

earlier Expert Working Group,[1] or any other proposals that they felt had not received proper consideration by that Expert Working Group.

9. Resolution WHA63.28 specified that the working group should examine the appropriateness of different financing approaches and the feasibility of implementation in each of the six WHO regions. The Consultative Expert Working Group underscored that it would be very challenging to analyse the regional appropriateness of different proposals within its time limits, and stressed that a full assessment would need to take regional and national issues into account and should thereby be carried out by local policy-makers. Resolution WHA63.28 also requested the Director-General to provide upon request and within available resources, technical and financial support for regional consultations to inform the work of the Consultative Expert Working Group. In the time available to it, the Consultative Expert Working Group thought it most appropriate to explore the possibility of organizing side meetings during the sessions of the WHO regional committees which are being held from August to October 2011 – should such meetings be requested by the WHO regional offices. The side meetings would involve the members of the Consultative Expert Working Group belonging to a particular region, the Regional Office concerned and the Secretariat at headquarters; invitees would include Member States and regional stakeholders. These regional meetings, if held, would enable the Consultative Expert Working Group to incorporate regional perspectives into its deliberations.

Analytical framework

10. The Consultative Expert Working Group decided that it would provisionally categorize proposals under two headings:

- Financing mechanisms – including both financing and allocation proposals in the terminology of the earlier Expert Working Group
- Coordination mechanisms – including those to improve efficiency, networking arrangements, and mechanisms with overarching implications that include global governance issues.

11. The Consultative Expert Working Group also decided that in reviewing proposals before it (i.e. proposals from the earlier Expert Working Group, or new, improved or resubmitted ones), it would not seek to give them a ranking or score as its predecessor had done. No proposal would be rejected unless clearly agreed to be outside the Consultative Expert Working Group's mandate. Rather, the Consultative Expert Working Group would provide a qualitative appraisal of each proposal, based on the evidence, where available, and its own judgment, according to its own criteria. On the basis of this analysis the Consultative Expert Working Group would aim to provide concrete recommendations on how Member States, the Secretariat and other stakeholders could take the agenda forward to improve financing and coordination in research and development.

12. The Consultative Expert Working Group considered a number of criteria that should inform its analysis, bearing in mind that their applicability would vary according to the type of proposal involved, and the diverse set of constraints in the research and development process that different proposals set out to address. These criteria included:

- potential public health impact in developing countries
- rational and equitable use of resources/efficiency considerations
- cost-effectiveness

[1] See "Methodology Used by the EWG": www.who.int/phi/explanation_of_methodology_used_by_the_EWG.pdf.

- technical feasibility, scaling-up potential, replicability, speed of implementation
- financial feasibility and sustainability
- additionality
- intellectual property management issues
- potential for delinking research and development costs and the price of products
- equity/distributive effect, including on availability and affordability of products and impact on access and delivery
- accountability/participation in governance and decision making
- impact on capacity building in, and transfer of technology to, developing countries
- potential synergy with other mechanisms/potential for combining with others.

Invitation to submit proposals

13. The Consultative Expert Working Group decided to issue an invitation to submit proposals at the end of April which would solicit the following: any improved versions of the 22 proposals considered by the earlier Expert Working Group; any proposals from that Expert Working Group's wider list of 109 that Member States or other stakeholders felt should be reconsidered by the Consultative Expert Working Group; and any new proposals, or any other proposals that were felt not have received proper consideration by the earlier Expert Working Group. The Consultative Expert Working Group asked the Secretariat to issue the call for proposals using a standardized template that required a self-assessment of each proposal according to agreed criteria, including the evidence base, where available, supporting the proposal. The call would in addition ask for submissions from academic institutions or others concerning any independent reviews and assessments of existing or new proposals.

Appendix 2

MAPPING OF EWG AND CEWG PROCESSES

Summary

This appendix explains which R&D financing and coordination proposals were considered by the CEWG and how we grouped them into our 15 assessments.

Pursuant to World Health Assembly resolution WHA63.28, we examined all 22 grouped proposals found in the report of the EWG. In order to understand better the scope of the 22 grouped proposals, the first part of this appendix explains how the EWG compiled an inventory of 109 incentive proposals[1] for promoting R&D financing and/or coordination, how it reduced these proposals from 109 to 91 (mainly by grouping proposals of a similar nature), and how most of these 91 proposals are reflected in the 22 grouped proposals that feature in Chapter 5 of the EWG report. Because the EWG did not fully describe its methodology, and particularly the final step, we analysed the 91 proposals and grouped them under the 22 grouped proposals to the best of our knowledge and ability.

In addition, we assessed and evaluated all proposals that were submitted to us in response to a call for submission of proposals announced on the CEWG's web page between 1 and 24 June 2011. Of the 22 proposals received, we found five to be essentially funding requests and outside our mandate. With regard to two other proposals, we found – as explained in the main part of the report – that they were insufficiently supported by empirical evidence and we were not convinced by the theoretical arguments which were used by the sponsors to justify the proposals. One proposal on coordination is discussed in the main text of our report. An analysis of the 14 remaining submitted proposals, together with the 22 grouped proposals featured in the EWG report, is contained in Appendix 2. The second part of this appendix explains these processes in more detail.

After examining all 22 grouped proposals in the EWG report and all 15 relevant submissions received in response to the call for submission of proposals, we regrouped all the proposals under consideration into 15 groups which we then assessed. The four EWG proposals relating to sources of financing (section 5.3 of the EWG report) and the submission relating to coordination are addressed in the main text of our report. The last part of the appendix explains which proposal has ultimately been grouped into which of the 15 grouped proposals evaluated by us.

The EWG's grouping of R&D financing and coordination proposals

The first step: creation of an inventory of 109 proposals

1. The EWG decided as a first step to create an inventory of proposals. Leading up to the second meeting of the EWG in June 2009, WHO contacted Member States to solicit proposals, and also set up a web-based public hearing between 7 March and 15 April 2009. This was open to individuals, civil society groups, government institutions, academic and research institutions, the private sector and other interested parties. In response to both of these initiatives, WHO received the following contributions:

For 15 contributions from Member States see: http://www.who.int/phi/mspublichearing_rdf/en/index.html.

[1] In this document the term "proposal" is used for all proposed, submitted or in other ways identified mechanisms that have been suggested to improve financing and/or coordination of R&D in this context, since this term has been used in the previous EWG. The term "grouped proposals" refers to those 22 groups of proposals analysed in the EWG report.

For 13 contributions from other stakeholders see: http://www.who.int/phi/shpublichearing_rdf/en/index.html.

2. In order to increase the breadth and depth of analysis, the EWG then conducted research to identify additional R&D financing proposals. The following sources were identified as containing additional proposals:

- proposals from EWG members;
- literature searches;
- proposals from the Commission on Intellectual Property Rights, Innovation and Public Health (CIPIH) (*1*), the Taskforce on International Innovative Financing for Health Systems (*2)*, and the Brookings Institution analysis of evaluation tools titled *Innovative financing for global health: tools for analysing the options* (*3*).

3. Proposals submitted to the Intergovernmental Working Group on Public Health, Innovation and Intellectual Property (IGWG) were not specifically listed by the EWG in the inventory of 109 proposals. However, most proposals submitted to the IGWG are reflected in the inventory of 91 proposals and/or in the final report of the EWG. For example, product development partnerships, patent pools and advanced purchasing commitments that were frequently referred to in the submissions to the IGWG are all reflected in the EWG's final report. In order to be as transparent as possible, the CEWG extracted all references to proposals submitted to the IGWG in the document entitled *IGWG public hearing – proposals recommendation* which is found on the CEWG web page at: http://www.who.int/phi/news/cewg_proposals/en/index.html.

4. An inventory of 109 proposals was generated as a result of the proposals received from Member States, other stakeholders and the above-mentioned other sources. This inventory can be accessed via the CEWG web page at: http://www.who.int/phi/inventory_of_proposals.xls (please see worksheet *All submissions alphabetically*).

The second step: from 109 proposals to 91 proposals

5. The inventory of 109 proposals was then reduced to 91 by grouping proposals that were essentially the same. For example, there were two items identified as “airline solidarity contribution”. Another example is the grouping of various prize funds (in the inventory of 109 see, for example, numbers 76 and 79) into the more general category of "prize funds" (number 69 in the inventory of 91). Yet another example was the grouping of various proposals relating to fast track reviews (see, for example, numbers 12, 19, 20 and 73 in the inventory of 109) into one or two proposals on fast tracks (see, for example, proposals 32 and 33 in the inventory of 91).

For a list of these 91 proposals, see the document entitled *Inventory* at: http://www.who.int/phi/public_hearings/ewg_2ndhearing_reldocs/en/index.html.

6. The EWG then decided to hold a second web-based public hearing open to Member States, individuals, civil society groups, government institutions, academic and research institutions, the private sector and other interested parties and, in this connection, to invite comments on the evaluation framework, evaluation criteria and the inventory of incentive proposals being considered by the EWG. The intention of this hearing was not to receive new proposals but rather to gather feedback. However, the feedback received from 18 groups, such as WHO Member States, funders, civil society groups, private industry, PDPs and regulatory authorities also included references to new proposals and restatements of proposals submitted during the first public hearing of the EWG or to the IGWG. It should be noted that the inventory of 91 proposals was not updated on the basis of the feedback received from the second hearing. However, in many cases the feedback was incorporated into the

final report. For example, the proposal related to UNITAID's patent pool was explicitly incorporated in the final report of the EWG.

For a list of documents published as part of the second hearing see: http://www.who.int/phi/public_hearings/ewg_2ndhearing_reldocs/en/index.html.

For details of feedback from two Member States see: http://www.who.int/phi/public_hearings/second/contributions/mspublichearing_rdf09/en/index.html.

For details on contributions from 16 other individuals and groups see: http://www.who.int/phi/public_hearings/second/contributions/shpublichearing_rdf09/en/index.html.

7. In order to be as transparent as possible, we extracted these proposals or references to proposals as received from the second hearing and listed them together with all other submissions received at this hearing in a spread sheet entitled *List of submissions to second hearing of EWG - not in inventory*, which can be found at the CEWG web page at: http://www.who.int/phi/news/cewg_proposals/en/index.html. This was done even if in some cases proposals were merely referred to briefly and even where no further explanation on a proposal was provided.

The third step: from 91 to 22 grouped proposals

8. Most of the 91 proposals were grouped into 22 broad groups of proposals (grouped proposals) mentioned in the EWG report and referred to in World Health Assembly resolution WHA63.28. There is no documentation on how the EWG performed this grouping nor a complete mapping of how the 91 proposals related to the 22 grouped proposals.

9. However, the CEWG deemed that this mapping was essential to understanding the scope of its work. We therefore analysed the 91 proposals and grouped them under the 22 grouped proposals to the best of our knowledge and ability. The results may be found in another spread sheet entitled *Inventory of 22 grouped proposals*, which can be found at: http://www.who.int/phi/news/cewg_proposals/en/index.html.

10. Worksheet 1 (entitled *Grouped proposals*) demonstrates how the majority of the 91 proposals found in the EWG inventory can be mapped into the 22 broad grouped proposals in the EWG report. Column A gives the numbering of the proposal as found in the EWG inventory of 91 proposals, columns B and C give the name and description of the proposal. Column D marks whether a proposal was considered an allocation (A) proposal or a funding (F) proposal. Column E indicates if proposals have been grouped under more than 1 of the 22 proposal groupings. Numbers under the title *Sources* in column F refer to the row of worksheet 2 (titled *Reading list*), in which further reading material on a respective proposal may be found.

11. The spread sheet *Inventory proposals not accounted* (to be found at the CEWG web page at: http://www.who.int/phi/news/cewg_proposals/en/index.html) lists all proposals in the inventory of 91 that could not be grouped into one of the 22 broad grouped proposals in the EWG report. It is worth noting that these proposals, which were not mentioned in the final EWG report, were almost entirely gathered from literature searches or other sources and not from proposals submitted to the EWG by Member States and other stakeholders. Numbers under the title sources in column F again refer to the row of worksheet 2 (titled *Reading list*), in which further reading material on a respective proposal may be found.

12. All grouped proposals can be found in Chapter 5 of the EWG report.

CEWG grouping of R&D financing and coordination proposals

The inventory of R&D financing and coordination proposals considered by CEWG

13. All 15 grouped proposals referred to in World Health Assembly resolution WHA63.28 can be found in Chapter 5 of the EWG report. In addition, Chapter 5 of the EWG report refers to seven further grouped proposals that are not specifically mentioned in resolution WHA63.28. During the first meeting of the CEWG in April 2011 we decided to examine all 22 grouped R&D financing and coordination proposals featured in Chapter 5 of the EWG report, including those not particularly mentioned in World Health Assembly resolution WHA63.28. These grouped proposals are listed in Table 1.

Table 1. Twenty-two grouped proposals considered by CEWG

Four innovative financing sources (section 5.3 of the EWG report) Mentioned in World Health Assembly resolution WHA63.28 under 2 (2) b i
A new indirect tax
Voluntary contributions from businesses and consumers
Taxation of repatriated pharmaceutical industry profits
New donor funds for health research and development
Five promising proposals (section 5.6) Mentioned in World Health Assembly resolution WHA63.28 under 2 (2) b ii
Open source
Patent pools (UNITAID model)
Health impact fund
Priority review voucher
Orphan drug legislation
Six further proposals (Annex 2) Mentioned in World Health Assembly resolution WHA63.28 under 2 (2) b iii
Transferable intellectual property rights
Green intellectual property
Removal of data exclusivity
Biomedical research and development treaty
Large end-stage prizes (impact-based rewards)
Neglected disease tax breaks for companies.
Five proposals relating to funding allocation (section 5.4) Not mentioned in World Health Assembly resolution WHA63.28
Product development partnerships
Direct grants to small companies and for trials in developing countries
“Milestone” prizes
“End” prizes (cash)
Purchase or procurement agreements
Two proposals to improve efficiency (section 5.5) Not mentioned in World Health Assembly resolution WHA63.28
Regulatory harmonization
Precompetitive research and development platforms

14. In addition to the 22 grouped proposals featured in the EWG report and in accordance with the mandate of the CEWG, we decided also to examine all proposals received in response to a call for submission of proposals on the CEWG web page between 1 and 24 June 2011. This call for submission of proposals invited relevant stakeholders to submit proposals that contained any improved versions of the 22 grouped proposals considered by the EWG, any proposals from the wider EWG list of 109 which Member States or other stakeholders felt should be reconsidered by the CEWG, any new proposals, or any other proposals that they felt had not received proper consideration by the EWG.

15. In response to this call for proposals we received the 22 submissions which are listed in Table 2. The full text of submissions can be found on the CEWG web page at: http://www.who.int/phi/news/cewg_submissions/en/index.html. We judged that 15 of these submissions (numbered 1–15) were of particular relevance to the CEWG mandate and these have therefore been grouped in the assessments with relevant proposals as shown in Table 2.

16. One of these submissions – *No.12: The ANDI model. African Network for Drugs and Diagnostics Innovation (ANDI)* – is dealt with in Chapter 5 of our report. Of the remaining submissions, five (numbers 16–20) were considered to be out of the scope of the CEWG terms of reference because they were requests for project funding rather than proposals for improving R&D financing and coordination. The two remaining proposals (21 and 22) were insufficiently supported by empirical evidence and we were not convinced by the theoretical arguments which were used by the sponsors to justify the proposals.[1]

Table 2. Grouping of submissions received through the call for submissions into the CEWG report and assessments

CEWG Submission		Related CEWG assessment
1	*Innovation inducement prizes.* Knowledge Ecology International.	Milestone and end prizes
2	*A global framework on health research and development.* All India Drug Action Network, Berne Declaration, CENTAD, Initiative for Health and Equity in Society, People's Health Movement, Third World Network.	1. Pooled funds 2. Global Framework on Research and Development
3	*Consideration of an essential health and biomedical R&D treaty.* Health Action International Global, Initiative for Health & Equity in Society, Knowledge Ecology International, Médecins Sans Frontières, Third World Network.	Global Framework on Research and Development
4	*Submission to the CEWG.* Universities Allied for Essential Medicines.	1. Open approaches to research and development and innovation 2. Patent pools
5	*Investing in small- and medium-sized enterprises in innovative developing countries.* COHRED and Global Forum for Health Research.	1. Direct grants to companies 2. Pooled funds
6	*International Fund for Innovation (IFI) (Green intellectual property).* Institut de Hautes Études Internationales et du Développement. Itaru Nitta.	Green intellectual property
7	*Fund for research and development in neglected diseases.* Novartis International	Pooled funds

[1] See above in Chapter 3

CEWG Submission		Related CEWG assessment
8	*A milestone-based prize to stimulate R&D for point-of-care fever diagnostics.* BIO Ventures for Global Health.	Milestone and end prizes
9	*Equitable licensing/med4all.* BUKO Pharma-Kampagne. Charité Universitätsmedizin Berlin. Universität Oldenburg.	Open approaches to research and development and innovation
10	*A new incentive system for technological innovation in developing countries.* Miguel Maito, Eduardo Franciosi.	1. Direct grants to companies 2. Pooled funds
11	*Submission to the CEWG.* Health Action International.	Global Framework on Research and Development
12	*The ANDI model. African Network for Drugs and Diagnostics Innovation (ANDI).* Special Programme for Research and Training in Tropical Diseases.	Dealt with in Chapter 5 of the CEWG report
13	*Financing & incentives for neglected disease R&D.* Drugs for Neglected Diseases Initiative.	1.Milestone and end prizes 2.Pooled funds 3.Open approaches to research and development 4.Regulatory harmonization
14	*Health Impact Fund.* Incentives for Global Health.	Health Impact Fund
15	*Open source drug discovery initiative*. Council of Scientific and Industrial Research, India	Open approaches to research and development and innovation
16	*Open source software for improving maternal, neonatal and child health services in Pakistan.* Ghulam Nabi Kazi. WHO Pakistan Country Office.	*Out of scope*
17	*Neglected tropical diseases management portal - epidemiological watcher*. Health Insight Ltd.	*Out of scope*
18	*Employees' food safety knowledge and practices in foodservice operations serving high-risk populations.* University of Costa Rica. Paola Paez.	*Out of scope*
19	*Limbal stem cell bioengineering.* Clinical Research, Dr Agarwal's Eye Hospital Ltd.	*Out of scope*
20	*Maternal mortality reduction proposal.* Clinical Research, Dr Argarwal's Eye Hospital Ltd.	*Out of scope*
21	*Optimal hedging against the premature obsolescence of available treatments.* Euromed Management, Centre National de la Recherche Scientifique, Groupement de Recherche en Economie Quantitative d'Aix Marseille, (IDEP). Patrick Leoni, Stéphane Luchini.	*Insufficiently supported*
22	*Reduction of patents' duration to prevent collusion at industry level.* Euromed Management. Kellogg School of Management, Northwestern University. Patrick Leoni, Alvaro Sandroni.	*Insufficiently supported*

The new landscape of proposals: 15 assessments and chapters on financing and coordination

17. The second meeting of the CEWG assessed the 22 grouped proposals featured in the EWG report and the 15 submissions deemed relevant to the mandate of the CEWG.

18. We then decided to regroup all proposals we had deemed relevant to our mandate into 15 new groups of proposals. On this basis, 15 assessments were prepared. For example, the various proposals

relating to pooling of funds were grouped together into the assessment of "Pooled funds" that provide additional finances to PDPs and other research organizations.

19. Table 3 shows which grouped proposals discussed in the EWG report and which submissions received in response to the CEWG's call for proposals were considered under each of the CEWG's 15 assessments presented in Appendix 3 of our report.

Table 3. Proposals considered under CEWG's 15 assessments

CEWG assessments		Relevant grouped proposals in the EWG report and other relevant submissions
1.	Global Framework on Research and Development	***Relevant section in the EWG report:*** Annex 2. ***Relevant submissions to CEWG:*** *Consideration of an essential health and biomedical R&D treaty.* Health Action International Global, Initiative for Health & Equity in Society, Knowledge Ecology International, Médecins Sans Frontières, Third World Network. *Comments by HAI Global.* *A global framework on health research and development.* All India Drug Action Network, Berne Declaration, CENTAD, Initiative for Health and Equity in Society, People's Health Movement, Third World Network. ***Other relevant submissions:*** *Health Action International 2009* (submission to the EWG). *Comments of Knowledge Ecology International (KEI) to the WHO public hearing for proposals for new and innovative sources of funding to stimulate R&D.* Knowledge Ecology International 2009 (submission to the EWG). *Proposal for WHO discussions on a biomedical R&D treaty.* Bangladesh, Barbados, Bolivia and Suriname 2009 (submission to the EWG).
2.	Removal of data exclusivity	***Relevant section in the EWG report:*** Annex 2 ***Relevant submissions to CEWG:*** None
3.	Direct grants to companies	***Relevant section in the EWG report:*** Section 5.4.2 on "Direct Grants to small companies and for trials in developing countries". ***Relevant submissions to CEWG:*** *New investment strategy: innovative developing country research awards*. Global Forum for Health Research. *A new incentive system for technological innovation in developing countries*. Miguel A. Maito, Eduardo Franciosi ***Other relevant submissions:*** *Concept note: Innovative financing mechanism for global health innovation*. Charles W. Wessner, US National Academies of Science, with support from the Global Forum for Health Research (submission to the EWG).

CEWG assessments		Relevant grouped proposals in the EWG report and other relevant submissions
4.	Green intellectual property	***Relevant section in the EWG report:*** Annex 2. ***Relevant submissions to CEWG:*** *International Fund for Innovation (IFI): An innovative financing mechanism for medicines in the developing world. Green intellectual property.* Itaru Nitta ***Other relevant submissions:*** *Patent insurance (Green intellectual property) scheme: a financial prescription for neglected diseases?* Itaru Nitta (submission to the EWG). *Patents and essential medicines: an application of the Green Intellectual Property project*. Itaru Nitta (submission to the CIPIH).
5.	Health Impact Fund	***Relevant section in the EWG report:*** Section 5.6.3 on "Health Impact Fund". ***Relevant submissions to CEWG:*** *Heath Impact Fund.* Incentives for Global Health. ***Other relevant submissions:*** *The Health Impact Fund: pay-for-performance 2009* (submission to the EWG).
6.	Orphan drug legislation	***Relevant section in the EWG report:*** Section 5.6.5 on "Orphan drug legislation". ***Relevant submissions to CEWG:*** None.
7.	Patent pools	***Relevant section in the EWG report:*** Section 5.6.2 on "Patent pools (UNITAID model)". ***Relevant submissions to CEWG:*** None
8.	Pooled funds	***Relevant section in the EWG report:*** Section 5.4.1 on "Product development partnerships". ***Relevant submissions to CEWG:*** *Fund for research and development in neglected diseases*. Novartis. *A global framework on health research and development.* All India Drug Action Network, Berne Declaration, CENTAD, Initiative for Health and Equity in Society, People's Health Movement, Third World Network. *Financing & incentives for neglected disease R&D: opportunities and challenges.* Drugs for Neglected Diseases Initiative. *A new incentive system for technological innovation in developing countries*. Miguel A. Maito, Eduardo Franciosi, ***Other relevant submissions:*** *The Fund for R&D in Neglected Diseases (FRIND) 2009* (submission to the EWG).

CEWG assessments		Relevant grouped proposals in the EWG report and other relevant submissions
9.	Open approaches to research and development and innovation	***Relevant section in the EWG report:*** Section 5.5.2 on "Precompetitive for Research and development platforms". Section 5.6.1 on "Open source". ***Relevant submissions to CEWG:*** *Universities Allied for Essential Medicines.* *Financing and Incentives for Neglected Disease R&D.* Drugs for Neglected Disease Initiative. *Equitable licensing/med4all*. BUKO Pharma-Kampagne, Charité Universitätsmedizin Berlin, Universität Oldenburg. *Open source drug discovery initiative.* Council of Scientific and Industrial Research, India ***Other relevant submissions:*** *"Open source drug discovery": an open collaborative drug discovery model for tuberculosis.* Council of Scientific and Industrial Research, India (submission to the EWG).
10.	Milestone prizes and end prizes	***Relevant section in the EWG report:*** Section 5.4.3 on "Milestone prizes". Section 5.4.4 on "End prizes". Annex 2. ***Relevant submissions to CEWG:*** *The global health innovation quotient prize: a milestone-based prize to stimulate R&D for point-of-care fever diagnostics.* BIO Ventures for Global Health. *Innovation inducement prizes.* Knowledge Ecology International.

CEWG assessments		Relevant grouped proposals in the EWG report and other relevant submissions
		Other relevant submissions: *Chagas disease prize fund for the development of new treatments, diagnostics and vaccines.* Bangladesh, Barbados, Bolivia and Suriname (submission to the EWG). *Prize fund for development of low-cost rapid diagnostic test for tuberculosis.* Bangladesh, Barbados, Bolivia and Suriname (submission to the EWG). *A prize fund to support innovation and access for donor supported markets linking rewards for innovation to the competitive supply of products for HIV-AIDS, TB, malaria and other diseases for humanitarian uses*. Bangladesh, Barbados, Bolivia and Suriname (submission to the EWG) *Prizes as a Reward Mechanism for New Cancer Treatments and Vaccines in Developing Countries*. Bangladesh, Bolivia, Suriname (submission to the EWG). *Response to the Expert Working Group on Alternative Financing*. Health Action International (submission to the EWG). *Comments of Knowledge Ecology International (KEI) to the WHO public hearing for proposals for new and innovative sources of funding to stimulate R&D*. Knowledge Ecology International (submission to the EWG). *Submission to the EWG*. Médecins Sans Frontières (submission to the EWG). *Priority medicines and vaccines prize fund*. Barbados and Bolivia (submission to the IGWG).
11.	Purchase or procurement agreements	***Relevant section in the EWG report:*** Section 5.4.5 on "Purchase or Procurement Agreements". ***Relevant submissions to CEWG:*** None.
12.	Priority review voucher	***Relevant section in the EWG report:*** Section 5.6.4 on "Priority Review Voucher". ***Relevant submissions to CEWG:*** None.
13.	Regulatory harmonization	***Relevant section in the EWG report:*** Section 5.5.1 on "Regulatory Harmonization". ***Relevant submissions to CEWG:*** None.
14.	Tax breaks for companies	***Relevant section in the EWG report:*** Annex 2. ***Relevant submissions to CEWG:*** None.
15.	Transferable intellectual property rights	***Relevant section in the EWG report:*** Annex 2. ***Relevant submissions to CEWG:*** None.

20. In addition we dealt with the "Four innovative sources of finance" (section 5.3 of the EWG report) in chapter 4 of our report, and with the proposal *The ANDI Model – African Network for Drugs and Diagnostics Innovation* in chapter 5.

References

1. *Public health, innovation and intellectual property rights*. Commission on Intellectual Property Rights, Innovation and Public Health. Geneva, World Health Organization, 2006 (http://www.who.int/intellectualproperty/report/en/index.html, accessed 5 March 2012).

2. Taskforce on Innovative Financing for Health Systems (2009). Raising and channeling funds. Working Group 2 report. http://www.internationalhealthpartnership.net/en/taskforce, accessed 5 March 2012).

3. De Ferranti D et al. (2008). *Innovative financing for global health: tools for analyzing the options*. Washington, DC, Brookings Institution, 2008 (Global Health Financing Initiative, Working Paper 2).

Appendix 3

ASSESSMENTS OF PROPOSALSs

Global Framework on Research and Development

Source: EWG Annex 2

Relevant submissions to CEWG

Consideration of an essential health and biomedical R&D treaty (in two parts): Health Action International Global, Initiative for Health & Equity in Society, Knowledge Ecology International, Médecins Sans Frontières, Third World Network.

A global framework on health research and development: All India Drug Action Network, Berne Declaration, CENTAD, Initiative for Health and Equity in Society, People's Health Movement, Third World Network.

Comments by Health Action International Global.

Other relevant submissions

EWG submission. Health Action International, 2009.

EWG submission. *Comments of Knowledge Ecology International (KEI) to the WHO public hearing for Proposals for new and innovative sources of funding to stimulate R&D*: Knowledge Ecology International, 2009.

EWG submission. *Proposal for WHO discussions on a biomedical R&D treaty*: Bangladesh, Barbados, Bolivia and Suriname, 2009.

EWG submission. *Submission of Third World Network*: Third World Network, 2009.

Proposal description

This assessment considers separately two proposals submitted to the CEWG although it is recognized that they espouse many common principles, contain common elements and have some shared sponsorship. These are:

- the submission by Health Action International Global et al on *Consideration of an essential health and biomedical R&D treaty"* – henceforth the "Treaty" (*1*);
- the submission by All India Drug Action Network et al on "*A global framework on health research and development"* – henceforth the "Global Framework" (*2*).

The other submission from Health Action International stresses the paramount importance of exploring and supporting an international instrument to address the coordination, financing and norm setting for biomedical R&D which it says is the only way to achieve a realistic structural change in R&D priority-setting focused on needs-driven research (*3*).

The Treaty

The sponsors' proposal is to begin negotiations for a treaty without delay under the auspices of WHO. The Treaty would seek to create a new global framework for supporting priority medical R&D, based on the fair and equitable sharing of costs, access to benefits of R&D, and incentives to invest in needs-driven R&D consistent with human rights and with the goal of all sharing in the benefits of scientific advancement. This will involve norms and obligations on both national governments and international institutions. While important details would need to be negotiated among Member States, the sponsors believe that certain principles and elements provide a sound foundation from which to begin such negotiations. Parties to the Treaty would seek to promote a sustainable system of medical innovation that would:

(1) ensure adequate and predictable sources of finance for needs-driven medical R&D relevant, in particular, to diseases and conditions which disproportionately affect developing countries;

(2) allocate fairly the costs of supporting needs-driven medical R&D, particularly to meet the health needs of developing countries;

(3) identify priority areas of needs-driven R&D;

(4) explore and promote a range of incentive schemes for health needs-driven R&D, addressing the delinking of the costs of R&D from the price of health products through, for example, the award of prizes that are designed to achieve the objective of delinking;

(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, with reference to the Declaration of Helsinki and other appropriate texts on ethical principles for medical research involving human subjects, including good clinical practice guidelines, and noting also that these ethical standards are in conflict with the ill-advised practice of granting exclusive rights in test data;

(7) enable medical researchers to build on 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;

(11) promote equitable access to new medical technologies so that all people share in the benefits of scientific advancement.

Possible elements of the Treaty would include:

(1) development of transparent and inclusive mechanisms and processes for facilitating health needs assessment, priority-setting and the assessment of funding needs;

(2) development of mechanisms for coordination of R&D actors, including developing appropriate networks, facilitating periodic assessments of R&D coordination, providing guidance to R&D efforts at national, regional and international levels, and advising on resource allocation following priority-setting;

(3) norms and mechanisms to ensure sufficient, regular, predictable and sustainable financing for R&D for types I, II and III diseases, with such financing primarily from government contributions based on a country's level of development, and managed by structures that are guided by the principles of transparency, inclusiveness (that stresses participation of developing countries in decision-making processes), equity and high governance standards; the financing of R&D should be for:

(a) R&D that results in quality health products that are accessible, affordable, acceptable and appropriate for the target populations;

(b) R&D incentive models that delink the cost of R&D from the price of the product and ensure that emerging R&D outcomes are available for promoting further research and facilitating generic competition, as well as affordable to those in need (Such models can be applied both across the range of current funding mechanisms such as grant funding and also to newer mechanisms such as prizes. These models must also ensure that outcomes and data generated from funded R&D are not monopolized but are available for follow-on research);

(c) the development and delivery of health products and medical devices to address the special health needs of developing countries, including the development of global health priority products such as antibiotics;

(d) all aspects of R&D, including basic health-related science and initiatives that facilitate wide dissemination of medical knowledge, such as open libraries for materials, open databases, open access medical publishing and other initiatives;

(e) conducting clinical trials associated with the development and independent evaluation of new health products with full disclosure of clinical trial data;

(f) initiatives that build and strengthen the local R&D capacity of developing countries;

(g) strengthening drug regulatory capacity regarding the safety and quality of medicines;

(4) measures to facilitate, encourage, and otherwise stimulate new incentives for R&D that are designed to delink R&D cost from high product prices to ensure that R&D outcomes are accessible and affordable, reward innovations that improve health outcomes (such as medical innovation inducement prizes and rewards to share access to knowledge, data, materials and technology) and do not rely on legal monopolies;

(5) norms for minimal levels of contributions to medical R&D from all Parties, considering factors such as each nation's level of development, size of economy and capacity to pay, through a variety of means, including taxes and contributions in kind;

(6) global norms to facilitate access to government-funded research;

(7) norms and measures regarding the transparency of global medical innovation, including but not limited to:

(a) standards for disclosure of information regarding clinical trials that are appropriate and beneficial, and regarding results and information on safety, quality and efficacy, in publicly and easily accessible registries;

(b) requirements for greater disclosure of the costs of R&D inputs, such as the costs of clinical trials;

(c) disclosure of prices and revenues of products in order to deepen analysis of the performance of mechanisms;

(d) standards for reporting and sharing of information on resource flows used to support R&D;

(e) where R&D outcomes are licensed, increased transparency on the terms and conditions of such licences;

(8) established and implemented norms for ethical standards for medical research as well as for clinical trials;

(9) measures and mechanisms to facilitate, encourage or otherwise stimulate local R&D capacity, including through the transfer of technology, particularly in developing countries;

(10) norms and mechanisms to ensure management of R&D outcomes and assets, including intellectual property rights, in a manner that promotes open sharing of knowledge, protects the public interest in access to knowledge and health-related innovation and ensures sufficient freedom to operate, and in a manner that meets the R&D needs of developing countries, protects public health and promotes access to health products.

(11) measures to overcome barriers and improve the availability of health products in the contexts in which they are needed, such as those relating to regulatory requirements, supply chain, health systems, and information;

(12) mechanisms to monitor and evaluate both the performance of R&D efforts and the implementation of the treaty, including appropriate reporting and amending systems (*1)*.

The Global Framework

The sponsors of the Global Framework highlight an urgent need for mechanisms for prioritization, coordination and sustainable financing of R&D, as well as for R&D models (push and pull mechanisms) that, inter alia, ensure availability of affordable treatments suitable for developing country conditions, promote further research and generic competition, and strengthen and build the R&D and production capacity of developing countries. Accordingly the sponsors call for a systematic and transparent global approach to R&D under the auspices of WHO.

The sponsors propose that the Global Framework should contain elements that provide predictable and sustainable financing, a dynamic R&D architecture and guiding principles that prioritize sharing of knowledge, access to affordable treatments, building of capacity in developing countries, and generic competition. The sponsors further elaborate on these elements.

On sustainable financing, the sponsors propose a fund:

- which would work to achieve collection of a specific amount of funds;
- where the primary source of financing would be from government contributions according to targets set to take account of countries' levels of development;
- where governments could generate their respective contributions by the use of mandatory levies on certain products and the use of tax-based systems, as nationally feasible;
- where government funding could be supplemented with other contributions such as donor funding.

The proposers note examples of successful levies and taxes of various kinds raised by developing country governments to finance health spending.

The sponsors further propose that a dynamic R&D architecture should guide and supervise the funding of R&D. It should engage in needs assessments and priority-setting, and should determine which activities and R&D are to be funded and which model of R&D, including incentives, should be the basis of the conduct of R&D. A summary description of these elements is as follows:

- **Needs assessment** aims to identify in a transparent and consultative manner at national, regional and international levels the health problems (and their determinants and severity), the availability of affordable and appropriate treatments, R&D gaps, and resources available for research.
- **Priority-setting** aims to improve the use of financial and human resources and to focus efforts on areas where needs are greatest and on products/technologies where R&D activity is too small or non-existent.
- **Funding R&D and determining an appropriate model, including incentives, for R&D,** means that the R&D architecture should engage in determining which R&D is to be funded, based on the needs assessment and priority-setting, and which model of R&D, including incentives, should be the basis of the conduct of R&D.

It is envisaged that the R&D architecture would make a call for proposals based on the R&D gaps identified, would evaluate applications and would fund the appropriate applicants on a step-wise basis.

Providing grants to conduct R&D is important for ensuring the participation of developing country entities. It is also important to explore other mechanisms that can facilitate R&D. For instance, there may be situations where a specific targeted technical challenge has been identified, and "prizes" may work either as a stand-alone mechanism or together with a grant. There could also be R&D gaps where collaborative research along the lines of an "open source" approach could be considered.

Different push and pull mechanisms can be used but these should be guided by the principle of delinking the cost of R&D from the price of the product and by other guiding principles elaborated below.

- **Scope of activities of the architecture:** It is envisaged that funding under the architecture will be provided for all aspects of R&D, including for conducting relevant clinical trials, building local research capacity in developing countries, and promoting transfer of technology to developing countries.
- **Intellectual property:** Under the R&D fund and architecture when funding is provided, the research outcomes should not be monopolized by the researcher/research entity through the use of intellectual property protection. The R&D architecture must allow others to build on the R&D outcomes that have emerged as a result of the efforts of the R&D fund and architecture.

- **Coordinating, monitoring and evaluating R&D:** A key objective would be to develop mechanisms to coordinate R&D efforts, including: developing appropriate networks; facilitating periodic assessments of these efforts; providing guidance and direction to these efforts at national, regional and international levels on the basis of knowledge and expertise generated in the needs assessment and priority-setting phase; and advising on appropriate priorities for resource allocation between R&D on different diseases and the balance between resources needed for R&D and delivery for each disease.

The architecture would develop mechanisms to monitor and evaluate R&D efforts generally including those undertaken with funds provided under the architecture as well as the impact of resources devoted to treatment and delivery.

The sponsors also propose guiding principles for R&D that should underpin the funding and architecture:

(1) The R&D fund and architecture must not be limited to Type III diseases but should also address other R&D gaps prevailing in developing countries. The fund and architecture should extend to R&D of medicines, diagnostic tools and medical devices.

(2) R&D efforts should be focused on the development of health products that are adapted to the needs of developing countries and patients of all ages, and that are simple (in terms of use, prescription and storage), accessible (in terms of availability and affordability), safe and of good quality.

(3) There must also be emphasis on strengthening regulatory capacity regarding the safety and quality of medicines and ethical standards of clinical trials in developing countries, as well as full disclosure of clinical trial data.

(4) Prices of products/technologies produced should be fixed on the basis that they are affordable to all who need those products/technologies, including in middle-income countries. Towards this end, push and pull mechanisms for the conduct of R&D should be designed to delink the cost of R&D from the price of the product.

(5) The R&D models should be designed to ensure that outcomes and data generated from R&D are not monopolized. The results of R&D should be widely disseminated to enable other researchers to engage in follow-on health research on condition that such follow-on R&D will also be readily accessible for others to build on.

(6) R&D models, including incentive mechanisms for the conduct of R&D, should be designed to ensure that, as a condition of receiving funding, the full ownership of research outcomes – including products and technologies emerging from R&D – will remain with the R&D fund and architecture in order to further promote research and generic competition.

(7) Activities should also aim to build and strengthen research and local capacity of developing countries. Where possible, such research and production should be undertaken in developing countries by the locals, or in collaboration with locals, in developing countries. For this purpose, effective measures to promote transfer of technology should also be set up.

(8) Where a product results from the genetic resource and/or associated knowledge of indigenous peoples and local communities the principles of prior informed consent and fair and equitable benefit-sharing should be adhered to at all stages of research, development and commercialization.

(9) High standards of governance and transparency are essential elements for the proper functioning of the R&D fund and architecture. For example, there should be transparency with regard to R&D funding provided and the R&D cost incurred.

(10) R&D fund and architecture should ensure sufficient and meaningful representation and participation of public and private institutions and researchers from developing countries. This includes providing developing countries with an equal voice in decision-making processes.

(11) Conflicts of interest must be disclosed and properly managed.

The sponsors argue that their proposal, as outlined above, offers a more comprehensive approach to R&D compared to other proposals. They are of the view that the proposed elements (i.e. the fund, the architecture and the guiding principles) could form components of an international framework instrument on R&D. Such an instrument could also additionally contain general norms/standards with regard to R&D and access that WHO Member States would have to follow and that would guide R&D initiatives such as:

- norms to facilitate access to government-funded research;
- norms/standards that promote transparency in global medical innovation, such as those that call for disclosure of the costs of the different stages of R&D and those that establish standards for reporting and sharing of information on resource flows used to support R&D;
- norms to facilitate and promote R&D incentives that delink prices from the cost of the product and that promote further research, generic competition and affordability;
- norms for monitoring and evaluating global R&D efforts, including implementation of the framework;
- ethical standards of clinical trials in developing countries as well as full disclosure of clinical trial data (*2*).

Public health impact

The Treaty

The sponsors of the Treaty say that their proposal would have a huge impact on public health, in that its aim is to create a new global framework for supporting priority medical R&D that is based on the equitable sharing of the costs of R&D and incentives to invest in needs-driven R&D.

The sponsors argue that the "international community needs an international legal framework to ensure (i) sustainable sources of financing for R&D focused on priority health needs, particularly the needs of developing countries and especially of the poorest or most vulnerable members of society, and (ii) an agreement that medical tools will be affordable and widely accessible to a global population of patients once they are developed".

"Our current system fails on both counts," the sponsors note, adding: "A binding international treaty that establishes a sustainable and predictable financing based on fair and equitable contributions from members could lead to increased total investment in R&D, advances in scientific progress, and a politically sustainable system for ensuring globally equitable access to health products. Guaranteeing fair contributions from all, and fair access to benefits for all, requires moving beyond an ad hoc system fuelled by donors and development aid.

The proposed treaty would provide the framework for ensuring that sufficient, regular, predictable and sustainable financing for R&D for types I, II and III diseases is secured; and that mechanisms to facilitate health needs assessment, priority-setting and the assessment of funding needs are developed and operationalized" (*1*).

The Global Framework

The sponsors of the Global Framework argue that its impact "is bound to be positive". They argue that the "proposal will put in place a comprehensive approach to the R&D problems of developing countries", adding that "the proposed solutions on financing should address financing issues, while the proposed R&D architecture as well as the guiding principles elaborated on address inter alia issues of affordability of R&D outcomes, building capacity of developing countries, IP management issues as well as delinking of R&D costs from the price of products" (*2*).

Overall, it is apparent that both approaches seek an international legal framework to improve public health by stimulating R&D more closely aligned to public health needs and by promoting access to the products of research.

Technical feasibility

The sponsors of the Treaty say that their proposal is for negotiations to be opened. The sponsors of the Global Framework also propose "the development of a framework instrument on R&D that addresses issues of financing, prioritization, conduct of R&D, coordination, monitoring and evaluation of R&D as well as that sets certain norms/standards in relation to R&D".

This would involve the facilitation of negotiations by WHO and active participation from Member States. Ultimately the content and scope of the international legal Framework on R&D would be decided in the process of these negotiations. The feasibility of negotiations will depend on the willingness of WHO Member States to embark on them. The feasibility of the outcome of any negotiations will depend on the form they will take (*1*).

Financial feasibility

The sponsors of the Treaty propose financing primarily from government contributions based on a country's level of development and managed by structures that are guided by the principles of transparency, inclusiveness that stresses participation of developing countries in decision-making processes, equity and high governance standards.

The sponsors say that the "financial feasibility of establishing the Treaty would have to be considered once negotiations on the shape and form of the Treaty had taken place. However, the establishment of such a Treaty must be seen in light of the WHO's mandate as outlined in its constitution, which states that in order to achieve its objectives, the functions of the Organization shall be:…(k) to propose conventions, agreements and regulations, and make recommendations with respect to international health matters and to perform such duties as may be assigned thereby to the Organization and are consistent with its objective" (*1*).

The sponsors of the Global Framework argue that the proposal is financially feasible as it proposes a fund and envisages financing to be obtained primarily from government contributions, with governments that are unable to contribute the amount putting in place certain levies to generate their contributions. The sponsors also envisage that the fund will receive supplementary financing from other sources.

It is proposed that the operation and implementation of the international legal Framework on R&D be funded through a fund financed primarily through government contributions, determined according to countries' levels of development. It is also being proposed that governments could meet the target of their contributions through various levies. It is further proposed that the fund could receive supplementary financing from other sources and that the fund be managed by structures that are guided by the principles of transparency, inclusiveness that stresses participation of developing countries in decision-making processes, equity and high governance standards.

Overall, because the scheme has not yet been precisely defined, or its potential impact modelled, it is not possible to say anything very meaningful about its financial feasibility.

Implementation Feasibility

A key step would be to get the agreement of governments actively to pursue negotiations on this proposal with a view to its eventual implementation. Table 1 provides a summary assessment of the proposal.

Table 1. CEWG summary assessment of the Global Framework on Research and Development

Criterion	Comment
Public health impact	Could be large if implementation successful.
Efficiency/cost-effectiveness	Difficult to assess.
Technical feasibility	Depends on willingness of WHO Members States to negotiate, and the shape of any final agreement.
Financial feasibility	Direct costs difficult to assess without final proposal.
Intellectual property	Aim is to remedy defects in IP system that might inhibit innovation or access.
Delinking	Basic principle is to incorporate delinking as integral feature of R&D financing.
Access	Promoting access is a guiding principle.
Governance and accountability	Governance principles are espoused, including transparency and inclusiveness.
Capacity-building	Capacity-building and technology transfer are emphasized in both proposals.

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Removal of data exclusivity

Source: EWG Annex 2.

Relevant submissions to CEWG

None.

Other relevant submissions

None.

Proposal description

Laws relating to data exclusivity exist in some countries. As an example, in the USA it means that, for a period of five years from the date when an originator non-biological product is approved for marketing, no other company may seek regulatory approval of an equivalent product on the basis of data submitted by the originator company without the latter's approval. During the period of exclusivity, drug regulators cannot use (rely on) the originator's data to approve a generic product, even if the product is demonstrated to be exactly equivalent in chemical composition and in its behaviour within the body. Some other countries have similar rules, although these may vary in the period during which they provide exclusivity and in other details. For example, the European Union has a longer period (between 8 and 11 years) and many developing countries have not adopted the practice. For instance, this is not the case in India (*1*).

Thus the effect of data exclusivity is to prevent, for a period of time, the entry of generic competition. This applies even if the originator product is not protected by a valid patent. Some argue that it is an additional incentive to undertake research, including for medical products where patent protection cannot, for one reason or another, be obtained. Pharmaceutical companies, and some developed country governments, are active lobbyists for the introduction of data exclusivity in developing

countries which do not have such regimes. Its introduction is a standard demand in free trade agreements between developed and developing countries. Others argue that data exclusivity constitutes an unnecessary additional barrier to generic competition and thus causes prices of products to be higher than they otherwise would be.

The TRIPS agreement imposes on WTO member governments an obligation to protect data relating to new chemical entities against unfair commercial use. In addition, they should protect such data against disclosure, except where necessary to protect the public or unless steps are taken to ensure that the data are protected against unfair commercial use. Some take this to mean that this requires countries to adopt a data exclusivity regime for a specified time period. They argue that data exclusivity encourages the development of new medicines. On these grounds, a recent industry-funded article in *Health Affairs* argued that data exclusivity should be extended to 12 years in the USA, consistent with the period that has recently been introduced there for biological drugs (which, it is argued, cannot easily be protected by patents) (*2*).

Others consider that TRIPS only requires data protection under the discipline of unfair competition (which is not based on, nor requires, exclusive rights) and that, if exclusivity was intended, the TRIPS agreement would have specified it (as it does in other areas of IP) and would have determined a time period during which regulatory authorities could not rely on data provided by the originator company to approve a generic competitor. For instance, this was included in the 1992 North American Free Trade Agreement but was not repeated in the 1994 TRIPS agreement (*1*,*3*). They argue that there is no evidence on the impact of data exclusivity in terms of promoting the development of new medicines, particularly in developing countries and for medicines needed in those countries, and that its implementation reduces access to medicines without benefits from a public health perspective.

Public health impact

The removal of data exclusivity could result in the reduction of prices and potentially greater availability of products that would otherwise have been under exclusivity.

In many developed countries the evidence suggests that there are relatively few cases where data exclusivity protects a product which is not patented. This is because in the majority of cases the data exclusivity period expires before the patent. Thus, the material effect of data exclusivity may be relatively limited both on prices and on innovation (*1*).

However, in developing countries, although the evidence is relatively limited, it is likely that there are many more products not protected by patents than in developed countries. This is partly because markets are small and, in many cases, companies may not consider it worth the cost of filing and then maintaining patents. In other countries which have relatively recently introduced a patent regime in accordance with the TRIPS agreement, there are a number of chemical entities that are not protected by a patent (but are elsewhere) but would be subject to data exclusivity if the rules existed (*1*). Evidence from Jordan suggests that companies often rely on data exclusivity introduced as a result of the USA-Jordan free trade agreement in 2001 rather than on patent protection, and that its implementation has led to a significant increase in the price of medicines (*4*). The advantage of data exclusivity for companies is that it is automatic, costs nothing and cannot be challenged in court as patents can be. It can also be a barrier to compulsory licensing (*1*).

In those circumstances there may well be considerable potential public health benefits from the removal of data exclusivity legislation, or by not introducing it. What circumstances these might be would very much depend on the country situation, as is evident from the above.

Technical feasibility

Because data exclusivity exists in many countries and not in many others its removal must be regarded as technically feasible. In cases where data exclusivity is provided for not only in the national law but in a binding international agreement, the review or renegotiation of such an agreement would be required.

Financial feasibility

Removing data exclusivity has virtually no cost in administrative terms, and saves the relatively small costs associated with a data exclusivity regime. By the same token it can result in savings to governments and patients to the extent that product prices are lower than they otherwise would be.

Implementation feasibility

Governments are free to change data exclusivity in ways that are consistent with their international obligations. Subject to the possible need for review or negotiation of any international agreement, the actual process of implementation would be relatively straightforward. Table 2 provides a summary assessment of the proposal.

Table 2. CEWG summary assessment of the removal of data exclusivity

Criterion	Comment
Public health impact	Potentially significant improved access to existing medicines where data exclusivity is the only exclusivity mechanism for a particular medicine.
Efficiency/cost-effectiveness	The removal of data exclusivity is low-cost, whereas renegotiating any existing international agreements may have high costs.
Technical feasibility	Easy to establish or remove, subject to renegotiating international agreements.
Financial feasibility	Potentially significant indirect cost savings in that public health authorities and patients may pay reduced prices for existing medicines.
Intellectual property	Removal promotes generic competition.
Delinking	Potentially reduces exclusivity period.
Access	Removal promotes generic competition and lower prices.
Governance and accountability	Not applicable (rules-based system).
Capacity building	Facilitates generic entry and helps build capacity by widening opportunities.

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Direct grants to companies

(EWG: Direct grants to small companies and for trials in developing countries)

Source: *EWG Five proposals relating to funding allocation.*

Relevant submissions to CEWG

New investment strategy: innovative developing country research awards: Global Forum for Health Research.

A new incentive system for technological innovation in developing countries: Miguel A Maito, Eduardo Franciosi.

Other relevant submissions

EWG submission. *Concept note. Innovative financing mechanism for global health innovation*. Charles W. Wessner, US National Academies of Science, with support from the Global Forum for Health Research.

Proposal description

Many countries have schemes, not necessarily focused on public health, which provide grant funds to small and medium enterprises (SMEs). These schemes are based on the premise that such enterprises find it difficult to raise funds on the capital markets (e.g. from banks or venture capitalists), even for worthwhile projects. Such schemes may, for instance, provide seed funding sufficient to bring a potential new medicine through Phase I trials, at which stage it may be possible to attract commercial funding in one form or another.

Examples of such schemes include the United States Small Business Innovation Research Initiative (SBIR). In respect of health, 2.5% of the extramural budget of the National Institutes of Health (NIH) is set aside to provide grants for small companies to conduct innovative research or R&D that has the potential for commercialization and public benefit. Small grants may be provided initially for feasibility studies (Phase I) and larger follow-up grants (US$ 0.5–1 million) may be provided subsequently (Phase II). Other schemes of a similar nature operate in several developed countries and in a few developing countries (e.g. India). (*1*)

The Wellcome Trust in the United Kingdom has begun implementing a £45 million project with the Indian Department of Biotechnology. Each side provides £22.5 million. The R&D for Affordable Healthcare initiative will support R&D projects aimed at delivering safe and effective health care products on a large scale at affordable costs. The aim is to bring together researchers from both the public and private sectors, largely working in India, to develop innovative new devices, diagnostics, medicines and vaccines that will reach the greatest numbers of beneficiaries without compromising on quality. (*2*)

The International AIDS Vaccine Initiative (IAVI) established a US$ 3 million fund aimed at biotech companies to pursue possible breakthroughs in the search for an AIDS vaccine. (*3*)

Two related proposals have been submitted to the CEWG:

- The first, on the lines of the SBIR, has been submitted by the Global Forum for Health Research for an international pilot project at a cost of US$ 30 million over five years to fund SMEs in "innovative" developing countries. (*1*)
- The second makes a proposal for a new innovation fund scheme to be run from local contributions from government, industry and other potential sources. A feature of this proposal is that products developed with its funding would be non-exclusively licensed with royalties payable to the fund. (*4*)

In addition, the EWG identified a need to provide funds for large-scale clinical trials by companies for products destined for developing countries, which might not otherwise take place. For instance, in 2005 the Bill & Melinda Gates Foundation provided over US$ 100 million to the Malaria Vaccine Initiative to help fund the cost of trials being undertaken in conjunction with GlaxoSmithKline (GSK). (*5*) The European and Developing Countries Clinical Trials Partnership (EDCTP) was created in 2003 "to accelerate the development of new or improved drugs, vaccines, microbicides and diagnostics against HIV/AIDS, malaria and tuberculosis, with a focus on phase II and III clinical trials in sub-Saharan Africa". (*6*) The proposals considered here are designed for earlier stages of R&D. Financing of later stages of R&D is considered elsewhere (see, for instance, pooled funding proposals).

Public health impact

The potential public health impact of SBIR-type schemes would depend on how they are formulated (e.g. they could specify disease areas, priority health needs and/or affordability criteria), the extent to which they stimulate new product development, and the extent to which there are reliable plans to promote access to new products in developing countries. Because some of these schemes (such as SBIR) are aimed at an early stage in the R&D process, the prospects of success are difficult to determine. On the other hand, the evidence from the United States SBIR scheme suggests that 60% of projects eventually reach the market, and that the award enabled nearly 80% of grantees to raise additional capital subsequently. (*1*) The Innovation Fund has delinking as a condition of funding, which could help to promote access.

Technical feasibility

Schemes such as the SBIR are tried and tested. There are no particular concerns regarding their implementability but they require administrative and technical capacity to make grants and monitor results.

Financial feasibility

Such schemes can be large or small. Schemes such as those proposed seem entirely financially feasible provided there are willing funders and an apex organization willing to run the scheme.

Implementation feasibility

There is a need to identify potential funders and implementers. Table 3 provides a summary assessment of the proposal.

Table 3. CEWG summary assessment of direct grants to companies

Criterion	Comment
Public health impact	Dependent on funding and implementation.
Efficiency/cost-effectiveness	Depends on scheme configuration. Grant-giving, particularly to SMEs, necessarily involves financial and transaction costs.
Technical feasibility	Schemes of this kind are common in developed and developing countries.
Financial feasibility	Can be large or small.
Intellectual property	Depends on scheme conditions.
Delinking	Depends on scheme conditions; possible in the case of the Innovation Fund.
Access	Depends on scheme conditions but no mechanism is proposed.
Governance and accountability	Need to be defined for each scheme.
Capacity-building	Could be designed to promote technology transfer and capacity-building.

References

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Green intellectual property

Source: EWG Annex 2.

Relevant submissions to CEWG

International Fund for Innovation (IFI): an innovative financing mechanism for medicines in the developing world. Green Intellectual Property, Itaru Nitta.

Other relevant submissions

EWG submission. *Patent insurance (Green Intellectual Property) scheme: a financial prescription for neglected diseases?* Itaru Nitta.

CIPIH submission. *Patents and essential medicines: an application of the Green Intellectual Property project.* Itaru Nitta.

Proposal description

The International Fund (previously Bank) for Innovation (IFI) proposes to create a substantive and sustainable fund both to finance unimpeded access to "indispensable" medicines in developing countries and to foster research to combat diseases that the people of those countries are suffering from. IFI would have three sources of funding: a "patent assurance premium", an allocation from the revenue of patent offices, and a 10% premium on the overseas income of patent-holders. In the form of the premium, IFI would impose a nominal levy on patent applicants and patentees, and would make a new allocation from fees currently collected for granting patents. It is estimated that these sources could generate annual revenue of over US$ 8.7 billion on a sustainable basis. The rationale seems to be that funds generated though an additional charge on patent-holders or applicants can be used, through the IFI, to mitigate possible adverse effects of the patent system on access to medicines or to stimulate innovation relevant to developing countries where the market provides inadequate incentives for innovation *(1)*.

Public health impact

There is no explicit assessment of the potential public health impact of this proposal. Examples are provided of cases where the IFI would pay a licence fee for a government which might otherwise resort to compulsory licensing, or subsidize the import of a patented medicine in countries without

manufacturing capacity. Alternatively IFI assistance might be provided to finance R&D institutions working on neglected diseases (*1*).

Technical feasibility

The proposal suggests a number of options for housing the IFI, including the World Bank, the World Trade Organization (WTO) and the World Intellectual Property Organization (WIPO). The preference is for the WTO and for some connection with the WTO's Dispute Settlement Mechanism (DSM) such that a request for funds from the IFI could be adjudicated by a modified DSM process. Moreover, the IFI would be supervised by the TRIPS Council, and it is suggested that the IFI should be established through an amendment to the TRIPS agreement (*2)*.

The technical feasibility of this scheme has not been established. The institutional structure proposed is complex. It is not clear that the IFI concept is compatible with the mandate and functions of the WTO and its various organs and mechanisms.

Financial feasibility

The proposal is for a premium of US$ 100 to be charged to patent applicants and grantees in developed countries and in emerging economies. It is not clarified if this means that US$ 200 would be charged in total when a patent is granted. The author estimates that this could raise US$ 88 million per annum. In addition he suggests that 10% of WIPO's income from the Patent Cooperation Treaty (about US$ 40 million) could be allocated to the IFI. Finally 10% of the overseas income of patent owners would be devoted to the fund.

Its achievement would depend on convincing decision-makers that the costs to patent owners (or WIPO) are justified by the likely benefits of the scheme. It is not clarified why or how 10% of overseas income of patent owners would be collected (*1*).

Implementation feasibility

A key first step would be to discuss the feasibility of this scheme with the international institutions envisaged to be involved and with other health and academic experts. Table 4 provides a summary assessment of the proposal.

Table 4. CEWG summary assessment of green intellectual property

Criterion	Comment
Public health impact	Not demonstrated.
Efficiency/cost-effectiveness	High transaction costs.
Technical feasibility	Feasibility not tested with stakeholders.
Financial feasibility	US$ 8.7 billion is very expensive.
Intellectual property	Impact not clear.
Delinking	Not addressed.
Access	Not addressed.
Governance and accountability	Very complex governance structure proposed.
Capacity-building	Not addressed.

References

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Health Impact Fund

Source: *EWG Five promising proposals*.

Relevant submissions to CEWG

Heath Impact Fund. Submitted by Incentives for Global Health.

Other relevant submissions

EWG submission. *The Health Impact Fund: pay-for-performance.*

Proposal description

The proposed Health Impact Fund (HIF) is a new way of paying for pharmaceutical innovation. All pharmaceutical firms worldwide would have the option of registering new medicines with the HIF. By registering, a firm agrees to provide its medicine at a price near the cost of production anywhere it is needed. In exchange, the company will be paid by the HIF annually for 10 years based on the fund's assessment of the actual global health impact of the medicine as a proportion of the global health impact achieved by all products registered with the HIF.

The sponsors of the HIF say it is designed to bridge an access-to-medicine gap created by the current system of medical R&D. Pharmaceutical companies traditionally recoup their investments on R&D by charging high prices for their medicines, facilitated by the exclusivity offered by intellectual property rules. Companies therefore have incentives to focus on drugs that sell, rather than on medicines that have the largest health impact. The current system thus fails in terms of medicines for diseases that mainly affect developing countries where market prospects are poor and uncertain.

For medicines to be widely accessible, prices need to be low, but low prices do not encourage innovation. The HIF is designed to provide long-term stable incentives to solve this problem. By paying for assessed health impact, the HIF will create a new stream of funding for research that is not currently financially feasible. In addition, the HIF gives firms incentives to ensure that medicines actually reach, and are correctly used by, the patients who need them.

Firms would register with the HIF if they thought the returns with the HIF would be higher than those expected with intellectual property protection. It would thus be especially attractive for products with high therapeutic potential but low expected commercial value, including for "neglected" diseases. The sponsors see the system as self-regulating in that rewards will be high if few firms register but this will then attract other firms and drive down the rewards. If the rewards become too low the reverse process would occur.

It is proposed that governments and other donors would finance the HIF. The proposal estimates an initial annual budget of US$ 6 billion, which is justified by the goal of enabling the HIF to maintain a reasonable portfolio of 20 medicines at a time. This portfolio implies that on average two new medicines are registered each year. With 20 medicines being rewarded at any given time, a HIF with US$ 6 billion annually would have USD$ 300 million available per medicine per year.

It is anticipated that the HIF will be governed principally by its funding governments, with some additional expertise from WHO or NGOs with field experience. The HIF board will need to make decisions on HIF payments on the basis of recommendations from the assessment branch of the HIF (*1*).

Public health impact

The proposal is based on the premise that companies which register products with the HIF will be paid in proportion to the incremental public health impact that the product has when used.

The standard measure of health impact is the quality-adjusted life year, or QALY. A drug that extends a person's life by 10 healthy years would be recognized as having created 10 QALYs. Assessing QALYs is difficult, and it will take a great deal of data to be able to make credible evaluations. The assessment process involves obtaining evidence on the incremental effect on health of the average consumer of the registered drug. When the registered drug simply displaces some existing medicine, the analysis is relatively straightforward. But typically a medicine's QALY impact would be more complex, arising from an improved therapeutic profile, from increased use due to a lower price, and from more effective use due to better prescription and patient instruction practices.

The assessments will start from information that is commonly available about medicines today. In addition, firms registered with the HIF would be required to provide information about their sales directly to the fund and would inform their distributors and this requirement. At the same time, the registrant would have a strong incentive to provide comparative data on its product's effectiveness in relation to others, since this would serve as evidence for payments from the HIF.

The sponsors are currently developing the health impact assessment methodology with a multidisciplinary team of experts. They recognize that there is no perfect metric for health or disease and no perfect algorithm for health impact assessment, and that any such assessment will inevitably rely on imperfect data. The sponsors say, however, that perfection is not the relevant standard. What matters, they say, is that pharmaceutical firms should have strong new incentives to deliver health improvements (and no strong new incentives to try to capture HIF rewards without health impact). The HIF assessment must be sound enough so that the best strategy for firms to capture HIF rewards is to deliver health improvements. The sponsors say that with a substantial investment in data collection and analysis, much larger than that of any national health system to date, the HIF would be in a position to make its assessments sufficiently consistent and reliable to ensure that payments are allocated fairly between registrants on the basis of health impact, and would thus provide meaningful incentives to innovators to develop products with large health impact (*1*).

Technical feasibility

The technical feasibility of the proposal rests on developing a practical and reliable method of determining health impact (on which depend the payments due to companies). It is proposed to base the measurement of health impact on QALYs, which is a methodology used in several countries (such as the United Kingdom) to value the health benefits of medical technologies. The challenge is to develop a credible and effective system for collection of the data that are needed to estimate incremental health benefits. This requires information not just on sales but also on the impact of medicines as used in developing countries. The HIF therefore envisages a very wide-ranging assessment mechanism which it estimates would cost US$ 600 million per year.

Part of this money would be allocated to evaluating clinical evidence. Current estimates of the cost of *head-to-head* studies can range in price from approximately US$ 2.5 million for relatively small studies to US$ 20 million for large studies. *Observational studies* range in cost from US$ 1.5 million to US$ 4 million. The HIF would require observational studies in different settings, so this could be quite costly. *Systematic reviews* of evidence tend to cost up to around US$ 0.3 million. The HIF would also require a substantial *auditing* function to ensure that the products are being distributed and used in ways consistent with the findings of the observational studies. Finally, there would be a significant *overhead* component related to obtaining the functions of the technical branch and other operational branches, which could be shared across products. Systems would also need to be put in place to monitor sales and to check that figures provided by companies were not overinflated. Thus, the sponsors say that "the HIF should require extensive reporting of sales volumes to it directly from wholesalers, with evidence from wholesalers on which retailers purchased the medicines" (*1*).

Overall the HIF "would be by far the largest health assessment agency in the world". The sponsors argue that, apart from providing information required by the HIF, such analysis would also be a public good in its own right (*1*).

There are two main interrelated questions raised by critics. First, even with a very costly assessment infrastructure that reaches down to the level of retailers and patients in developing countries, would it be possible to collect credible and reliable data on which payments can be based? Second, even assuming perfect data, would it be possible to isolate the independent impact of a medicine as distinct from the impacts of other concurrent health interventions? For instance, in one country there might be simultaneous use of bednets and other kinds of malaria treatment. The question would be asked as to how much of a measured improvement in health status could be attributed to one particular medicine (*2*).

Further details of the sponsors' ideas on technical feasibility are provided in their submission to the CEWG (*3*).

Other critics have suggested that the open licensing of products registered with the HIF would be a better way of ensuring that selling prices are as near to the cost of production as possible by encouraging competition between generic suppliers and brand owners (*4*).

Financial feasibility

The proposal requires annual financing by governments and other donors of about US$ 6 billion, estimated to be sufficient to maintain a portfolio of about 20 medicines.

As a comparison, it should be noted that in 2010 total development assistance for health was estimated to be US$ 26.9 billion in 2008 dollars (*5*). In 2011 the total global pharmaceutical market was estimated at US$ 880 billion (*6*).

Implementation feasibility

A key first step would be to develop a plan for the assessment of health impact that companies would find credible enough to indicate that they would be likely to use the system and would find it an attractive incentive. A second key step would be to convince governments that an annual cost of US$ 6 billion, including a large assessment organization, is worth paying in relation to the benefits. Table 5 provides a summary assessment of the proposal.

Table 5. CEWG summary assessment of the Health Impact Fund

Criterion	Comment
Public health impact	Potentially significant if registration of products with the fund is significant.
Efficiency/cost-effectiveness	The assessment apparatus represents 10% of proposed cost.
Technical feasibility	Reliable health impact assessment, on which success depends, is very challenging.
Financial feasibility	The direct costs of the proposal at US$ 6 billion are high.
Intellectual property	Allows voluntary partial relinquishment of some patent rights in exchange for reward payments.
Delinking	Fundamental principle based on delinking.
Access	Provides incentive for better access as reward is related to incremental health outcomes.
Governance and accountability	Governance arrangements unclear.
Capacity-building	No direct impact.

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Orphan drug legislation

Source: EWG Five promising proposals.

Relevant submissions to CEWG

None.

Other relevant submissions

None.

Proposal description

Orphan drug legislation already exists in Australia, Japan, the USA and the European Union. The proposal here describes mainly the scheme in the USA and draws comparisons as necessary.

An orphan drug scheme is a scheme designed to promote the development of products to tackle a rare disease on the premise that industry would have insufficient incentive to do so without special help. In the USA a rare disease is defined as one that affects fewer than 200 000 people. The law provides seven-year marketing exclusivity to sponsors of approved orphan products for the specific indication, a tax credit of 50% of the cost of conducting human clinical testing, and research grants for clinical testing of new therapies to treat orphan diseases.

The European Union scheme is similar but offers 10 years of market exclusivity.

Beyond the guarantee of market exclusivity, orphan drug legislation often includes an element of lowering statistical requirements for registration (e.g. sample sizes) because large trials are impossible for most rare diseases.

To date the USA's legislation has resulted in more than 2250 orphan drug designations, 361 of which have culminated in full marketing approval. In 2009, orphan drugs constituted 38% of the 29 new therapies that the United States Food and Drug Administration (FDA) approved for marketing (*1*).

Although orphan drug schemes aim to incentivise treatments for rare diseases in developed countries, they are potentially relevant to diseases that are rare in developed countries but prevalent in developing countries (e.g. tuberculosis).

Modifications to existing schemes in developed countries might enhance their impact in respect of developing country diseases. Alternatively, similar measures might be taken by developing country governments to provide additional stimulation to innovation relevant to their own disease profiles.

Public health impact

The general conclusion of recent reviews of orphan drug legislation in the USA is that it has been successful in stimulating R&D and making available new products or new indications for existing products, which would not otherwise have been developed, to treat rare diseases *(2)*. On the other hand these schemes have not materially helped to spur the development of treatments for diseases that mainly affect developing countries and are very rare in developed countries. The impact of orphan drug schemes on public health in developing countries has been extremely limited (*3*,*4*,*5*,*6*).

In the USA there has been a public health impact in the sense that more treatments are now available and used for rare diseases, but this is achieved at a cost to the patient, the insurer and/or the government. The price of orphan drugs – which include, for instance, many new cancer treatments – reflects their market exclusivity, which is why the market exclusivity is regarded by companies as the most effective incentive in the orphan drug package. Developed countries are better placed to afford the cost of such incentives, although in every country health-care costs are under extreme scrutiny.

On the other hand, in both the USA and the European Union there are examples of compounds which were previously available cheaply but subsequently have received orphan drug approval for a particular indication and their price is then raised. Thus there is scope for companies to game the system in ways that do not conform to the objectives of the legislation *(7*,*8*).

While orphan drugs need to meet FDA criteria for marketing approval, they are by their nature likely to have been tested in much smaller populations than drugs for "major" illnesses (*3*). Typically orphan drugs may also include treatments at the cutting edge (e.g. for rare cancers) which will be eligible for accelerated or fast-track approval by the FDA – i.e. with less regulatory oversight justified by the potential benefits of early introduction. Thus the nature of orphan drugs may make them more susceptible to the post-marketing discovery of side-effects than is the case with other treatments. Where an orphan drug is addressing a disease affecting millions of people in developing countries rather than thousands in developed countries, the regulatory authorities would need to take account of this in approving the drug for marketing.

Technical feasibility

An orphan drug scheme is technically feasible in developed countries and has been implemented in several of them. The issue is whether a scheme of this nature that would incentivize R&D relevant to the needs of developing countries would be technically feasible.

Most of the literature suggests that the key deficiency is the absence of an effective "pull" mechanism because the demand in the developed country for the product is small or non-existent. Thus most analysts suggest that, although there are various improvements one could make to these schemes, their impact could be substantially transformed only by linking them to another "pull" mechanism such as a priority review voucher, a transferrable intellectual property right or a prize fund (*3*,*4*,*5*). In view of this, the technical feasibility of the scheme will largely depend on the technical feasibility of the pull mechanism to which it is linked.

As regards improvements to existing schemes, suggestions include:

- explicitly including diseases that mainly affect developing countries in eligibility criteria, or products directed at the needs of developing countries in relation to Type I diseases;
- ensuring that overseas trials are eligible for grants or tax breaks;
- harmonizing developed country schemes and/or reciprocal approval arrangements;

– ensuring that regulatory approval criteria are appropriate to developing countries.

It is not clear how orphan schemes could be adapted for use by developing countries to meet their own needs. Their main priority is likely to be for diseases that are not "orphan" in their own countries. The schemes' feasibility would thus depend on the circumstances and needs of different developing countries. However, such schemes would not help to provide a "pull" factor – the distinguishing feature of which in the developed world is market exclusivity linked to a market with an ability to pay often very high prices.

Financial feasibility

Orphan drug schemes are relatively cheap for governments to implement in terms of outlays on administering the scheme which relies on adding functions to an existing organization – the regulatory authority. On the other hand the cost of grants under the scheme and tax credits may be significant. However, the heaviest cost will be borne by the purchasers of medicines as a result of the exclusivity granted and/or the cost of the complementary pull mechanism designed to stimulate R&D relevant to developing countries.

Implementation feasibility

One key step would be for those countries with orphan drug schemes to consult on moves they could take, preferably in harmony, to increase incentives for R&D on products to meet the needs of developing countries. Table 6 provides a summary assessment of the proposal.

Table 6. CEWG summary assessment of orphan drug legislation

Criterion	Comment
Public health impact	No real impact demonstrated in developing countries.
Efficiency/ cost-effectiveness	Only assessable if impact generated.
Technical feasibility	Demonstrated in developed countries; unclear relevance to developing countries.
Financial feasibility	Low direct costs but market exclusivity potentially very costly to purchasers.
Intellectual property	Imposes new exclusivity rights, and existing rights to patentability in developing countries unaffected.
Delinking	If anything, has opposite effect.
Access	No impact.
Governance and accountability	Rules-based governance according to legislation.
Capacity-building	No impact.

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Patent pools

(EWG: Patent pools (UNITAID model))

Source: *EWG Five promising proposals.*

Relevant submissions to CEWG

UNITAID.

Other relevant submissions

None.

Proposal description

The EWG considered patent pools (UNITAID model) as a promising low-cost approach, which scored well on efficiency, feasibility and on potential public health impact. The EWG highly recommended this model for further exploration in terms of its adaptability to other disease areas.

The "UNITAID model" is essentially a "downstream" pool which deals with patents related to products for the treatment of HIV/AIDS. Traditionally patent pools have more often been related to "upstream" research as a means of facilitating product development, particularly where different entities own large numbers of patents that need to be utilized in the research process.

This assessment reviews the evidence on one downstream initiative which is now being implemented by the Medicines Patent Pool Foundation (MPP). It also reviews the evidence on an upstream initiative, the Pool for Open Innovation (POI), established by GlaxoSmithKline (GSK) and now managed by BIO Ventures for Global Health. In addition, the World Intellectual Property Organization (WIPO) has recently launched another upstream initiative called Re:Search.

Medicines Patent Pool

Over six million people in developing countries receive antiretroviral treatment today, up from a few thousand a decade ago. A further 10 million people need medicines now but do not have access to them. Recent research has shown that earlier treatment can also protect the partners of people living with HIV, reducing the likelihood of transmission by as much as 96% (*1,2*).

The latest WHO guidelines for the treatment of HIV recommend newer, safer, and more effective medicines (*3*). However, a changing intellectual property climate over the past few years means that many of these newer medicines are, or will be, patented in potential manufacturing and consuming countries and priced out of reach of people living in developing countries. Many people already on first-line treatment will need second- and third-line therapies where current prices are a multiple of first-line treatments.

Many needed fixed-dose combinations (FDCs) are not being developed by the current patent-holders and those interested in conducting R&D do not have access to the patents needed to do so. The component medicines included in FDCs are nearly always owned by several different patent-holders. Negotiating for all the needed licences carries high transaction costs and uncertainty, both of which can represent significant barriers to innovation and the development of FDCs.

Other technologies oriented to the needs of developing countries – such as paediatric or heat-stable formulations – face similar problems. While the medicines exist, the adapted formulations are not being made, and lack of licences is one of the barriers that prevent product developers from making them.

The Medicines Patent Pool (MPP), established with the support of UNITAID in July 2010, aims to stimulate needed R&D on HIV treatments that are specifically geared to the needs of developing countries – such as paediatric or heat-stable formulations, or FDCs – as well as to increase access to existing, but currently unaffordable, treatments. The MPP does this through the negotiation of public-health oriented patent licences on critical HIV medicines (*4*).

In the last decade generic competition was instrumental in causing a precipitous drop in the cost of antiretrovirals – as much as 99% – and allowed for unprecedented access to medicines (*5*). It was possible for this competition to occur because India's patent law at that time allowed the production of key medicines although they were patented elsewhere. Now, with changes in Indian patent law in line with the TRIPS agreement, this kind of competition and resultant price reduction is no longer possible with new treatments unless widespread licensing is available or intellectual property obstacles are otherwise overcome. Easier access to needed patents, facilitated by the MPP, will allow potential generic manufacturers to enter the market more easily, thus stimulating competition with potentially large price reductions based on the experience with existing antiretrovirals.

Easier access to needed patents also facilitates the development of FDCs and can open the door to new formulations for children and help meet the particular treatment needs in developing countries. It can also eliminate the need for product developers to undertake uncertain and often costly negotiations with several patent-holders in order to obtain all the necessary intellectual property rights. The MPP, therefore, could play a key role in enhancing access to, and promoting innovation in, HIV medicines needed in resource-poor settings.

The MPP works through voluntary negotiations with patent-holders on the terms on which they will license their patents to the pool. Such negotiations will typically cover the geographical scope of the pool, royalty payments and the detailed terms of the licence agreement. Once licensed to the pool, generic manufacturers may take out licences from the pool allowing them (subject to any special restrictions that may have been negotiated) to manufacture and sell licensed products within the geographical area covered by the licence agreement with the originator. Similarly, they may develop new combinations or other improvements that suit the needs of developing countries.

To date the MPP has signed licence agreements with the United States National Institutes of Health concerning its patents on darunavir and with Gilead Sciences for its patents on four antiretrovirals. It has also reached sublicense agreements with three generic companies – Aurobindo, Medchem and Emcure.

Pool for Open Innovation

The Pool for Open Innovation (POI) seeks to motivate innovative and efficient drug discovery and development by opening access to intellectual property or know-how in neglected tropical disease research. It seeks to make the patents and, at the discretion of a pool contributor, know-how of companies and organizations more widely available for the development of therapeutics for neglected tropical diseases (NTDs). It is based on the premise that there are no or few commercial returns for NTD therapies but that the social returns will be enormous. Therefore, the main objective of the POI is to incentivize research into NTDs by making patents and know-how more widely available, on terms that facilitate the development of new therapeutics, and to make the process efficient and effective. Its scope is limited to therapeutics to treat the 16 NTDs in humans (as defined by the United States Food

and Drug Administration). Any products developed would be sold free of royalties in least developed countries. There are currently more than 2300 patents in the POI. Apart from GSK, contributors of intellectual property to the POI include Alnylam, Massachusetts Institute of Technology, University of California, Caltech and Stanford University. There have been no licences awarded from the POI to date (*6*).

WIPO Re:Search

WIPO Re:Search is a new consortium through which public-sector and private-sector organizations around the world are making intellectual property available to qualified researchers anywhere in the world who are seeking to develop new solutions for NTDs, malaria and tuberculosis. These include:

- compounds;
- compound libraries;
- unpublished scientific results;
- regulatory data and dossiers;
- screening technologies;
- platform technologies;
- expertise and know-how;
- patents and patent rights.

Services such as access to company research facilities are also offered through WIPO Re:Search. Licences will be royalty-free for product distribution in least developed countries.

To support the use of the resources made available in WIPO Re:Search, BIO Ventures for Global Health serves as the nonprofit administrator of the partnership hub. The responsibility of BIO Ventures for Global Health is to reach out to potential users and licensees of WIPO Re:Search resources to ensure that all assets are being used as productively as possible.

WIPO Re:Search is supported by a wide range of organizations including Alnylam, AstraZeneca, California Institute of Technology, Center for World Health and Medicine, the Drugs for Neglected Diseases initiative, Eisai, GlaxoSmithKline, Massachusetts Institute of Technology, Medical Research Council (South Africa), Medicines for Malaria Venture, MSD, National Institutes of Health (USA), Novartis, Oswaldo Cruz (Fiocruz) Foundation, PATH, Pfizer, Sanofi, Swiss Tropical and Public Health Institute, the University of California, Berkeley and the University of Dundee.

Public health impact

Medicines Patent Pool

Widespread licensing, backed by sufficiently attractive market prospects, can help to bring down the prices of new medicines by enhancing competition.

In addition, FDCs – simplified, combined treatments – are essential to the scale-up of antiretroviral treatment in developing countries. FDCs improve adherence to treatment regimens by reducing the number of pills a person is obliged to take, and lighten the burden on the health infrastructure, including distribution and storage facilities, relied on by people living with HIV in resource poor-settings.

Access to affordable, adapted medicines represents the difference between leading longer and healthier lives or succumbing to a treatable illness. Earlier treatment can also lead to lower rates of transmission, protecting sexual partners and reducing the spread of the epidemic.

A recent independent review concluded:

"Since IP for AIDS drugs has considerable value for originator companies, a system in which such IP can be widely licensed to generic manufacturers for low-income and some middle-income markets, as soon as possible after the drug is registered in rich countries, would have significant public health benefits for the millions of HIV-positive persons in the developing world who need anti-retroviral therapy. In addition, such a system should make multiple ARVs available for generic manufacture, so that fixed dose combinations can be produced." (*7*)

Pool for Open Innovation/WIPO Re:Search

The potential public health impact of these initiatives depends on whether they overcome a real barrier to innovation for neglected diseases. The analysis below suggests this will be the case only in rather exceptional circumstances.

Technical feasibility

Medicines Patent Pool

The MPP is now fully operational and has signed two licence agreements with patent-holders and two sub-licence agreements with generic companies. In addition, it is in serious negotiations with several other brand-name companies. The MPP has thus demonstrated its technical feasibility to date, but a key issue for the future is whether it can secure a critical mass of patents on products that will feature in treatment programmes. Concerns have been raised by a number of activist groups about the nature of the agreement reached with Gilead Sciences (*8*). These concerns include the restricted geographical scope of the agreement, other restrictions imposed on licensees, and the alleged undermining of the use of the flexibilities contained in the TRIPS agreement. The MPP shares a number, but not all, of these concerns, but emphasizes that the agreements it reaches are voluntary, and in its judgement and that of its Board and Expert Advisory Group the agreement with Gilead is a step forward.

Pool for Open Innovation/WIPO Re:Search

The independent review quoted above considered that the main barrier to drug development for NTDs was the lack of a large market and that, with a few exceptions, patents were less of a barrier. Their interviews with product development partnerships (PDPs) spearheading drug R&D for five NTDs – namely Chagas disease, leishmaniasis, human African trypanosomiasis, malaria and tuberculosis – suggested that patents have not impeded to any great extent their pursuit of development activities. These organizations have been able to identify existing intellectual property and harness it, developing fruitful relationships, following up on leads and successfully negotiating licences with pharmaceutical and biotechnology companies and universities. For these PDPs, the main issue has not been the paucity of valuable intellectual property for the drug candidate they are aiming to develop, but rather the lack of funding. However, where there was a pre-existing or potential commercial market for drugs for some NTDs, such as drugs for tuberculosis or Chagas disease, dual-use drugs (that can be used to treat a disease that has a lucrative market and also an NTD), access to the necessary patented compounds could be impeded, and the POI could therefore help to facilitate licensing free of royalties or at low rates, along the lines of what the MPP is trying to achieve. However, as with the MPP, a key issue would be the incentive for patent-holders to place their patents in the pool if that would potentially diminish their commercial value. The POI could also help to improve access to know-how

and data for the discovery of NTD compounds, which is more of a concern for universities, PDPs and companies interested in the early stages of drug development. The POI is well-designed to make it easier for academic laboratories dedicated to drug discovery to scan the intellectual property landscape, by providing a centralized source for intellectual property, and by negotiating the necessary licences for their work (*7*).

While the analysis above relates to the POI, the same considerations are likely to apply to WIPO Re:Search. Apart from those above, the criticism has been raised that a geographical scope limited to least developed countries is too restrictive given the prevalence of these diseases in other developing countries (*9*).

Financial feasibility

Medicines Patent Pool

The MPP is fully funded under a five-year memorandum of understanding with UNITAID. The current annual cost is under US$ 4 million per annum, less than 0.5% of current costs of antiretroviral treatment in developing countries (*4*). The cost of the MPP is likely to rise considerably as its portfolio and activities expand (to perhaps double the current level) but the potential savings in treatment costs and enhanced health benefits could be a large multiple of this *(10)*.

Pool for Open Innovation/ WIPO Re:Search

The costs of these initiatives are unknown but at present are unlikely to be significant.

Implementation feasibility

The MPP is already operational, as are the POI and WIPO Re:Search. The issue is the extent to which both initiatives will prove cost-effective and deliver public health benefits. Table 7 provides a summary assessment of the proposal.

Table 7. CEWG summary assessment of patent pools

Criterion	Comment
Public health impact	Potentially significant for MPP but upstream pool benefits are less easy to establish.
Efficiency/cost-effectiveness	Potentially significant benefits in relation to costs of MPP. Upstream pools probably cheaper but benefits less certain.
Technical feasibility	MPP already operational but there are issues concerning voluntary collaboration from companies, geographical scope and feasibility of obtaining "best" licensing terms. Upstream pools operational but there are issues about whether they address major constraints to R&D and geographical scope.
Financial feasibility	Relatively low cost to establish and run.
Intellectual property	MPP reduces transaction costs for licensing, and involves an innovative use of intellectual property. Upstream pools involve less innovative use of intellectual property.
Delinking	MPP can contribute to delinking if prices are lower than they would otherwise have been. Upstream pools have less direct connection to delinking.
Access	MPP could lower prices and promote new formulations to improve access. Upstream pools could promote availability of new products if successful.
Governance and accountability	MPP is a non-profit Swiss foundation with a memorandum of understanding

Criterion	Comment
	with its main funder UNITAID. Upstream pools have not specified their governance arrangements.
Capacity-building	MPP can promote technology transfer to licensees. Upstream pools involve no technology transfer obligation.

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Pooled funds

Source: *EWG Five proposals relating to funding allocation – Product development partnerships.*

Relevant submissions to CEWG

Fund for Research and Development in Neglected Diseases. Novartis.

A global framework on health research and development. All India Drug Action Network, Berne Declaration, CENTAD, Initiative for Health and Equity in Society, People's Health Movement, Third World Network.

Financing and incentives for neglected disease R&D: opportunities and challenges. Drugs for Neglected Diseases Initiative (DNDi).

A new incentive system for technological innovation in developing countries. Miguel A Maito, Eduardo Franciosi.

Other relevant submissions

EWG submission. *The Fund for R&D in Neglected Diseases (FRIND), 2009.*

Proposal description

The CEWG considered the three funds featured in the EWG report as ways to provide additional finance to PDPs and other research organizations. These were:

- the Product Development Partnership Financing Facility (PDP-FF), originally proposed by the International AIDS Vaccine Initiative (IAVI) and collaborators (*1*);
- the Industry R&D Facilitation Fund (IRFF), which was originally proposed in a report by the Pharmaceutical R&D Policy Project in 2005 (2);
- the Fund for Research in Neglected Diseases (FRIND) proposed by Novartis (3,4).

Novartis has submitted an updated proposal for FRIND to the CEWG.

The Third World Network and others have submitted a proposal for a fund within "a global framework on health research and development" (*5*). This assessment also takes account of the submission from Maito and Franciosi on "a new incentive system for technological innovation in developing countries" (ISTI) (*6*). It also draws on the recent evaluation by Results for Development of pooled funds (*7*).

The **PDP-FF** aims to deliver a substantial new source of secure long-term funding for PDPs. As presented, the proposal focuses on vaccines and the needs of three PDPs (IAVI, the Malaria Vaccines Initiative, and AERAS – the PDP for tuberculosis vaccines) but the principle could be generalized. Under the scheme, donors make a commitment to guarantee bonds issued by the PDP-FF. This enables the facility to issue bonds, the proceeds of which finance PDP activities. At the same time the facility would aim to earn revenue from royalties from sales in high- and middle-income countries, a fee charged to donors in low-income countries and other donor grants. Resources would be allocated long-term to PDPs on the basis of agreed expenditure plans. For the proposal concerning three PDPs, the projections assume that each PDP could receive US$ 29–73 million annually.

The **IRFF** is a proposed long-term grant fund of between US$ 130 million and US$ 190 million per year to underwrite industry participation in PDPs, with the dual aims of increasing industry R&D for neglected diseases and improving PDP outcomes. The IRFF aims to provide secure and predictable funding to PDPs, particularly to secure collaboration with industry. To that end it would operate by refunding a proportion, say 80%, of the cost of PDP contracts with industry. It would provide funding to PDPs on a five-year cycle against an agreed business plan. Various common services could be added to the core functions of receiving and disbursing donor money.

On the basis of its submission to the CEWG, **FRIND** will focus on the financing of diagnostics, treatments and vaccines in late-stage clinical development (Phases II and III). All research organizations, and not just PDPs, will be eligible for funding. It will use portfolio management techniques on the industry model to select the strongest compounds, and will finance them from milestone to milestone. An independent scientific advisory committee will be tasked to select the best compounds for investment from the different organizations. FRIND will focus on attracting government funds from new donors who currently do not have the capacity to perform portfolio management. They propose a pilot phase at funding levels of US$ 50–100 million annually, with a view to doubling that amount if the first phase is successful.

The Third World Network proposal is less well developed but emphasizes the following features:

- sustainable and predictable financing financed by some form of mandatory levy on products or services (e.g. indirect taxes);
- the importance of the fund in assessing needs and setting priorities;
- different pull and push mechanisms might be used but should be guided by the principle of delinking R&D costs from pricing;
- financing of capacity-building and technology transfer;
- outcomes and data generated should not be monopolized.

The proposers take the view that the elements described (i.e. the fund, architecture and guiding principles) could form components of an international framework instrument on R&D.

The ISTI proposal is for a grant fund, which could be financed nationally from a number of sources. This fund would meet a proportion of the cost of R&D proposals submitted by companies in return for which the companies would provide an open licence for other manufacturers with royalties being paid to a national innovation fund.

The DNDi proposal similarly concentrates on mobilizing innovative and sustainable financing, and has a mechanism for allocating funds based on global health priorities. It also makes proposals for reducing the costs of R&D through better mechanisms for sharing knowledge and better regulatory pathways.

All proposals involve subsidising R&D costs and thus involve an element of delinking. The proposals differ on how they will deal with intellectual property – from all rights accruing to the recipient, to various provisions on licensing back to the funder (e.g. exclusive licensing under FRIND), or completely open licensing. The Third World Network proposes that the resulting products should not be protected as intellectual property. Thus the extent to which they address the access issue for developed products varies considerably. Some of the proposals explicitly include provisions to promote capacity-building and technology transfer (TWN, ISTI, DNDi), while in others it is either implicit or absent (e.g. the EWG proposals).

Public health impact

It is difficult to identify with any certainty the public health impact of pooled fund proposals. Impact could come in two ways: through attracting additional resources into R&D by PDPs and other research organizations, and through improving the efficiency with which existing resources are utilized (e.g. through more rigorous portfolio management, better information-sharing or eliminating duplication). The proposals have varying provisions relating to access to products developed, although most PDPs have policies that emphasize affordability as a product characteristic and devote resources to eliminating barriers to product introduction in developing countries. PDPs have developed 16 products in the course of a decade or so and have over 100 products at various stages of development (*8*).

Technical feasibility

The technical feasibility of these proposals varies. In general, none of the proposals has probed very deeply into the issues that will arise as implementation is attempted. Nevertheless, there are some common issues regarding feasibility:

- Pooling is meant to be attractive to donors, including new ones, who lack the in-house capacity to decide on an optimal allocation to different PDPs and other research organizations and could rely on this mechanism to ensure that their money is well spent. On the other hand, even small donors may be concerned that the pool mechanism will not reflect their priorities. It is highly unlikely that established donors would channel their existing or additional funding into a pooled mechanism due to the loss of control that this entails.
- There is a tension between generating long-term predictable funding and providing an environment where hard decisions on priorities need to be taken in response to changing circumstances. For example, unpromising projects might be continued with little scientific justification. Much will depend on the criteria for releasing funds adopted by each pooled fund mechanism and on the quality of its decision-making.
- Whether a pooled fund will help to improve coordination and resource allocation, and will eliminate duplication, depends on whether the pooled fund both dominates the funding "market" and achieves better results than the current situation where individual donors decide how to allocate their money to different research organizations and what conditions to attach to it.
- In reality, none of the three EWG proposals will provide a very large share of the nearly US$ 500 million that flowed to PDPs in 2010, of which the Bill & Melinda Gates Foundation provided over half and over 90% was provided by the top 12 donors (*9*). In that situation, a pooled fund could be regarded as just another player, adding to complexity for PDPs and other research organizations and only justified if it delivers additional funds.

PDP-FF

This is the most challenging proposal because it relies on obtaining donor guarantees over an extended period of time. A similar model was used successfully in the International Finance Facility for Immunisation (IFFm) which was established in 2006 to allow bonds to be issued to support immunization with repayments guaranteed by donors. The IFFm involves the World Bank as treasury and required the establishment of a United Kingdom charity. Funds raised are channelled to the Global Alliance for Vaccines and Immunization (GAVI) (*10*). Establishment costs were therefore quite high. However, in spite of its success in raising funds in this way, there are no current proposals to replicate

it in other areas (except for the present proposal). The PDP-FF is, on the face of it, more complex than the IFFm because:

- The PDP-FF involves generating revenues from royalties in higher-income countries, and premiums (in effect royalties paid by donors) in lower-income countries. The latter is also a new concept which will require negotiations with donors and purchasing agencies. In effect, donors are being asked to do separate things: guarantee bond repayment and establish a new system for paying premiums on sales in low-income countries.
- While the IFFm is simply a vehicle for channelling resources to GAVI which manages its expenditure, the PDP-FF needs to decide how to channel funds to three or more entities in a way that is predictable over the longer term but is also flexible enough to cope with the uncertainty inherent in the R&D process.
- The need to generate revenues may bias the facility towards products that will have significant markets in higher-income countries, rather than those specifically addressed at developing countries.

IRFF

The IRFF is based on the premise that industry collaboration with PDPs is suboptimal. It therefore ties expenditures to the PDP costs of joint projects with industry. However, apparently the sponsors might now propose widening the original scope (*7*). If so, the distinguishing feature of the IRFF will be that it would reimburse a proportion of expenditures (e.g. 80%) against agreed targets in a five-year business plan. It is not entirely clear how this system would coexist with conventional funding from existing donors, who would, in effect, be financing the proportion (e.g. 20%) not reimbursed by IRFF. Nor is it clear how the IRFF business plan would relate to a PDP's overall business plan.

FRIND

The distinguishing features of FRIND are:

- emphasis on attracting new or existing donors who lack in-house capacity;
- a focus on late-stage development (Phases II and III);
- application of a rigorous methodology in project selection and pruning through an independent scientific advisory committee;
- it would be open to all research entities, and not just PDPs.

In its original conception, FRIND would become the dominant source of funding for neglected disease R&D. It was argued that research in this area was very fragmented and that even within single diseases there were several actors working in parallel and with limited communication between them. A major objective of FRIND was therefore to seek to improve overall portfolio management and the efficiency of spending across the board by applying a rigorous scientific methodology, underpinned by its ability to provide or withhold funding. It should be noted that some have questioned whether in reality a single funder allocating resources would necessarily result in a better portfolio than the current arrangements. In 2010 the Bill & Melinda Gates Foundation provided nearly US$ 450 million to neglected disease research other than HIV/AIDS, under 25% of total expenditure by all research organizations (*9*).

However, given the lack of enthusiasm of major donors to pool funds, the current proposal is more modest, envisaging a maximum expenditure of US$ 200 million annually (less than 10% of current spending on neglected diseases other than HIV/AIDS). That being so, the objective of improving

overall portfolio management for neglected disease research is no longer very relevant (except within FRIND's own portfolio).

Third World Network proposal

The TWN proposal has more ambitious objectives than the others but its scale and modus operandi are not described.

The ISTI proposal

As a national proposal, although intended to be extended, the feasibility will depend on national circumstances. Detailed implementation would raise a number of issues concerning the proposed arrangements.

Financial feasibility

All of these proposals are to a large extent scalable, but for each to commence there would need to be a critical mass of funders willing to participate. The conclusion of the evaluation of the three EWG schemes by Results for Development was as follows:

"Based on our analysis of the three pooled funding ideas ... and our assessment of the current environment and the mood of the donors, we are fairly pessimistic about the prospects of seeing one or several of these ideas launched in the next few years. The case for investing time and resources in establishing any of the three funds, in their current form, is weak at present". (7)

The analysis was that much would depend on the number of potential new funders who were most likely to be attracted to the pooled fund concept. There is no guarantee that donor resources channelled to a pooled fund will not be at the expense of existing flows.

The other proposals (TWN, DNDi, ISTI) rely to a greater extent on other innovative sources of finance, which are discussed elsewhere.

Implementation feasibility

The required key step is to identify donors and governments who are interested in contributing to a pooled fund process. Although some of these proposals have been in existence for up to five years, donor champions of pooled funds have not yet been identified. Other than political will, there are no overriding technical obstacles to creation of a pooled fund. Table 8 provides a summary assessment of the proposal.

Table 8. CEWG summary assessment of pooled funds

Criterion	Comment
Public health impact	Little evidence for assessing additional impact arising from pooled funds in general.
Efficiency/cost-effectiveness	All proposals involve elements of coordination and prioritization which could add to cost-effectiveness, or alternatively add to complexity.
Technical feasibility	Proposals are technically feasible to different degrees, but with different issues involved in implementation.
Financial feasibility	Depends on raising money on the scale required from existing donors or new sources of finance.
Intellectual property	Differs according to fund proposal.

Delinking	Differs according to fund proposal.
Access	Differs according to fund proposal.
Governance and accountability	In most cases these arrangements are yet to be defined with any clarity.
Capacity-building	Differs according to fund proposal.

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Open approaches to research and development and innovation

Source: *EWG Two proposals to improve efficiency, Five promising proposals.*

Relevant submissions to CEWG

Universities Allied for Essential Medicines.

Financing and incentives for neglected disease R&D. Drugs for Neglected Disease Initiative (DNDi).

Open source drug discovery initiative. Council of Scientific and Industrial Research, India.

Equitable licensing/med4all. BUKO Pharma-Kampagne, Charité Universitätsmedizin Berlin, Universität Oldenburg.

Other relevant submissions

EWG submission: Open source drug discovery: an open collaborative drug discovery model for tuberculosis. Council of Scientific and Industrial Research, India.

Proposal description

This assessment covers a number of approaches to the use and licensing of intellectual property characterized by a common theme of making new knowledge as freely available as possible. The purpose of these approaches would be to seek to ensure that products embodying new knowledge, such as medicines, are made as available and affordable as possible. The submissions above all make proposals covering the different aspects of these approaches. Patent pools, dealt with in separate assessments, may also be regarded as an important element of these approaches. Together these approaches can cover the spectrum from upstream to downstream research to promoting access.

There are a number of open approaches to innovation.

The "open innovation" approach was originally pioneered by Henry Chesbrough, a professor from the USA. He defined the approach as "a paradigm that assumes that firms can and should use external ideas as well as internal ideas, and internal and external paths to market, as the firms look to advance their technology. Open Innovation combines internal and external ideas into architectures and systems whose requirements are defined by a business model" (*1*). In essence a company looks to, and opens itself up to, external partners in order to better reach its innovation objectives. This is in contrast to the previous "closed" models where R&D was essentially in-house. The pharmaceutical industry has embraced an open innovation approach, particularly as a result of current difficulties in the development of new treatments (*2*). The approach involves no change in the intellectual property system but may necessitate a more flexible use of it.

"Open source" drug discovery is an idea based upon the successful example of open source software development. Generically, "open source" refers to a programme in which the source code is available to the general public for use and/or modification from its original design free of charge. Open source code is typically created as a collaborative effort in which programmers improve upon the code and share the changes within the community. Software is developed virtually by independent programmers. Anyone is allowed to use, distribute and modify the freely-available software code so long as the original author(s) are properly credited. Typically, open source initiatives are governed by a General Public Licence which guarantees the freedom to utilize and share software with others.

Open source drug discovery borrows two components from software development. These are 1) collaboration – organizing and motivating a group of independent researchers to contribute to a research project, and 2) an open approach to intellectual property – making the output of that research publicly available usually through open publication or deposit on a website or by using customized licences. It therefore bears a close relation to the concept of precompetitive platforms, discussed below, where results are meant to be shared freely among collaborators without intellectual property barriers (*3*,*4*,*5*).

India's Council for Scientific and Industrial Research funds the Open Source Drug Discovery (OSDD) initiative (focused on tuberculosis) (*6*,*7*). OSDD has chosen tuberculosis as its first target disease and plans to expand into malaria. It seeks to cover all stages of drug discovery from early-stage discovery up to lead identification. In the clinical development stage it will partner with other organizations supported by public funds. OSDD, while committed to making technologies it has developed freely available to generic manufacturers, does not entirely rule out the use of patents in specified situations (*8*).

An example of how this works in practice can be demonstrated through the synthetic *praziquantel* project hosted by Synaptic Leap. This project aims to make a better synthetic version of the schistosomiasis drug *praziquantel*. The initial web page of the project summarizes "what is needed right now" and displays recent postings to the website. Scientists can contribute either by performing peer review of the postings or performing specific tasks independently. After each task is performed (e.g. in a laboratory), the findings are posted publicly on the web site. All postings are considered part of the public domain (*9*).

Currently there are several other open source drug discovery projects, including Sage Bionetworks (focused on human disease biology) (*10*).

Another open approach to making research results more widely available is **open-access publishing**. Traditional fee-for-access journals may limit the access of researchers (in particular in developing countries) to new knowledge. There are two main types of open access publishing. "Green open access" is where authors publishing in a fee-for-access journal self-archive their articles in an agreed open-access repository. "Gold open access" is where authors publish in an open-access journal. Open-access journals use a business model that charges authors a fee (usually well over US$ 1000) to cover costs but allows free online access to readers, although sometimes externally-funded subsidies may be involved. In addition, many publishers will waive fees for authors from developing countries. There are now many open-access publishers. Well-known examples include BioMed Central and the Public Library of Science (PLoS). *PLoS ONE* is the largest scientific journal in the world, publishing 7000 articles in 2010 (*11*). Fee-for-access publishers are now launching their own open-access journals in response to the perceived success of the model. For example, the *British Medical Journal* has recently launched *BMJ Open* and *Nature* has launched *Scientific Reports,* both based on the *PLoS ONE* model. Some fee-for-access publishers, including Elsevier – the world's largest scientific publisher – also now offer the option of open-access in particular journals if the author pays a fee. Many research funders have instituted policies that allow author fees to be a legitimate cost in grant awards and demand that published research is made freely accessible within a certain period of time (e.g. 12 months) via archiving or open-access publication. For example, the National Institutes of Health in the USA and the Medical Research Council and Wellcome Trust in the United Kingdom have publishing policies along these lines.

Precompetitive R&D platforms are designed to contribute to R&D, possibly in several fields, by collaboratively developing technologies which overcome problems and bottlenecks in the overall research process. Essentially they are an aspect of open innovation. Platforms can take many forms. For example, the Human Genome Project (*12*), the International HapMap Project and the SNP

Consortium (*13*), and the Structural Genomics Consortium (*14*) have provided classic platforms for further biomedical research across the board. Other platform technologies might include, for instance, an animal model that more accurately predicts the value of a tuberculosis vaccine in humans, or surrogate markers that accurately predict the effect of an HIV drug, without requiring months or years of follow-up. Such findings are described as precompetitive as they are designed to be available to many developers rather than being proprietary to one company. Advances such as these could potentially save large sums on R&D for a single product, both by decreasing the development time and by early detection and elimination of leads with low performance.

Examples of precompetitive platform research projects cited by the EWG included:

- The European Commission's Innovative Medicines Initiative, co-funded by the European Union and the European Federation of Pharmaceutical Industry Associations, awards research grants to European public–private collaborations working on platform breakthroughs.
- The Program for Appropriate Technology in Health (PATH) is a United States-based product development partnership, which develops enabling and platform technologies and makes them available to all companies with products relevant for its programmes. For example, new assays and cell cultures are available to all manufacturers of a rotavirus vaccine for developing countries, and a consensus animal model is used for all candidate pneumococcal vaccines.
- The United States National Institutes of Health have developed many platforms to support R&D for neglected diseases, such as distributing parasites and biological materials, including infected animals, vectors and snails and transgenic parasites that express fluorescent labels, through three resources centres – one for schistosomiasis, one for filariasis and one for malaria and reference reagents (*15*).

The submission by Universities Allied for Essential Medicines (UAEM) highlighted a new initiative, Arch2POCM, which seeks to develop a new business model for the pharmaceutical industry based on precompetitive and collaborative research which would improve the efficiency and productivity of the industry's traditional competitive research model. It thus seeks to extend the sphere of precompetitive research up to the identification of molecules in Phase II trials. It is described as follows:

> "The Structural Genomics Consortium and Sage Bionetworks are spearheading an effort to build a precompetitive, pharma-backed public–private partnership to optimize the clinical validation of new therapeutic targets. By removing IP and data-access restrictions, the group hopes to create an environment that will eliminate redundant discovery programs and reduce the overall cost of R&D. A newly established public-private partnership called the Archipelago to Proof of Clinical Mechanism (Arch2POCM) hopes to improve the efficiency and lower the costs of drug development by generating a portfolio of small molecules that hit new therapeutic targets and by carrying out early clinical work – up to Phase II clinical trials. Both the discovery and the trials would happen in a precompetitive environment." (*16*)

The emphasis of this initiative is to develop a new commercial business model for the pharmaceutical industry focused on therapies for diseases in developed countries. Nevertheless, the methodology is potentially applicable to products to meet the needs of developing countries (*17,18*).

Equitable licensing is typically used to define an approach to the licensing of publicly-funded intellectual property that is developed in a university or a public research institution. It is also commonly known as "humanitarian" or "global access" licensing. It recognizes that publicly-funded research is very important in the development of new medical technologies, particularly for diseases

that mainly affect developing countries. For instance, almost two thirds of funding for neglected diseases was provided by public funders in 2010 (*19).* A recent article suggested that 9.3% of products approved by the FDA in the last 40 years were the product of publicly-funded research (*20*).

The global licensing framework set out in Box 1 below describes the main elements of equitable licensing. It can apply both to intermediate technologies which are needed in further research to develop products required by developing countries and to the licensing of health-care products suitable for use in developing countries

Box 1. Global access licensing framework

Every university-developed technology with potential for further development into a drug, vaccine or medical diagnostic should be licensed with a concrete and transparent strategy to make affordable versions available in resource-limited countries for medical care. Licences are complex and each will be unique. Universities should therefore implement global access policies that adhere to the following six principles:

Goals

1. Access to medicines and health-related technologies for all is the primary purpose of technology transfer of health-related innovations. This includes protecting access to the final end-product needed by patients (e.g. formulated pills or vaccines).

2. Technology transfer should preserve future innovation by ensuring that intellectual property does not act as a barrier to further research.

Strategies

3. Generic competition is the most efficient method of facilitating affordable access to medicines in resource-limited countries. Legal barriers to generic production of these products for use in resource-limited countries should therefore be removed. In the cases of biological compounds or other drugs where generic provision is forecast to be technically or economically infeasible, "at-cost" or other provisioning requirements should be used as a supplement to generic provisioning terms but should never replace those terms.

4. Proactive licensing provisions are essential to ensure that follow-on patents and data exclusivity cannot be used to block generic production. Other barriers may need to be addressed for the licensing of biologicals.

5. University technology transfer programmes should facilitate future innovation by patenting only when truly necessary to promote commercialization, utilizing non-exclusive licensing, creating streamlined processes for materials transfer, and reserving broad rights to use licensed technology in future research.

6. A global access licensing policy should be systematic in its approach, sufficiently transparent to verify its effectiveness, and based on explicit metrics that measure the success of technology transfer by its impact on access and continued innovation.

Source: http://essentialmedicine.org/archive/global-access-licensing-framework-galf-v20.

Public health impact

Open approaches tend to be most applicable at the earlier stages of the discovery and development cycle and/or have only recently been attempted. Thus there is little direct evidence on their potential public health impact. However, in different combinations they are identified by many researchers and stakeholders as ways to overcome current obstacles in biopharmaceutical R&D and therefore have the potential to impact public health, including in developing countries. Genomics has been, and is being, applied in many fields but, as frequently noted, has taken longer than initial expectations to accelerate the development of new products.

UAEM cites the case of Yale's licence of stavudine in which pressure from students, researchers and Médecins sans Frontières resulted in a renegotiation of its licensing agreement with Bristol-Myers

Squibb and contributed to a subsequent large price reduction for this widely used antiretroviral. A number of universities, particularly in the USA, have since adopted these principles, although it is difficult to trace exactly how many equitable licences have been executed or to document their impact on public health. UAEM lists its successes on its web site (*21*).

Technical feasibility

Open approaches have generally demonstrated their technical feasibility. Projects involving both the public and private sector, such as the SNP Consortium, have been successful where it is recognized there is a collective benefit in undertaking fundamental research of this nature, which will then be publicly available. "Open innovation" approaches have been widely adopted in the pharmaceutical industry in recent years. The feasibility of extending precompetitive and collaborative research downstream, as proposed in Arch2POCM, has yet to be tested.

As noted above, open-access publishing and self-archiving have demonstrated their technical feasibility in practice. Open-access growth has been relatively fast but open-access articles still represent a minority of all those published, although the landscape is rapidly changing. Critics argue that the open-access model may result in a reduction in quality, partly because there is a vested interest in acceptance of publications and an incentive to reduce the standard of peer review to cut costs and increase turnover.

Financial feasibility

Many of these approaches are simply different ways of doing things in R&D and their direct financial costs are generally small, although some of the precompetitive platforms mentioned above have incurred significant costs that have been met be foundations and governments as well as the private sector. These may involve more transaction costs because of the necessity for greater interaction with external partners. To the extent that they are successful they should help lower the costs of R&D by, for example, reducing the failure rates experienced in Phase II or III trials and/or by reducing labour costs through the use of volunteer labour.

Open-access publishing has proved to be something that can be financially viable without external subsidies. For instance, PLoS was initially heavily supported by foundations but is now largely financially self-sufficient and *PLoS ONE* is said to be extremely profitable, enabling PLoS to cross-subsidize its less popular titles. BioMed Central, a for-profit organization, was not profitable for many years and was taken over by Springer, a fee-for-access publisher, in 2008. Since the takeover, BioMed Central has continued to expand, suggesting it is a viable business in its own right.

Implementation feasibility

A key step would be to identify particular challenges in research for a particular disease or diseases suitable for a collective approach and to develop a fundable project proposal. Table 9 provides a summary assessment of the proposal.

Table 9. CEWG summary assessment of open approaches to research and development and innovation

Criterion	Comment
Public health impact	Has potential but is largely untested as yet.
Efficiency/cost-effectiveness	The rationale is that they are potentially more efficient and cost-effective than current R&D models.
Technical feasibility	Working models exist; new approaches need to be tested.
Financial feasibility	Difficult to generalize. Many are low-cost but others may require significant subventions (e.g. precompetitive platforms).
Intellectual property	Generally involve much greater flexibility and innovation with respect to intellectual property.
Delinking	Can contribute to delinking depending how the final product development is financed – whether it is patented, and whether and how the patent is licensed.
Access	Potential impact on access if innovation is promoted and costs lowered, and if prices delinked.
Governance and accountability	Depends on the design of individual schemes.
Capacity-building	Can contribute by widening opportunities for participation in R&D.

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Milestone prizes and end prizes

(EWG: "Milestone" prizes, "End" prizes (cash), Large end-stage prizes (impact-based rewards))

Source: *EWG Five proposals relating to funding allocation, EWG Annex 2.*

Relevant submissions to CEWG

The global health innovation quotient prize: a milestone-based prize to stimulate R&D for point-of-care fever diagnostics. BIO Ventures for Global Health.

Innovation inducement prizes. Knowledge Ecology International.

Other relevant submissions

EWG submission: *Chagas disease prize fund for the development of new treatments, diagnostics and vaccines.* Bangladesh, Barbados, Bolivia, Suriname.

EWG submission: *Prize fund for development of low-cost rapid diagnostic test for tuberculosis.* Bangladesh, Barbados, Bolivia, Suriname.

EWG submission: *A prize fund to support innovation and access for donor supported markets linking rewards for innovation to the competitive supply of products for HIV-AIDS, TB, malaria and other diseases for humanitarian uses.* Bangladesh, Barbados, Bolivia, Suriname.

EWG submission: *Prizes as a reward mechanism for new cancer treatments and vaccines in developing countries*. Bangladesh, Bolivia, Suriname.

EWG submission: *Response to the Expert Working Group on Alternative Financing.* Health Action International.

EWG submission: *Comments of Knowledge Ecology International (KEI) to the WHO public hearing for proposals for new and innovative sources of funding to stimulate R&D.* Knowledge Ecology International.

EWG submission: *Submission to the EWG.* Médecins Sans Frontières.

Submission to the IGWG 2008: *Priority medicines and vaccines prize fund.* Barbados and Bolivia.

Proposal description

Prizes are rewards for successful completion of a specified set of R&D objectives. There are basically two kinds of prizes – for reaching specified milestones in the R&D process, or for reaching a specified endpoint such as a new diagnostic, vaccine or medicine with a specified profile in terms of performance, cost, efficacy and/or other important characteristics. The EWG also distinguished between small end-stage prizes (such as might be offered for a diagnostic) and large end-stage prizes such as might be offered for a completely new drug or vaccine. Prizes may be offered in two main circumstances, both of which may apply in the area of neglected diseases:

- where it is considered that incentives for R&D are too small because the potential market is insufficient to stimulate needed innovations;

– where the R&D process has encountered a technological obstacle that needs a new approach.

The case for offering prizes (a form of "pull" incentive), rather than grants (a form of "push" incentive), is made in several ways. First, from the point of view of the prize sponsor, payment is made only for success, whereas in push funding failure is also rewarded. Thus in the prize model the risks are transferred to the product developer. Secondly, the model can open up a research field to new researchers who might have new and innovative ways of addressing a research problem. Thirdly, some view the conditions attached to prize award as a means of promoting subsequent access to the product. For instance various licence requirements relating to the intellectual property may be imposed on the prize winner, including allowing free use of the technology by others to promote competition in supply. For example, proposals by Bangladesh, Barbados, Bolivia and Suriname to the EWG incorporate the latter aspect.

Various other prize-type mechanisms have been proposed which have the objective of partially or wholly replacing the patent system as an incentive for biomedical R&D. For instance, two bills *(1,2)* were recently introduced into the United States Senate containing prize proposals which have the explicit objective of delinking the costs of R&D from prices:

"The proposed legislation would eliminate patent and other intellectual property barriers to the introduction of generic medicines. Replacing product monopolies would be a new Medical Innovation Prize Fund, that would provide more than US$ 80 billion in annual rewards for useful investments in R&D for new medicines and vaccines". (*1*)

The Health Impact Fund, or HIF, described separately, is also in effect a voluntary prize mechanism which would substitute for patent rewards in the products that it covers.

Other forms of prize do not aim to substitute for market incentives as such, but rather to stimulate R&D by signalling and rewarding personal or group achievements. In recent times the X Prize Foundation posted a US$ 10 million prize for a reusable manned spacecraft launched successfully into space twice within two weeks. This prize was won in 2004 and is said to have generated investment of US$ 100 million on the part of the participants. Thus the value of the prize did not compensate for the investment involved. The X Prize Foundation is currently developing a prize for a tuberculosis diagnostic (*3*). Innocentive is a for-profit company that awards prizes on behalf of sponsors to solve particular R&D problems (challenges), including in the life sciences. It has some 250 000 registered "solvers", about 1200 challenges have been launched since 2001, and US$ 7 million has been awarded in prizes ranging from US$ 5000 to US$ 1 million. The company claims an average success rate of 50% (*4*).

Many other types of prize seek mainly to reward individual achievement and may or may not include monetary rewards. These range from the Nobel Prize (based on past achievement) to those that may be awarded by universities or foundations. Typically in these cases, it is the prestige rather than the monetary reward which is the principal incentive. The use of such prizes in all fields of human endeavour has become widespread in recent years (*5*).

This assessment takes advantage of the recent assessment of prize fund proposals by Results for Development (*6*).

It is also accompanied by a submission to the CEWG by BIO Ventures for Global Health entitled *The global health innovation quotient prize: a milestone-based prize to stimulate R&D for point-of-care fever diagnostics* (*7*).

Knowledge Ecology International has submitted a paper on *Innovation inducement prizes* (*8*) which helpfully summarizes the various proposals submitted to the IGWG and EGWG *(9–14)*.

Public health impact

The choice of disease and specification of a prize will ultimately determine its public health impact. In some cases, such as the HIF and the Medical Innovation Prize Fund, it is sought to link the value of the prize to the incremental therapeutic or health impact of the product developed. Some prize proposals lay greater emphasis on facilitating access to the products developed than do others. Given the diversity of prize fund proposals it is very difficult to say anything meaningful in general about their public health impact.

The submission by BIO Ventures for Global Health concerns a fever diagnostic that would identify malaria, pneumonia and other bacterial infections, including tuberculosis and ideally HIV. Two particular health benefits would be accurate diagnosis of pneumonia, particularly in relation to an assumption of the presence of malaria, and reduction in over-prescription of antibiotics, thus mitigating the development of antibiotic resistance. BIO Ventures for Global Health estimates that globally the lives of 355 000–460 000 children under five years of age could be saved annually with full roll-out. They also estimate that about 50 million inappropriate antibiotic prescriptions would be saved (*7*).

Technical feasibility

Prizes are certainly technically feasible but the likelihood of success, and in a manner that is cost-effective as compared to possible alternative incentives, will depend very much on the suitability of the prize design in relation to the intended purpose. The target product profile needs to be defined precisely. There is an example of such a profile in the BIO Ventures for Global Health submission which also includes a target cost. The overall conditions attached to the award of a prize must also be considered, particularly from the perspective of whether the prize is sufficient to induce effort on the part of firms, or whether there may be aspects of the profile or conditions that will put off potential respondents. For example, an unrealistic target cost may be a disincentive to participation, as would too small a prize in relation to the effort expected.

A great number of design features need to be considered in relation to a prize. These are discussed at some length in the Results for Development report which looked also, as a case study, at the two proposals for a diagnostics for tuberculosis from the XPrize and the proposals by Bangladesh, Barbados, Bolivia and Suriname.

Important general points from the study by Results for Development included:

- An end prize will attract only companies which can mobilize funds up-front and accept the risk of failure. Small companies, such as many biotechnology companies, may therefore not be incentivized.
- On the other hand, small companies which find it difficult to find funding might be more attracted to milestone payments at intermediate stages and may be familiar with such arrangements in their commercial partnerships.
- Prizes are most useful where the way forward is not clear and new ideas are needed.
- The size of the prize needs to take account of the fact that there may be more than one winner – but too large a prize may induce too many potential winners, and this will create uncertainty in the minds of potential entrants as to their reward. The BIO Ventures for

Global Health proposal specifies the value of each prize and the number of awards it will make at each milestone stage, which is a way to reduce this uncertainty.

- A requirement to give up or license intellectual property rights on the product may deter some entrants, particularly where the technology developed may be valuable in other areas of their business (platform technologies). The authors believe that requiring winners to grant non-exclusive licences for relevant intellectual property, restricted by geography, could be a way to drive down prices and ensure sustainable supply so long as a satisfactory way can be found to deal with platform technologies.

In respect of the two tuberculosis proposals the study concludes:

- The X-Prize prize of US$ 5–20 million is probably too small to attract new entrants to the field, or to intensify existing efforts. However, the prize of US$ 100 million proposed by Bangladesh, Barbados, Bolivia and Suriname is probably attractive to a wide range of firms, and may even be larger than necessary.
- The conditions in the prize proposed by Bangladesh, Barbados, Bolivia and Suriname obliging all winners to put their intellectual property in a patent pool and meet manufacturing cost targets might deter some participants. By contrast, the X-prize proposal has no obligation on intellectual property and no cost target which the authors of the report consider too weak.
- A prize of the right size and design could be successful, particularly if it included milestone payments as well as an endprize. Biotechnology companies might respond to smaller prizes rather than large ones and may be open to new business models (*6*).

Financial feasibility

Prizes can be set at any level, dependent on context. Large schemes, such as the Medical Prize Innovation Fund, involve large sums but this is predicated on public funding replacing funds for R&D which are currently recovered from patients and taxpayers through high medicine prices. At the other extreme, prizes offered through Innocentive can be as low as US$ 5000. The two tuberculosis diagnostic proposals range from US$ 20 million to US$ 100 million. The BIO Ventures for Global Health multiplex diagnostic proposal is costed at US$ 155 million. The pneumococcal AMC, which has prize-like characteristics, costs US$ 1.5 billion. The HIF, with similar characteristics, is budgeted at US$ 6 billion.

To a large extent the financial feasibility of a proposal is likely to be inversely related to its cost. The proposals for diagnostics at a medium cost, combining milestone and end prizes, and/or support for specific activities such as clinical trials or specimen-testing, seem eminently feasible if policy-makers can be convinced of the case.

The key issue is to determine whether a prize proposal is likely, given the circumstances in a particular field, to be the most cost-effective way of addressing a particular challenge in product development compared to alternative push and pull incentive mechanisms.

Implementation feasibility

For prizes where the cost is in the tens or hundreds of millions of dollars, the key step is to make a good case and find funders who back that case. For the most part, given the potential for finance, there are no insuperable technical barriers. Similar things are already being done in a variety of fields, including the life sciences.

In order to make a good case, there may be a need for further evidence-building, but it needs to be considered whether the existing evidence base is, in fact, sufficient for the case to be made. It should be noted that many schemes are mutually exclusive and there is a potential for several prizes to be progressed simultaneously. For the larger schemes, which have also a transformative effect on the current system of financing R&D, the key step is to identify advocates who will wield influence with the governments who need to make such strategic decisions. Table 10 provides a summary assessment of the proposal.

Table 10. CEWG summary assessment of milestone prizes and end prizes

Criterion	Comment
Public health impact	Potential for impact but little evidence to date.
Efficiency/cost-effectiveness	More likely with milestone prizes than with end prizes.
Technical feasibility	Commonly used in diverse fields.
Financial feasibility	Size varies enormously – prizes have already been offered over a wide range.
Intellectual property	Arrangements differ according to design.
Delinking	Can be incorporated as a feature of design.
Access	Access can be promoted, dependent on design.
Governance and accountability	Procedures and triggers for prize award need to be carefully designed.
Capacity-building	Can contribute but contingent on the prize design.

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Purchase or procurement agreements

Source: *EWG Five proposals relating to funding allocation.*

Relevant submissions to CEWG

None.

Other relevant submissions

None.

Proposal description

Purchase or procurement agreements are contracts between a purchaser (normally a government or an international financing agency) and suppliers which involve some form of guarantee with regard to price and/or volume. By creating a market and greater certainty, such agreements may have the effect of offering incentives for product improvement or R&D. Although most are simply agreements to elicit reliable supplies of quality products at the best possible prices, one variant of such an agreement is the Advanced Market Commitment (AMC) which seeks to promote R&D and accelerated introduction into developing countries by offering an enhanced price to suppliers if they offer a product which meets a particular specification in terms of its public health impact. A pilot AMC for a pneumococcal vaccine is currently being implemented by GAVI which offers an enhanced price of US$ 7 per dose for 20% of supplies in return for producers agreeing to supply in the long term at a maximum price of US$ 3.50 per dose (*1*). Another variant is the agreement between GSK and FIOCRUZ in Brazil, the latest in a long partnership between the two organizations, which is reported to involve a €1.5 billion contract to supply GSK's pneumococcal vaccine and transfer technology to allow domestic production, along with technology transfer for a dengue vaccine (*2*).

Public health impact

GAVI estimates that the pilot pneumococcal AMC could save some 900 000 lives by 2015 and up to 7 million lives by 2030 (*1*). However, this may be a considerable overestimate and does not take into account the investment in competing interventions to reduce child mortality (*3*). Given the variety of purchase and procurement agreements for different kinds of product, it is difficult to provide an overall estimate of public health impact. Much will depend on the design and targeting of particular agreements.

Technical feasibility

Purchase and procurement agreements are very common and are therefore technically feasible. However, the more sophisticated agreements, such as the pilot AMC, involve quite complex legal agreements between various entities, independent committees for assessment and adjudication, and the involvement of several different international institutions and multiple donors. Heavy transaction costs can therefore be involved, particularly in the establishment of these arrangements.

This raises a question mark as to the scalability of schemes such as the AMC, although there remains the intention among some donors to launch a second AMC for an "early stage" product, such as a malaria vaccine. Indicatively this may involve a much larger AMC value in order to stimulate R&D.

While the first vaccines have now been delivered under the AMC, it is too early to judge whether the AMC is a success in terms of its stated objectives. A benchmark evaluation study was completed in

2010 which defines indicators and counterfactual situations against which success can be measured (*4*).

Financial feasibility

Schemes designed to secure supplies of existing products at lowest possible prices are entirely financially feasible and may indeed be self-financing in that the cost of setting them up is outweighed by the savings to the purchaser(s) arising from lower product costs than would otherwise have been the case. At the other extreme, schemes designed to elicit an R&D response, such as the AMC, can be very costly in terms of the cost of the incentive itself, and the associated cost of the institutional arrangements necessary to implement the scheme. Thus, the estimated cost of a second AMC for an "early stage" product is estimated at US$ 3 billion (*5*).

As regards the AMC, there is vigorous debate as to whether the pilot project is correctly specified to achieve its objectives at minimum cost. Critics argue that the size of the premium payable to companies is too high, given that these products were already in development when the AMC was conceived. Thus the incentive is not so much designed to stimulate R&D as to encourage accelerated introduction of a new product into developing countries by offering price and volume guarantees to suppliers (*6,7,8*). Supporters say that traditionally new vaccines do not filter through to developing countries and that the AMC stimulates immediate introduction. It is also argued that the long-term price premium offered to suppliers by the AMC (a maximum of US$ 3.50 per dose) may be too high, particularly because there are currently only two suppliers meeting AMC criteria (GSK and Pfizer) and the AMC has done too little to encourage more competition, in particular by promoting technology transfer to potentially lower cost suppliers in India or elsewhere (*8*). Supporters say that the price is set appropriately, and may reduce as competition develops. In any case, the price is less than one tenth of prices paid for equivalent vaccines in developed countries.

While the AMC donors fund the US$ 1.5 billion supplement payable to manufacturers, GAVI itself (with only a small contribution from recipient countries – 20 US cents per dose for low-income countries) is expected to finance the actual purchase of the vaccines. While the AMC adds US$ 1.5 billion to GAVI's income, GAVI estimates that between 2010 and 2030 it will, in addition, have to devote more than five times that amount (US$ 8.1 billion) to subsidising country purchases. This can happen only if countries also spend US$ 6.2 billion of their own resources on vaccine purchase. Thus the headline cost of the AMC is a fraction of the overall cost of supplying AMC vaccines to people who need them (*8*).

Implementation feasibility

There are no particular key steps to be identified for any sort of purchase or procurement agreement other than willing partners. In the case of AMC-type arrangements, this would also require funders willing to commit substantial sums of money over an extended time period. Table11 provides a summary assessment of the proposal.

Table 11. CEWG summary assessment of purchase or procurement agreements

Criterion	Comment
Public health impact	To the extent that availability and prices are lower.
Efficiency/Cost-effectiveness	Unresolved debate about whether or not the costs are justified by the benefits, relative to other possible investments.
Technical feasibility	AMCs are quite complex – others less so.
Financial feasibility	Individual AMCs are expensive.
Intellectual property	No change to the status quo.
Delinking	An AMC can delink prices from recovery of R&D costs through subsidy arrangements.
Access	To the extent that availability and prices are lower.
Governance and Accountability	AMC governance arrangements are complex – pure procurement agreements less so.
Capacity building	No impact.

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Priority review voucher

Source: *EWG Five promising proposals.*

Relevant submissions to CEWG

None.

Other relevant submissions

None.

Proposal description

A priority review voucher scheme has already been introduced in the USA but could potentially be introduced in any jurisdiction. In the United States scheme, those who obtain marketing approval from the FDA for a product to treat or prevent one of 16 neglected tropical diseases are entitled to receive a priority review voucher which entitles the bearer to receive priority review of another product that would not otherwise qualify for priority review. By this means, a company could advance the approval of a potentially "blockbuster" product with correspondingly increased revenues during the lifecycle of the product (i.e. until patent expiry). The FDA provides for priority review of products which it considers are a significant improvement over currently marketed products. It aims to complete 90% of such reviews in six months (although approval may take longer if scrutiny raises issues to be resolved). The FDA aims to complete reviews for 90% of other (standard) products in 10 months (*1*).

The priority review voucher can be used by the recipient or sold to another company. The original authors of the proposal estimated that the average difference in approval time between priority and standard products was about one year and that the average value of a voucher could be over US$ 300 million (*2*,*3*).

The legislation was passed in 2007. One priority review voucher has been issued to date – in April 2009 to Novartis for the antimalarial drug Coartem. Novartis used this voucher in February 2011 to accelerate FDA review of one of its own drugs for arthritis. The application was given priority but was not successful as a result of the advice of the FDA's Advisory Committee. Novartis also paid a US$ 4.6 million fee for priority review of the product (*4*).

Proposals have been made for a similar scheme in Europe.

Public health impact

The potential public health impact of the proposal is based on:

- the additional incentive for companies to devote resources to investment in R&D for neglected diseases;
- the potential benefit to patients in the USA from the earlier introduction of new therapies;
- benefits to United States travellers and the military.

Turning potential public health impact into reality depends, in the first place, on the effectiveness of the scheme in stimulating additional R&D on neglected diseases. This is unproven so far. While the potential value of a priority review voucher is significant, many argue that it is too small to have any meaningful impact on the allocation of R&D resources by large pharmaceutical companies. Such a sum might be more attractive to smaller biotechnology companies but in their business model it is quite rare to take a product right through to marketing approval, and the incentive effect will be diluted if, for instance, the product is licensed out at Phase III trials. Comparison also needs to be made with the US$ 1.5 billion incentive offered for late-stage development and manufacture of pneumococcal vaccine under the AMC of GAVI, or the US$ 3 billion incentive often discussed (and disputed) as the incentive required to stimulate early-stage research (e.g. for a more effective malaria vaccine).

Secondly, it has to be demonstrated the voucher is actually worth its estimated value in the marketplace. Companies with a suitable product eligible for standard review who cannot benefit from use of a voucher have to weigh the risk that ultimately their product may not be approved, that in reality the time saved in review may be much less than one year (the FDA can offer no guarantees), and that its commercial prospects may not be such as to justify the purchase of a voucher. In reality, therefore, the amount companies are willing to pay for a voucher may be considerably less than estimated (*5*). The experience of Novartis illustrates the potential for lower returns than anticipated.

The only empirical evidence relates to the priority review voucher obtained by Novartis. This involved the first registration in the USA of Coartem, a medicine which had been in use elsewhere since 1998 and was placed on WHO's Essential Drugs List in 2002. Thus the incentive effect of the priority review voucher has not been tested and no incremental health benefit will occur in developing countries. The only direct health benefit will be to users in the USA, but Novartis claims it would have registered the product without the incentive of the priority review voucher. The use of the voucher by Novartis for one of its own products also means the market value of its voucher has not been tested (*4*).

Thirdly, assuming the priority review voucher scheme is effective in accelerating product development for neglected diseases, a defect is that there are no provisions that relate to promoting access to patients in developing countries. Without such access there can be no health benefit. Again, this may be compared with the AMC which contains provisions for long-term supply at agreed prices even after the incentive payment has ceased (*6,7*).

Fourthly, because the scheme depends on effectively paying for accelerated review of a product that the FDA would otherwise have reviewed as standard, it has been argued that this carries a risk that the FDA will scrutinize such products less stringently and/or a risk of distortion of the FDA's allocation of resources on grounds other than public health. Although the research shows that, in the 1990s, 15 out of 29 best-selling drugs with sales over US$ 1 billion were classified by FDA as "standard review" (*2*), there is an apparent contradiction in accelerating the approval of products judged by the FDA to offer "at most, only minor improvement over existing products". In addition there is no necessary direct correlation between the sales revenue generated by a product and its public health impact.

Finally, the incentive does not distinguish between products with potentially very different public health impacts in developing countries; the only criterion is that it should be for the treatment of specified diseases. Companies will have an incentive to do the minimum necessary R&D to qualify for a voucher rather than tackle harder problems with a potentially greater public health impact (*6*).

Technical feasibility

The proposal is technically feasible to introduce, as demonstrated in the USA. The simplicity of the scheme, and the way it uses existing regulatory mechanisms, made it possible to introduce it in a very

short space of time in the USA. In other jurisdictions, such as Europe where regulatory and other institutional characteristics differ considerably, a version would also be technically feasible but implementation would probably be much more complex (*9*).

However, as noted above, it is still not clear that the proposal will achieve its objective because the mechanism has only been utilized once. In that sense, it has not yet been demonstrated that the scheme, in its current form, is correctly technically specified to achieve the intended objective. Changes that might be made to the scheme to increase its public health impact would tend to make it more complex and thus possibly much more technically difficult to implement.

Financial feasibility

The proposal is also financially feasible. There was an initial set-up cost for the FDA (e.g. issue of guidelines) but the proposal is essentially self-financing. Companies using a voucher also have to pay the FDA a fee for the priority review *(1*).

Implementation feasibility

As is apparent, implementation of a scheme of this nature can be relatively straightforward. In the USA it took little more than a year from genesis to legislation.

Were the scheme to be extended, or indeed modified in the USA, questions would arise as to whether the basic idea is sound. One question is whether the incentive potentially offered is adequate and, in reality, whether vouchers will have a market value similar to their potential theoretical value.

For implementation in other jurisdictions, the scheme would need to be adapted to their own institutional characteristics. In addition, there would need to be consideration of how the scheme could be adapted to encourage access to developed products in developing countries. Table 12 provides a summary assessment of the proposal.

Table 12. CEWG summary assessment of priority review voucher

Criterion	Comment
Public health impact	No demonstrated impact in developing countries.
Efficiency/cost-effectiveness	Dependent on evidence of impact and use to which the voucher is put.
Technical feasibility	Demonstrated in the USA, but doubts about its effectiveness.
Financial feasibility	Low direct costs; there may be indirect costs associated with use of the voucher.
Intellectual property	Does not alter the status quo.
Delinking	No impact.
Access	Not addressed by the scheme.
Governance and accountability	Rules-based governance according to legislation.
Capacity-building	Not addressed by the scheme.

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Regulatory harmonization

Source: *EWG Two proposals to improve efficiency.*

Relevant submissions to CEWG

None.

Other relevant submissions

None.

Proposal description

A large proportion of the cost of developing and marketing new products in developed countries is used to meet the costs of clinical trials required by regulatory authorities to establish that the product is safe, effective and of high quality. Costs can be increased further when different countries have different regulatory requirements, each requiring its own set of information as the basis for national approval and use. The aim of regulatory harmonization is to improve this situation by aligning the requirements of a number of developing countries (*1*).

WHO has long played a role in bringing together regulators through the International Conference of Drug Regulatory Authorities. This provides an important platform to develop international consensus and to assist WHO and drug regulatory authorities in their efforts to harmonize regulation and improve the safety, efficacy and quality of medicines. To seek to ensure that good quality pharmaceuticals are available, WHO sets norms and standards, develops guidelines and advises Member States on issues related to quality assurance of medicines in national and international markets. WHO assists countries in building national regulatory capacity through networking, training and information-sharing.

A WHO prequalification project was set up in 2001 to give United Nations procurement agencies, such as UNICEF, the choice of a range of good quality products that meet the standards laid down by the project. It does not intend to replace national regulatory authorities or national authorization systems for importing medicines but draws on the expertise of some of the best national regulatory authorities to provide a list of prequalified products that comply with unified international standards. Over time, the growing list of products that have been found to meet these standards has proved useful for countries and organizations purchasing medicines in bulk. For instance, the Global Fund to Fight AIDS, Tuberculosis and Malaria disburses money for medicines that have been prequalified by the WHO process, as well as those meeting other regulatory standards. This has proved useful to developing countries without the means themselves to conduct similar assessments. However, responsibility for decision-making and the processes required for that decision-making remain matters of national sovereignty (*2*).

Harmonization of regulation in developing countries has begun in some regions, although progress is slow. For instance, in Africa early steps were taken by the African Union and by various regional economic communities – such as the Economic Community of West African States which acknowledged the value of a harmonized regulatory dossier, the East African Community which harmonized standards and practices for quality assurance, and the Southern African Development Community which developed a pharmaceutical business plan for full regulatory harmonization over the period 2007–2013. An African drug registration harmonization consortium has been formed – led by the New Partnership for Africa's Development, the Bill & Melinda Gates Foundation, the United Kingdom's Department for International Development, the Clinton Foundation and WHO – which assists African regional economic communities and organizations in formulating high-level plans to attract donor support for harmonization. A trust fund has now been established in the World Bank with the objective of mobilizing funds from multiple donors (*3*).

Other regional regulatory harmonization initiatives include those of the Association of South-east Asian Nations, the Gulf Cooperation Council, and the Pan American Network for Drug Regulatory Harmonization.

The core members of the International Conference on Harmonisation (ICH) are the research-based industry and developed country regulators, which have sought with some success to harmonize the information requirements required by regulators, thus mitigating some of the problems associated with differing requirements of regulatory authorities in developed countries. The ICH has so far been less successful in involving developing countries, particularly because harmonization implies a reasonable parity in existing capacities for regulation. While patients in developing countries should expect to receive medicines and vaccines of the same quality, safety and efficacy as those in developed countries, the applicability and relevance of each and every ICH requirement to the needs of the developing countries is questionable (*4*). The European Medicines Agency has developed a partly harmonized registration system but this followed a very long political process over several decades (*5*).

The CIPIH report recommended that "developed countries, and their regulatory institutions, should provide greater financial and technical assistance to help attain the minimum set of regulatory standards needed to ensure that good quality products are available for use" and that "developing country governments and regulatory institutions should give support to regional initiatives, tailored to the current capacities of their member countries, which offer more scope for lifting standards over time, exploiting comparative advantages, avoiding duplication, sharing information and facilities, and promoting appropriate standardization without erecting barriers to competition."(*6*)

Public health impact

The EWG concluded that harmonization of regulation in developing countries would have an impact on health in those countries as it could lead to more rapid registration of many products (both generic and brand-name) and may lead to product registration in countries that would otherwise not have access to the product. It is likely to increase patient access since developers are more likely to register products that are to be offered for sale in many developing countries if the cost and difficulty of doing so are decreased; and it may have a broader impact if lower development costs mean lower prices (although this is far from being a certainty).

Technical feasibility

The EWG felt that regulatory harmonization was technically feasible, as shown by the advances made by developed countries in this area. However, the ability to regulate medicines effectively is determined by a number of factors, including the state of economic development, availability of infrastructure, and a country's prevailing health-care system. At root, the problem in developing countries lies in a lack of human and financial resources devoted to regulation. Among other things, this is often the result of inadequate political commitment, exacerbated by the interest groups that benefit from loose regulation. Hence, although the policy options to rectify this situation are relatively straightforward in principle, implementation may well be much more difficult. Countries need resources, both human and financial, but political leadership is also very important. Even if more financial resources are allocated to ensuring appropriate regulatory development within a region, the availability and expertise of human resources will remain a challenge over the medium term.

Financial feasibility

Regulation has a cost which in most countries is met by a mix of government subsidies and fees payable by companies for registration. Yet many regulators in developing countries, as noted above, are short of both human and financial resources. In addition, establishing harmonized systems and running them properly has a significant investment cost. For instance, setting up harmonized systems across Africa could have an investment cost of the order of US$ 100 million. The NEPAD-led project

for harmonization in Africa has to date only one donor – the Bill & Melinda Gates Foundation – and few other donors have demonstrated any significant interest in funding it.

Implementation feasibility

The key step will be to generate greater political support for improved regulation among developing country governments and funding agencies. Table 13 provides a summary assessment of the proposal.

Table 13. CEWG summary assessment of regulatory harmonization

Criterion	Comment
Public health impact	Has the potential to impact.
Efficiency/Cost-Effectiveness	Dependent on impact.
Technical feasibility	Improved regulation and harmonisation is a long term proposition.
Financial feasibility	Relatively costly and donor community does not assign high priority.
Intellectual property	Does not alter status quo.
Delinking	No impact.
Access	Better regulation may improve availability of quality products, but not necessarily access.
Governance and Accountability	Depends on local decisions.
Capacity building	Intended to build local capacity in regulation.

References

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Tax breaks for companies

Source: *EWG Annex 2*.

Relevant submissions to CEWG

None.

Other relevant submissions

None.

Proposal description

This is a provision in national tax laws which allows companies to set expenditures on R&D for neglected diseases against their tax liabilities. For example, the United Kingdom introduced a scheme in 2002 (called Vaccines Research Relief, though it also covers treatments) which allowed companies to deduct an additional 50% of eligible expenditures from their taxable income for R&D on vaccines and/or medicines for malaria, tuberculosis and HIV/AIDS (*1*). This percentage was reduced to 40% in 2008, 20% in 2011, and the scheme will be abolished for small and medium enterprises in 2012. For firms that make losses and pay no tax, there is provision for an equivalent grant to be provided. This is in addition to general tax credits which R&D expenditures may attract. Other examples of schemes specifically targeted at neglected diseases are not known.

Presumably the proposal would be to consider encouraging countries across the world to adopt this type of scheme in order to provide better incentives for relevant R&D – i.e. related to Type II and Type III diseases and the specific R&D needs of developing countries in relation to Type I diseases.

Public health impact

The impact on public health will depend entirely on the extent to which the proposal would increase R&D and the development of new products which will be made available and used in developing countries. There is no evidence on this to date.

Technical feasibility

Tax credits for R&D expenditures exist in many countries and are therefore technically feasible. The available evidence suggests that general R&D tax breaks may, in the long term, increase R&D expenditures by as much as the cost of the tax subsidy. In the relatively simple form introduced in the United Kingdom, the credit is based on all eligible R&D expenditures. The disadvantage of this is that it may simply subsidize R&D that a company would have undertaken anyway. It may not in practice be a sufficiently strong incentive to induce companies to shift more resources into neglected disease research. To overcome these defects it is possible to offer the incentive only for incremental R&D expenditures. However, experience of a general R&D subsidy on these lines in the USA suggests there are multiple problems in determining eligibility of expenditures and high compliance costs. Focusing the scheme thus makes it considerably more complex to administer and leads to disputes over qualifying expenditures and baselines (*2*).

In the United Kingdom it was estimated at the time of the introduction of the tax credit that between 10 and 50 companies might make use of it and that R&D might increase by £20–50 million annually on the basis of experience of R&D tax credits elsewhere which suggested that, for every tax dollar spent, companies would on average spend an additional dollar on R&D (*1*). In reality, only about 10

companies have made use of the system in the United Kingdom, and the annual amount claimed has been less than £5 million (*4*). This is to be compared with an estimate of over US$ 40 million of qualifying research undertaken in the United Kingdom annually (*2,3)*.

In the USA, claims by the pharmaceutical industry under the incremental tax credit scheme (Research and Experimentation Tax Credit) represent 3% of total domestic expenditures by the pharmaceutical industry on R&D. This does not suggest that, as currently structured, it is a powerful incentive. In the USA also, the orphan drug legislation offers a 50% tax credit on clinical trial expenditure for rare diseases, but most observers regard the market exclusivity offered by the legislation as the most powerful incentive (*2*). Another recent scheme in the USA (Qualifying Therapeutic Discovery Research Project) offers a grant or 50% tax credit for R&D to small firms meeting unmet medical needs. This one-off scheme with a cost cap of US$ 1 billion was very popular, attracting 5600 applications and 3000 awards. However, the amount of tax credits awarded was under US$ 19 million so it was the grant component that was overwhelmingly more popular (*5*).

Overall, therefore, the experience with targeted tax credit schemes to date is not very encouraging.

Financial feasibility

It is estimated that the private sector spent over US$ 500 million globally on neglected disease research in 2010 (*6*). This provides an indicator of the order of magnitude of the cost of a global tax credit scheme – the exact cost would depend on the structure of the schemes adopted and the degree of take-up by companies. On the basis of the information above, the cost of the scheme would probably be very much less than US$ 400 million. However, this would not necessarily be an indicator of cost-effectiveness.

Implementation feasibility

Because tax credits are a feature of most national tax regimes, it should be relatively straightforward for many countries to introduce such a scheme, should they decide it is a good way to stimulate R&D. Table 14 provides a summary assessment of the proposal.

Table 14. CEWG summary assessment of tax breaks for companies

Criterion	Comment
Public health impact	Not demonstrated for existing schemes.
Efficiency/cost-effectiveness	Not demonstrated in absence of impact.
Technical feasibility	Relatively easy to establish as part of tax regimes.
Financial feasibility	Limited direct costs.
Intellectual property	Not addressed in schemes considered.
Delinking	Not addressed in schemes considered.
Access	Not addressed in schemes considered.
Governance and accountability	Subject to normal rules procedures relating to tax credits.
Capacity-building	Not addressed in schemes considered.

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Transferable intellectual property rights

Source: *EWG Annex 2.*

Relevant submissions to CEWG

None.

Other relevant submissions

None.

Proposal description

The proposal for transferable intellectual property rights (TIPR) is similar in many respects to that for priority review vouchers. The idea is that a reward would be offered to companies which develop a product to fight neglected diseases in the form of an extension of market exclusivity that could be used on another top-selling product. Such a reward would be tradable and thus could potentially be monetized.

There are various ideas about exactly how this could be implemented. The trigger for the reward could be the licensing of a product for neglected diseases by the regulatory authority, as is the case with the priority review voucher. The reward could be a voucher for extension of a patent or some other form of exclusivity right on a product.

As with the priority review voucher, at the cost of more complexity, rewards could be made dependent on measures going beyond licensing, such as:

- specifying product profiles by disease, which would meet certain standards for potential health impact;
- differentiated rewards for products with different potential health impacts;
- making the award of a voucher dependent on, for instance, licensing the product in a number of developing countries;
- requiring non-exclusive licensing or relinquishing of intellectual property rights altogether on the product.

Public health impact

The potential public health impact will depend, as with the priority review voucher, on the effectiveness of the scheme in stimulating additional R&D on neglected diseases, and the extent to which rewarded products are actually made accessible in developing countries.

However, unlike the priority review voucher, which is intended to accelerate introduction of products onto the developed country market, TIPR will work by extending market exclusivity for top-selling products in developed country markets. This will delay the time at which generic companies can enter the market and increase health-care costs accordingly.

Technical feasibility

The proposal in its simplest form, whereby a voucher is provided on licensing a qualified product, is technically feasible, as has been demonstrated in the case of the priority review voucher.

The TIPR has an advantage over the priority review voucher as an incentive mechanism in that the value of the tradable voucher is potentially more certain. It can be applied, for instance, to a patent extension on the best-selling medicine on the market and its value in the marketplace should reflect this. In the case of the priority review voucher, by contrast, there are two uncertainties – the length of additional marketing time gained through priority review and having to choose a product for priority review without knowing how successful it might be in the market.

The other aspect is the value of the reward necessary to stimulate additional R&D. This would depend on assumptions about the costs of R&D and the margin on existing sales. One estimate for Europe is that the required additional exclusivity would be 1–6 years (*1*) on the basis of an estimated TIPR value varying between €350 million and €1130 million.

As noted above, technical feasibility may be affected by otherwise desirable measures to improve specificity and impact which would considerably add to complexity.

Financial feasibility

The proposal is financially feasible in its simplest form in that, like the priority review voucher, it imposes few direct costs on governments. However, the cost of the additional market exclusivity will be a substantial burden on health-care costs borne by patients, insurers and/or governments. This is one reason some people oppose the TIPR on grounds of equity. The impact could be mitigated if the health-care budget was subsidized, for example, by that of the government's development agency.

However, that would then raise the question as to why a monetary reward was not offered directly to a company rather than through a more complicated TIPR regime with its attendant costs.

Implementation feasibility

This proposal has not yet generated significant support. More work would need to be done to define the details of the scheme, particularly:

- the size of the incentive required, possibly differentiated according to the public health value of the product;
- what additional criteria and conditions might be necessary to promote appropriate innovation and access to products in developing countries;
- appropriate ways to address the issue of equity arising from the impact of extended market exclusivity in the developed country.

Table 15 provides a summary assessment of the proposal.

Table 15. CEWG summary assessment of transferable intellectual property rights

Criterion	Comment
Public health impact	No evidence of impact.
Efficiency/cost-effectiveness	Dependent on evidence of impact.
Technical feasibility	Feasible.
Financial feasibility	Low direct costs, but high indirect costs in developed countries.
Intellectual property	Extends exclusivity period on best-selling product, and beneficiary may acquire and exploit intellectual property rights in developing countries.
Delinking	No impact.
Access	Does not promote access.
Governance and accountability	Would involve rules-based governance according to legislation.
Capacity-building	Not addressed.

Reference

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Appendix 4

Regional Consultation Meetings

In accordance with World Health Assembly resolution WHA63.28 we convened regional consultation meetings. These meetings were held in order to examine the appropriateness of different R&D financing approaches under review by us and to examine the feasibility of implementing these approaches in each of the six WHO regions. The regional consultation meetings also served to familiarize Member States with our work in the context of the Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property and to elicit feedback to our work from Member States in each of the WHO regions.

Issues raised in the regions were diverse, reflecting different national situations and the mix of people participating. We took account of these issues in reaching our conclusions.

Regional meetings took place on 27 August 2011 in Abidjan, Cote d'Ivoire, for the African Region; on 7 October 2011 in New Delhi, India, for the South-East Asia Region and on 13 October 2011 in Manila, Philippines, for the Western Pacific Region. A virtual conference for the Americas Region was held on 7 November 2011.

No dedicated regional consultation meeting was convened in the WHO European Region. However, the group's work was presented and discussed on 5 October 2011 at the 7th European Congress on Tropical Medicine & International Health which was held from 3 to 6 October 2011 in Barcelona, Spain.

No regional consultation meeting took place in the WHO Eastern Mediterranean Region. Attempts to hold such a meeting failed due to the limited time frame and the busy working schedules of regional members.

Reports of all meetings can be found at: http://www.who.int/phi/news/cewg_regional_consultations/en/index.html.

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