

Public health, innovation and intellectual property: global strategy and plan of action

Report of the Expert Working Group on Research and Development Financing

The Director-General has the honour to transmit to the Sixty-third World Health Assembly the full Report of the Expert Working Group on Research and Development Financing¹ (distributed separately) and its executive summary (Annex).²

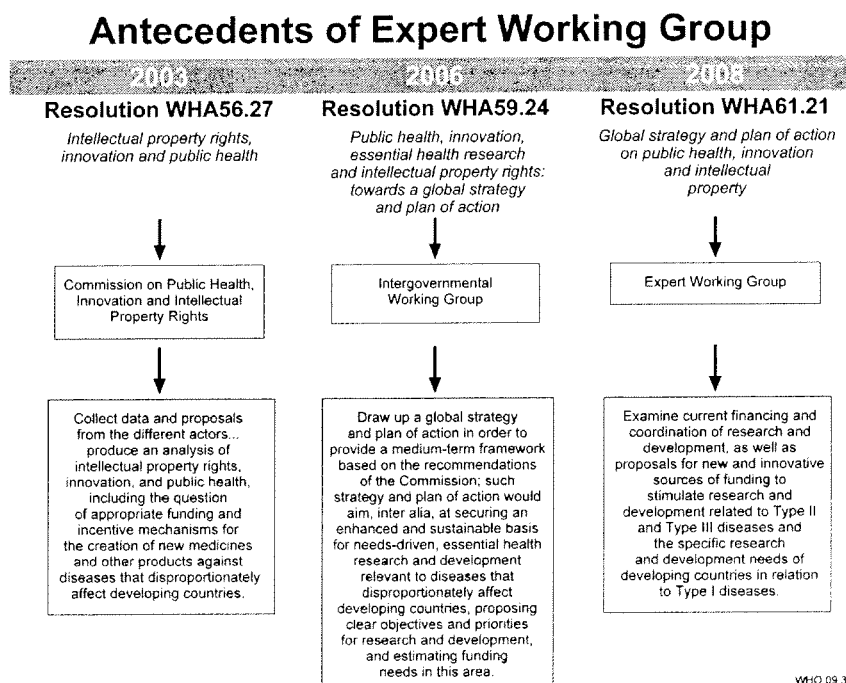
¹ World Health Organization. Report of the World Health Organization expert working group on research and development financing. Geneva, World Health Organization, 2010.

² Originally issued as document EB126/6 Add.1.

ANNEX
**REPORT OF THE EXPERT WORKING GROUP ON RESEARCH
 AND DEVELOPMENT FINANCING**

Executive summary

1. There is persistent and growing concern that the benefits of the advances in health technology are not reaching the poor. The emphasis of the developed world is naturally on the solution of the problems that affect it predominantly. This is in spite of the evidence of the heavy burden of disease on the poor, which in addition to being one of the more egregious manifestations of inequity, could undoubtedly affect overall global stability. There is convincing evidence of the poor bearing a double burden of disease, but there is still no indication of adequate research and development to address the Type II and III diseases.¹ This growing focus on the diseases of the poor has led to examination of the relationship between intellectual property rights,² innovation and public health, and the gap in the innovation cycle with the concern that the commercial incentives provided by intellectual property rights have not resulted in sufficient improvements in public health in developing countries or to access to the benefits of innovations that take place in the developed world. The Director-General of WHO established an expert working group to address some of these challenges in the context of the Global strategy and plan of action on public health, innovation and intellectual property. The chart below gives a description of the evolution of the Expert Working Group (EWG).



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.

² Intellectual property rights include copyright, patents, trade marks, and trade secrets. In the context of this report, they primarily concern patent rights.

2. The Working Group decided from the beginning to adhere strictly to the mandate as given and not to address the several issues that remained unresolved from the work of other groups. Thus the report is structured to address:

- current financing of research and development;
- coordination of research and development;
- proposals for new and innovative sources of financing to stimulate research and development.

3. The Working Group had to complete its work within a year. It held three face-to-face meetings in Geneva in January, June/July and November/December, 2009, and much of its work was done by soliciting public comment and submission electronically as appropriate.

4. The Group commissioned several background papers to inform its work. The first meeting entertained a series of presentations from groups and organizations which have interest or expertise in the area. All presentations as well as the background papers and the individual submissions to the group are available on the WHO web site. Subsequent meetings discussed and evaluated the extensive material presented. Most of the work between meetings was conducted by virtual consultations on various proposals and report drafts. It was gratifying and an indication of interest that there was much comment through public hearings. The membership of the Group was drawn from a wide cross-section of countries and disciplines.

5. The following represents a synthesis of the Group's work and conclusions/recommendations in line with its mandate.

I. FINANCING OF RESEARCH AND DEVELOPMENT

6. There is a need for incentive structures to stimulate research and development when there is no market or there is market failure in the production and diffusion of knowledge. The EWG examined this in the context of the nature of knowledge as a public good and pointed out the two main incentive structures available, which basically are the intellectual property rights and public support. The relevance of the integrity of intellectual property rights is well documented with respect to the need to foster and favour research and development. However, attention was paid more specifically to the role of public support and the need to reinforce this in both developed and developing countries in the provision of knowledge leading to appropriate technologies of particular interest to the developing countries. Direct public support is through grants, procurement contracts and prizes. The use of one or the other is highly context specific. Indirect public support may be through such measures as tax exemptions. A framework for financing options for research and development considers two dimensions.

- (a) The first is whether the knowledge required by the poor already exists. If it does, then the challenge is mostly associated with ensuring the diffusion of knowledge. If it does not exist, then the challenge is to ensure that it is generated.
- (b) The second is whether the innovations (knowledge) are relevant for the poor only, or are relevant both for the developing and developed countries.

7. The most troubling situation occurs when knowledge that is predominantly applicable to the problems of the poor developing countries does not exist and therefore needs to be generated.

8. The financing of research and development was examined, dividing diseases into the noncommunicable and the communicable groups (NCDs and CD, respectively) for ease of analysis and because the data sources lent themselves to this analysis more readily than if the taxonomy of Types I, II and III had been used. Three categories of funding were examined: public (France, Germany, Japan, United Kingdom of Great Britain and Northern Ireland and United States of America), industry and charity/private foundations. There were limitations in the data sources, but there are enough data to allow general conclusions; see Figures 1–3.¹ Figure 1 shows the allocation of funding by the public sectors of five countries to research on NCDs and CDs. Figure 2 indicates the number of drugs in development by 10 major pharmaceutical companies for CDs, NCDs and other diseases; the research and development budget of these companies in 2008 (US\$ 43 900 million) was 62.4% of the whole pharmaceutical industry's research and development budget. Figure 3 shows the split of the US\$ 2500 million investment by private not-for-profit institutions into research and development for CDs and NCDs.

Figure 1. Allocation of funding by the public sectors of five countries

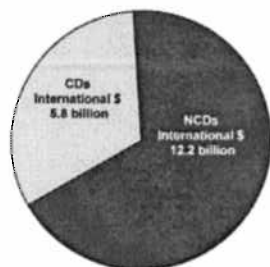


Figure 1 shows the allocation of funding by the public sectors in the five countries: International \$ 12.2 billion to research on NCDs and 5.8 billion to CDs.

Figure 2. Number of drugs in development by 10 major pharmaceutical companies for communicable, noncommunicable and other diseases

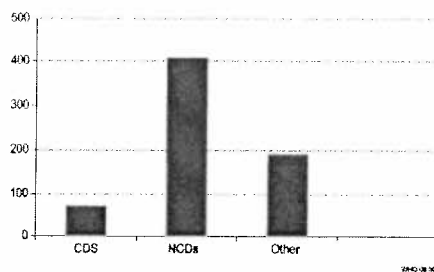


Figure 2 shows the number of drugs in development by 10 major pharmaceutical firms for communicable, noncommunicable and other diseases. The research and development budget for these companies for 2008 (US\$ 43.9 billion) was 62.4% of the whole pharmaceutical industry's budget for research and development.

¹ Figures 1–3 were derived from Feletto, M. & Matlin, S. in *Global R&D Financing for Communicable and Non-communicable Diseases: A Report to the WHO Expert Working Group on R&D Financing* (October 2009).

Figure 3. Percentage distribution by private not-for-profit institutions for R&D into communicable and noncommunicable diseases



Figure 3. A total of US\$ 2.5 billion was identified as investment by private not-for-profit institutions and the Figure shows the percentage distribution.

9. The total sector investments in research and development by category reflect the predominance of funding dedicated to noncommunicable diseases. Cancer funding dwarfed expenditure in all categories (Table 1).

Table 1 Total sector investments in health research and development (R&D) by category in International \$ million (2008)

| Category | Public Sector | | Private Sector | | Not-for-profit | | Total | |
|----------------------------|-----------------|--------------|-----------------|--------------|----------------|--------------|-----------------|--------------|
| | R&D (\$ mn) | % | R&D (\$ mn) | % | R&D (\$ mn) | % | R&D (\$ mn) | % |
| Noncommunicable total | 12 168.7 | 67.8 | 29 390.0 | 68.4 | 1 650.4 | 66.7 | 43 209.1 | 68.2 |
| Communicable Disease Total | 5 766.2 | 32.2 | 13 590.0 | 31.6 | 822.9 | 33.3 | 20 179.1 | 31.8 |
| Total | 17 934.9 | 100.0 | 42 980.0 | 100.0 | 2 473.3 | 100.0 | 63 388.2 | 100.0 |

10. Resource tracking is seen as indispensable for any attempt at monitoring coordination of financing for research and development. This relatively new field has been pioneered by the then Commission on Health Research for Development, which initially in 1986 estimated that the world spent US\$ 80 billion on health research and development but about 5% of that sum was being applied to the health problems of the developing countries. Currently there are increasing amounts of data on official development assistance (ODA) and the financial flows to health but a comprehensive system for analysis of the flows to research and development is lacking and should be established.

II. COORDINATION OF RESEARCH AND DEVELOPMENT

11. There is no global coordination of research and development for diseases generally and less so for Types II and III. Analysis of coordination by disease, health area or by product could elucidate examples in each area, but there was no overall coordination mechanism. Each of the examples chosen could demonstrate coordination internal to the area usually through committees, boards and technical specialist groups.

12. There has been more progress in policy coordination for research and development and various forums have been established to allow international funders and agencies for international development to coordinate and harmonize their efforts. One such example is Enhancing Support for Strengthening the Effectiveness of National Capacity Efforts (ESSENCE), which is a collaborative framework for funding agencies to ensure synergies in addressing research capacity needs. It aims to

improve the impact of investment in institutions and enabling mechanisms that address the identified needs and priorities within national strategies on research for health.

13. Mapping tools for initiatives in research and development have been developed and provide information to interested donors and researchers. One such example is the Health Research Web, a web-based, interactive and growing source of information from the Council on Health Research for Development on the structure and organization of research for health in and for low- and middle-income countries. The tool, which is aimed at maximizing the impact of research on health, equity and development in low- and middle-income countries, is a response to the problem that there is no single source of information on research for health that is organized from the perspective of those countries.

14. WHO itself has recognized the need for coordination of research internally¹ and the Secretariat has initiated a process for coordination of the eight health research organizations and initiatives that have some role in the oversight and reporting on research globally, although they are not themselves engaged in research.

15. Any global coordination of research and development is challenging and will need to identify priority areas for action; the distribution of the needed research effort between the different competent entities and the financing of the research and development.

16. A global health research and innovation coordination and funding mechanism should be created with support from various sources including voluntary, business, government, and consumer contributions, including contributions that may arise from those listed in recommended action 8 below, in order:

- (a) to target research and development for new drugs, vaccines, diagnostics, and intervention strategies against priority health conditions of the poor;
- (b) to support a range of research areas that are essential for improving health including health policy and health systems research;
- (c) to enhance innovation capacities and environments in low- and middle-income countries;
- (d) to operate a health research observatory with regional expression to monitor disease and track research and development resources regularly.

III. PROPOSALS FOR NEW AND INNOVATIVE SOURCES OF FINANCING

17. More than 90 proposals are currently in circulation or have already been implemented. Around half of these are pure financing proposals; a further nearly-half are not financing proposals at all. They include proposed structures to centralize, manage and disburse funds to health research and development (if funds were to be available), but they do not have mechanisms to raise these funds. A small number of proposals both raise and allocate funds. Each proposal was assessed for suitability to

¹ At its 124th session in January 2009, the Executive Board considered a draft WHO strategy on research for health and, in resolution EB124.R12 it recommended the Health Assembly to endorse that strategy. In May 2009, the Sixty-second World Health Assembly decided to postpone discussion of the matter, proposing that it be included on the provisional agenda of the Sixty-third World Health Assembly in May 2010.

its stated disease and product target, and for its likelihood of incentivizing developers to commence or increase their research and development activities.

18. Taking into account considerations related to health inequity, it is important to note that the amount of funding needed for any health research and development activity depends on several key factors:

- Does the solution for the health problem have a substantial market/some market/no market?
- Does the solution for the health problem have a sound science and technology base?
- What kind of research and development is needed?
- How well does the proposal match the needs of the target group?

19. For each of these factors there are very different cost structures, business models and needs. As a result of these differences, it is unlikely or impossible that a single allocation proposal could efficiently address all disease and product needs, and the requirements of all relevant development groups.

20. A suite of proposals has been chosen that cover research and development from basic research through to distribution; that are best suited to maximizing research and development activity by all potential target groups and that deliver maximum public health return for any given investment. The three main criteria for analysis were developing country impact, financial aspects and operational efficiencies. On this basis a shortlist was drawn up of:

- three proposals for financing mechanisms that will more than double available funds for research and development for neglected diseases of the developing world;
- five proposals for funding allocation mechanisms that should optimally allocate both existing funds and new funds raised by the three proposed financing mechanisms;
- two efficiency proposals aimed at cutting research and development costs across the board.

Financing proposals

21. Having considered a wide range of options, the EWG put forward the following fundraising proposals based on the likelihood they can generate new funds for health research and development in a sustainable way:

- (a) a new indirect tax (a consumer-based tax)
- (b) voluntary business and consumer contributions
- (c) new donor funds for health research and development.

(a) A new indirect tax

22. Indirect taxes involve a small tax being imposed on specified products or transactions and could potentially raise very significant amounts of revenue. Examples given include the following:

- a 10% tax on the arms trade market, which might net about US\$ 5 billion per annum;
- digital tax or “bit” tax: Internet traffic is huge and likely to increase rapidly; this tax could yield tens of billions of US dollars from a broad base of users;
- Brazil’s financial transaction tax – Contribuição Provisória sobre Movimentação ou Transmissão de Valores e de Créditos e Direitos de Natureza Financeira (CPMF): a tax on bank account transaction, set at 0.38% levied on paying bills online and major withdrawals, it was raising an estimate US\$ 20 billion per year and funding some 87% of the Government’s key social protection programme, Bolsa Família, before it was voted down;
- the UNITAID airline tax has raised around US\$ 1 billion since it was launched in September 2006; 13 countries have already passed the necessary legislation and several are in the process of doing so. UNITAID attests to the fact that an international solidarity micro-levy is well accepted by the public and causes no economic distortion.

23. Using the airline tax as a guideline, the introduction of an indirect tax (e.g. a very low digital tax) could be estimated to raise funds in the low billions of dollars. Introducing a new tax or expanding an existing tax may require legal changes, nationally and internationally, depending on the tax, and ongoing regulation to ensure compliance. As with the introduction of any tax there are trade-offs. For example, there is only moderate certainty over revenue forecasts as actual revenue will depend on the response of providers and consumers to price rises associated with the tax and scope of the tax.

(b) Voluntary business and consumer contributions

24. Voluntary consumer contributions are donations made by individual consumers and operate in three different ways:

- voluntary linking of a donation to the payment for a service (e.g. payment of mobile phone bills or payment of income tax);
- automatic donations directly to a particular recipient (e.g. standing order payments to Oxfam);
- voluntary but non-automatic donations (e.g. private-giving campaign or endowment). An income tax donation allows an individual to make a contribution from their income which government will match with the income tax that would have been paid.

25. Voluntary contributions have less-certain funding streams than a tax, but once established are reasonably predictable. The size of revenue raised varies:

- airline ticket voluntary solidarity contribution is expected to raise about US\$ 980 million per annum, although these expectations have since been revised downwards¹
- mobile-phone voluntary solidarity contribution would raise from € 200 million to € 1.3 billion, according to the Millennium Foundation
- contributions from credit cards
- De-Tax could raise up to US\$ 2.2 billion calculated on a base of 26 countries and 5% business uptake.¹

26. Using the Product Red initiative as a guide, the introduction and use of the voluntary business-sector contribution could be estimated to raise in the order of US\$ 40 million annually. Using the airline voluntary solidarity contribution as a base to estimate voluntary consumer contributions, these could raise around US\$ 1 billion per annum. A combined estimate of both brings this to around US\$ 1 billion or more per annum. Introducing voluntary contribution schemes, like the airline ticket voluntary solidarity contribution, is not expected to have any legal obstacles nor require amendments to international laws. However, other mechanisms, like De-Tax, do require changes to law.

(c) New donor funds for health research and development

27. This mechanism considers three main sources of funding:

- additional funding from new donors, non traditional donors, who are not currently included in OECD's Development Assistance Committee (DAC), such as China, India and Venezuela
- additional funding from existing DAC donors (for example, earmarking a percentage of GDP for health research and development)
- additional funding from philanthropic organizations.

28. This differs from diverting existing resources in that it is based on projected additions to funds raised that could be allocated to health in the future. The High-Level Taskforce on Innovative International Financing for Health Systems estimates that additional funding for health might grow to some US\$ 7.4 billion per annum by 2015 from traditional donors² (under optimistic assumptions and if donors meet their commitments to aid) and that developing country contributions *might be* in the range of US\$ 9.5–12.1 billion per annum. However, there would be a gap in available additional funds until then, as additional resources rise from US\$ 2.8 billion in 2009 to US\$ 7.4 billion in 2015. Using these estimates and removing the potential for double counting from the indirect tax,³ and assuming 10% could be earmarked for health research and development, new donor funds could amount to about

¹ http://www.internationalhealthpartnership.net/CMS_files/userfiles/FS_DeTax_raffaella%20final%20final.pdf.

² Taskforce on Innovative International Financing for Health Systems, 2009 – Constraints to Scaling Up and Costs, Working Group 1 Report.

³ About US\$ 3 billion.

US\$ 440 million per annum by 2015. An argument for directing some of this new stream of funding to health research and development can be made, as some countries already direct part of their health aid budget towards research and development for developing countries. However, channelling these resources in this way can only be achieved if there is political will to do so and a convincing case is made. These funds do not include additional contributions from philanthropic organizations, nor innovative developing countries themselves, and as such the estimates are conservative.

29. The proposed suite of mechanisms provides a balance between:

- developing and developed country contributions
- consumer, government and the pharmaceutical industry contributions
- voluntary and non-voluntary (i.e. taxes) contributions
- some that would require managed and sustained political commitment: new donor funds and taxes; while others would not: voluntary consumer and business contributions
- those that would need effort to be operationalized (new taxes) and those that have less operational requirements (voluntary contributions).

Taxes would provide greater certainty once in place than voluntary contributions.

30. Potential estimates of funds raised from these combinations are in the order of US\$ 4.6 billion (by 2015). All these funding alternatives and decisions ultimately rest with national governments and individual philanthropic organizations.

Funding allocation proposals

31. The following five proposals provide funding allocation across most research and development stages and developers in a manner that is best designed to maximize public health returns in the developing world:

- (a) funding via product development partnerships;
- (b) direct grants to small and medium-sized enterprises and grants for developing country trials;
- (c) milestone prizes;
- (d) end-prizes (cash);
- (e) purchase or procurement agreements.

(a) Funding via product development partnerships

32. Product development partnerships operate on a not-for-profit basis and as “quasi venture capital funds” in the domain of developing world health. They raise funds from a wide range of public and philanthropic sources, select the projects that offer the likely highest health return for investment, and closely monitor and manage the progress of the portfolio they have invested in. They have large product portfolios across many Type II and III disease areas (but only marginal activity in Type I disease

areas), and currently manage around nearly 30% of global neglected-disease research and development grant funding in 2007; and around half of global grant funding, if the National Institutes of Health in the United States of America is excluded. As a result, they act as a major consolidator of public funding, investment risk, and global coordination of research and development in their given field. These partnerships invest predominantly in product discovery and development. Currently, they have no reliable revenue stream, being entirely reliant on annual donor funding. As a result, three proposals are in circulation to provide reliable, long-term funding to product development partnerships, and to automate or centralize funding decisions across product development partnership portfolios to a lesser or greater degree. These are:

- Fund for Research and Development in Neglected Diseases
- Industry Research and Development Facilitation Fund
- Product Development Partnership Financing Facility.

33. The proposed product development partnership funding mechanisms performed variably in the evaluation on developing country impact, operational efficiency and feasibility. Overall, product development partnerships score very highly on developing country impact because of their focus on developing affordable suitable products for developing country use; their routine practice of working with developing country researchers and developers; and, to varying degrees, their capacity building efforts in developing countries. Donors are increasingly favouring product development partnerships as their vehicle of choice to disburse neglected-disease funding, while smaller donors may disburse virtually all their funding in this manner (likely reflecting the ability of product development partnerships to minimize donor management needs).

34. The product development partnership route offers high developing-country health impact and operational efficiency, and is the only mechanism that successfully stimulates early and ongoing involvement of multinational corporations. However, a mechanism is needed to assist donors to fund across product development partnerships in a far simpler manner than is currently possible. Product development partnerships do not cover all areas of Type II and III needs, and all are not equally efficient.

(b) Direct grants to small and medium-sized enterprises and grants for developing country trials

35. Many countries and some philanthropists provide direct grants or contracts to small and medium-sized enterprises in areas of public health importance where venture capital may be either suboptimal or lacking entirely. Direct grants are vital for cash-constrained small firms, which need push funding in order to conduct research and development. Funding schemes for small and medium-sized enterprises fall into two categories: grants or contracts to developed-country companies to conduct research and development relevant to developing countries; and grants within developing countries (especially innovative developing countries) to conduct locally relevant research and development.

36. Typical schemes in circulation or submitted to the Expert Working Group include:

Developed-country grant/contract schemes for small and medium-sized enterprises

- the Small Business Innovation Research Programme: funded through the United States Government National Institutes of Health to provide early-stage finance for small innovative businesses to bring technologies to market
- the Small Business Research Initiative in the United Kingdom: a programme that provides innovative solutions to specific issues identified by the public sector by engaging a broad range of companies in competitions for ideas that result in short-term development contracts.

Developing-country/Innovative developing-country grant schemes

- Projeto Inovar (Project Innovate) is a strategic action of Financiadora de Estudos e Projetos, an agency of the Brazilian Federal Ministry of Science and Technology, aimed at promoting the development of small and medium-sized businesses
- in India, the Small Business Innovation Research Initiative, initiated by the Department of Biotechnology, promotes high-risk pre-proof-of-concept research and end-stage development by small and medium-sized enterprises.

37. In terms of health impact in developing countries, developed country-based schemes performed less well, since they do not clearly and specifically target developing country needs and define developing country-relevant outputs. Small developers (small and medium-sized enterprises, innovative developing countries and diagnostic firms) gave unanimous support to direct grant programmes, rating this as one of the two incentives most likely to stimulate them to commence or expand developing country research and development programmes. Large companies were less likely to respond, although they noted that grant programmes would be a very welcome support to subsidize the costs of large-scale clinical trials in developing countries. These grant schemes were rated very highly by all donors, public and philanthropic, developed and developing countries.

38. Developed- and developing-country grant schemes are a clear priority to encourage broad participation of small and medium-sized enterprises in developing country-relevant research and development, with developing country-based schemes being particularly promising.

(c) Milestone prizes

39. Milestone prizes are cash prizes given for reaching interim steps along the development pathway and are best suited to solving basic research and technical questions, but are unlikely to be useful for clinical development. Only one pure prize proposal was presented to the EWG. However, a number of more complex proposals include a milestone prize element.

40. InnoCentive, for example, is a pure prize. It is an online marketplace where “seekers” (public, private and philanthropic) can post challenges. The award is paid to the solver who best meets the solution requirements, and a commercial agreement is then negotiated with the seeker. InnoCentive performed particularly well in terms of developing country capacity building, with over one third of InnoCentive’s solvers being located in the developing world.

41. Milestone prizes are easy to put in place, scalable and have no administrative or legal hurdles. Their operational efficiency and feasibility scores were therefore high, and would likely be higher if

data gaps had not existed. The InnoCentive milestone prize system is also strikingly cost effective, with an average of 300 problems posted per year (and around 130 solved) for an annual cost of US\$ 6–9 million. InnoCentive-style milestone prizes are a highly cost-effective way to encourage small firms to generate innovative solutions to basic research questions and technical problems up to the point of clinical development. However, maximum buy-in from the private sector is likely to be obtained by managing prizes within the intellectual property system. Prize design is crucial to generating high developing country impact.

(d) End-prizes (cash)

42. Cash end-prizes propose providing a large lump sum at the end of the development process as a reward for product development. The prize can be awarded as a pure reward for innovation, allowing the intellectual property-holder to retain rights to their product, or as a “fee” to purchase the intellectual property rights from the developer to allow free exploitation by the prize-giver. Although the notion of cash end-prizes has been generally discussed, only one such proposal was submitted to the EWG, the prize fund for development of a low-cost rapid diagnostic test for tuberculosis.

43. End-prizes are likely only suitable for diagnostic development, where prizes sufficiently large to reward developers are within reach of public funders. The developing country health impact of the prize would be optimized by intellectual property-buyout prizes rather than prizes purely as a reward for innovation.

(e) Purchase or procurement agreements

44. Purchase or procurement agreements are contracts between a purchaser (often a government, regional or multilateral group) and product developers, which set the price at which a product will be purchased and/or the volume of product that will be supplied. Most agreements apply to generic products and are designed to secure bulk price discounts and security of supply, but they do not stimulate research and development. A more recent innovation is purchase agreements for novel products or products still in development. Examples of such agreements include:

- minimum volume guarantee
- minimum volume guarantee for a novel product
- affordable medicines facility – malaria
- advance market commitment pilot, whereby donors commit to price and volume purchase contracts with companies for as-yet-undeveloped vaccines that meet public health requirements.

45. Performance of purchase agreements for novel products varies significantly depending on the design of each agreement. The advance market commitment performs least well, because of its failure to preferentially incentivize low cost-of-good products and thus low prices, and its weak technology-transfer stimulus; it is also operationally complex and scored low on political feasibility as it would be extremely difficult to scale up for broad use.

46. The affordable medicines facility – malaria gained the highest rating of all, since it uses bulk procurement to secure lowest price, and also requires participating countries to ensure access to even the poorest populations as part of their national product roll-out plans.

47. All purchase commitments for novel developing-country products struggle to achieve financing, with donors and recipients historically accepting a long wait for cheaper generic versions. Developers gave purchase commitments the highest ranking of all the proposals reviewed, with a unanimous top rating by large and small companies, innovative developing country firms, diagnostic companies and product development partnerships. All developers felt that purchase commitments – or rather, demonstrated government willingness to purchase products – was the best advance signal of demand they could have, and would incentivize them to conduct research and development.

48. Purchase funds for novel products are a vital factor in stimulating increased research and development and providing large-scale access to new products; they are also well suited to steering existing programmes towards developing country needs, for example, research and development programmes for Type I diseases that would otherwise focus on developed country product profiles and on production capacity to meet developed country needs. However, purchase agreements do not have a mechanism to decrease the price of new products, particularly if there is limited or no competition with similar products. Better outcomes may be achieved by pooled price negotiations or by early signals to developers as to the desired developing-country-friendly (and developing country price-friendly) profile for the final product.

Efficiency proposals

49. The following two proposals reduce research and development costs across the board, and thus reduce overall future research and development funding needs and expedite access to new products by the developing world:

- (a) regulatory harmonization (developing country-focused);
- (b) pre-competitive research and development platforms.

(a) Regulatory harmonization (developing country-focused)

50. A large proportion of the cost of developing and marketing a new product relates to regulatory requirements to establish that the product is safe, effective and of high quality before it is administered to patients in large numbers. An additional “quasi-regulatory” stage is in place courtesy of WHO processes aimed at assessing registered products for their suitability for developing-country use. Developing-country regulatory harmonization has begun in some regions, but progress is slow. Developing-country regulatory harmonization is likely to have a very high developing country impact, since the single act of harmonization facilitates more rapid registration of many products (both generic and brand) in many countries, and may lead to product registration in countries that would otherwise not have had access to that product at all.

51. Harmonization is feasible. However, it ranks only moderately in terms of operability. Disparate national legislative frameworks are a substantial obstacle. Countries may not have sufficiently high levels of trust to move to a harmonized system regionally (it took the European Medicines Agency nearly 40 years to do so); national sovereignty issues may emerge; and loss of income from regulatory fees can pose difficulties for resource-poor nations. Product developers consistently rated regulatory efficiencies as a number one priority.

52. Political will to move forward on developing-country regulatory harmonization and integration would be a major cost-saving and greatly increase developing-country access to quality products.

(b) Pre-competitive research and development platforms

53. Development of pre-competitive research and development platforms, which are tools to increase the efficiency of research and development across many products and deliver high-value efficiencies, requires up-front investment. Examples of pre-competitive platform research include:

- the European Commission's Innovative Medicines Initiative, co-funded by the European Union and the European Federation of Pharmaceutical Industry Associations, which awards research grants to European public-private collaborations working to develop platform breakthroughs;
- the non-profit organization PATH, a product development partnership based in the United States of America, develops enabling and platform technologies that are made available to all companies making relevant products for its programmes;
- the US National Institutes of Health has a number of mechanisms for developing and distributing research platforms for neglected-disease research and development such as animal models, unique materials, and genomic sequence databases. Several organizations such as the National Institutes of Health and the UNICEF/UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases also offer free pre-clinical compounding testing for academic and industrial scientists.

54. Both companies and product development partnerships ranked investment into pre-competitive platforms as a top priority, noting for instance that "ways to reduce the cost of, and simplify, research and development is a real gap", and that "surrogate marker work is incredibly important to accelerate research and development".

55. Investment into pre-competitive research and development platforms targeted at developing-country products can deliver substantial cost-savings for all development programmes in that disease area, but tends to be poorly supported because of public-good/free-rider issues. Political will in this area would make a substantial difference.

Other proposals

56. A number of promising proposals were analysed which included: open source; patent pools (UNITAID model); Health Impact Fund; priority review voucher scheme; and orphan drug legislation.

Comment

57. The proposed allocation and efficiency mechanisms provide coverage of Type II and III diseases in an efficient manner, and are well suited to maximizing developer activity. If the provisos noted are taken into account, they are also expected to provide good public health and capacity building results for the developing world. Some of the recommended approaches are already in place, or the general approach is in place to act as a framework, host or model for a developing country-specific version of the mechanism (e.g. product development partnerships; grant schemes; milestone-prize vehicles; purchase or procurement funds hosted by the GAVI Alliance, the Global Fund to Fight AIDS, Tuberculosis and Malaria and others; regulatory harmonization and integration initiatives; and isolated pre-competitive platform initiatives within individual organizations). Other proposals would require implementation, including mechanisms to fund product development partnerships and cash end prizes.

58. Unlike many lower-performing proposals that have been discarded, *none* of the recommended mechanisms has a revenue stream, with all currently relying on donor contributions and philanthropy. The financing mechanisms proposed in the report are, however, well suited to address these funding deficits.

59. Type I disease products do not fare so well. The recommended mechanisms cover developing country-relevant adaptations of Type I products fairly well, but are less effective in ensuring low prices for these. However, as noted above, there were no effective proposals to address gaps in developing country access to patented Type I products.

IV. RECOMMENDATIONS

60. WHO should undertake the actions outlined below, including, where appropriate, linking these to the implementation of the Global strategy and plan of action on public health, innovation and intellectual property in order to support achievement of the goals of the United Nations Millennium Declaration:

- (1) develop information for dissemination on the background to the development of incentives for the production of knowledge as a basis for developing the tools necessary to address health problems in developing countries including health systems research as an essential underpinning for the development of equitable and universal health services;
- (2) take note of the relationship between research and allocation of funds and burden of disease and health risks that disproportionately affect developing countries within the context of reducing health inequity;
- (3) support efforts at resource tracking, which is indispensable to an understanding of the distribution and coordination of financing for research and development;
- (4) support the creation of a global health research and innovation coordination and funding mechanism with support from various sources, including voluntary, business, government, and consumer contributions and contributions that may arise from those listed in recommended action 7 below, in order to:
 - (a) target research and development for new drugs, vaccines, diagnostics, and intervention strategies against priority health conditions of the poor;
 - (b) support a range of research areas that are essential for improving health including health policy and health systems research;
 - (c) enhance innovation capacities and environments in low- and middle-income countries;
 - (d) operate a health research observatory with regional expression and ownership to monitor disease and track research and development resources regularly;
- (5) build on and promote in countries, the adoption of locally relevant public policy choices to bring together the technological capabilities of the public and private actors, in order to

generate missing knowledge and create incentive structures to stimulate research and development for appropriate technologies of interest to the developing countries;

(6) facilitate regional approaches to research collaboration and funding in developing countries, making full use of the potential of innovative developing countries to break new ground in research collaboration, capacity building including training in clinical and translational research, serving to facilitate partnerships with other research institutions, private industry collaborators and product development partnerships;

(7) follow up the work of the Expert Working Group and:

(a) conduct an in-depth review of proposals with appropriate groups within both the recommended and promising approaches;

(b) mobilize appropriate groups with adequate representation from developing countries and including the international financing institutions to test the acceptability of some or all of the final proposals for implementation;

(c) begin matching revenue streams to allocation mechanisms and involve donors in a formal process to conduct this exercise;

(d) begin discussion on a mechanism to coordinate funding allocated by proposals outside the product development partnership model;

(e) determine which mechanisms best suit specific health problem areas, and prioritize their implementation by disease and product;

(f) examine in detail developing-country access to products that address Types I, II and III diseases and which may require different combinations of solutions in addition to research and development;

(8) promote the following suite of approaches:

(a) financing proposals

(i) indirect consumer tax;

(ii) voluntary and individual business contributions;

(iii) new donor funds for health research and development;

(b) funding allocation approaches

(i) product development partnerships-linked funding;

(ii) pure prize proposals, to encourage small firms to generate innovative solutions to basic research questions and technical problems up to the point of clinical development; and end prizes sufficiently large to reward developers for diagnostic development;

- (iii) purchase funds, which are a vital factor in stimulating increased research and development and providing large-scale access to new products;
 - (iv) developing country “regulatory harmonization and integration” in order to facilitate rapid registration of products, in the interest of cost saving, thereby greatly increasing developing country access to quality products;
 - (v) investments in pre-competitive research and development platforms targeted at developing-country products, which can deliver substantial cost-savings for all development programmes in the relevant disease area;
 - (vi) developing-country grant schemes to facilitate direct grants to encourage broad participation of small and medium-sized enterprises in developing country-relevant research and development;
- (9) efforts should be made to examine other promising proposals in their local contexts, such as open source products; patent pools; Health Impact Fund; priority review voucher scheme; and orphan drug legislation.

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