

Note



**Jean-Hervé Bradol**

## **Medical and health innovations within a global health framework**

### **Three questions and some food for thought**

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## Three questions and some food for thought

### By Jean-Hervé Bradol

Research Director  
 MSF Foundation. CRASH

The english translation of this working paper could not be revised by his author. We apologize in case of any inconsistencies or misinterpretation from the original text. The french version is available upon request.

This paper begins by briefly introducing three questions around which the seminar discussion should be arranged:

How are priorities decided?

What kinds of organization and institutional cooperation favor the emergence of new medical and health practices?

How can access to medical and health products and services be ensured?

It goes on to consider other questions in the hope that they will contribute to informed discussion:

What kind of diseases are we talking about?

What are the different categories of innovation?

What were the principal pharmaceutical R&D results for developing countries over the last ten years?

What is the state of R&D for developing countries in 2011?

What are the basic stages of the innovation process?

How should the innovation process be managed?

How are potentially successful innovations identified?

In which fields might medical innovations prove decisive in the next ten years?

## Three questions How are priorities decided?

Over the last few decades, transnational health institutions have made undeniable contributions to the identification of national health priorities in a number of fields. This has also brought about a standardization of national health plans, especially since foreign aid is often conditioned on the adoption of policies promoted by transnational institutions like the WHO.

Priorities were for some time determined in camera by political decision-makers after hearing from relevant experts and enterprises involved. Today, users and practitioners are sometimes invited to the discussions, which take on a public dimension.

Priorities must in the first instance be compatible with the state of science and technology. Funds to cover the additional cost of their implementation must be identified. According to global health institutions, the use of funds should be optimized using a list of priorities which will guarantee the greatest effect at a set cost: i.e., the largest possible reduction of mortality and morbidity on a limited budget. Users and practitioners are rarely consulted. Such decisions are in good part unhindered by the democratic process.

Such an approach, at the end more economic than health-related, means the poorest, who have no say in the matter, are offered primary care (vaccination, nutrition, treatment for common infections in children, and pregnancy monitoring) in limited domains. The emphasis is on prevention (vaccination, mosquito nets, and health information deemed by experts to be the most useful). In short, priority is given to prevention and some inexpensive treatments. The reasoning behind this seems to meet demands that are at once moral and political: save the most lives using a budget that is, by definition, limited.

In fact, there are other parameters affecting government choices lurking behind this financial analysis which seems naturally to determine priorities. Will the implementation of certain priorities forestall the negative effects of certain health events on public security, economic growth, or political stability? Will they be able to avoid enough death and illness before public security is not compromised? Can an epidemic be avoided that would otherwise paralyze the economy and bring enormous losses? On the other hand, will the economic effect of certain health interventions be advantageous to certain economic sectors (chemical, pharmaceutical, insurance, etc.)? Will the chosen priorities help governments avoid accusations of having failed to foresee or plan for health crises?

AIDS upset the balance of power between the participants in these discussions about which medical and health innovations to prioritize. On the one hand, it soon became morally untenable to allow millions to die when a treatment was available, despite the high cost of antiretrovirals. On the other hand, there were a number of economic studies showing that controlling the AIDS epidemic would have a positive effect on economic growth.

Malnutrition, infections, and poor pregnancy management certainly contribute to a large number of deaths in countries with limited resources. Efforts in these areas must, without any doubt, be pursued. But at a time when two-thirds of deaths worldwide are now caused by chronic pathologies (notably cardiovascular disease, cancer, and diabetes), how long can we wait to offer preventative and curative care for such diseases in low- or middle-income countries just to save money?

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## What kinds of organization and institutional cooperation favor the emergence of new medical and health practices?

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With the aim of achieving better results a new institutional model, Products Development Partnerships (PDPs), was proposed and a new philanthropic source of funding became available (the Bill & Melinda Gates Foundation, BMGF, which has spent \$15 billion USD on global health since 1994). The new model establishes economic incentives in the form of research organizations that are likely to improve the performance of both economic and scientific actors. PDPs bring together the private sector (pharmaceutical laboratories, non-profit organizations, philanthropic organizations, etc.) and the public sector (universities, research centers, government agencies, international organizations, etc.). Between 1999 and 2003, more than 15 PDPs were created. Each centered its work on a specific type of product (e.g. medicine, vaccination, or diagnostic test) and on certain diseases (e.g. the Global Alliance for Tuberculosis).

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## How can access to medical and health products and services be ensured?

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A number of conditions must be met to guarantee large-scale use of a new medical service or product.

First, for an innovation to win support, it must meet a need. To this end, users (patients and their families, practitioners) should contribute early in the process to the specifications of the innovation. This means a social and political approach to the creation of the innovation that goes beyond its technical details.

The standards required to produce the object, ensure its effectiveness, and assess its toxicity should be adjusted based on a risk analysis taking into account not only the potential for innovation but also the risk that persistent absence of the innovation would bring about.

If the risk analysis favors the introduction of the innovation in response to demand, the stage of implementation at population scale requires the creation of a new and appropriate economic model.

The innovative object must then be produced regularly, in sufficient quantity, and to a certain level of quality without incurring a cost that would make it too expensive for potential consumers.

The final stages are writing protocols, obtaining administrative authorizations, organizing continuous supply, training personnel, informing users, evaluating efficacy, and pharmaco-vigilance.

Even briefly summarized, the process is long and complex, and requires a multitude of interventions, each decisive, which must be synergized. What is the principal proposition that would allow the streamlining of such an undertaking?

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## Food for thought

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Scientific medicine originated in Europe around 200 years ago. It has only more recently become an efficient approach to personal care and public health. It remains accessible primarily to urban populations with incomes of a certain level or above. For most people, access to scientific medical products and services is limited to consuming – without a prescription – medical products purchased someplace other than a pharmacy. The poor quality or even toxicity of these medicines, which are prescribed irrationally, often leads to disastrous consequences. This doesn't stop the promoters of science from mocking non-scientific medicines as dangerous and inefficient. Scientific medicine is, however, only one of the world's treatments, and not the world's only treatment. Take, for example, the use of artemisinin derivatives, borrowed from traditional Chinese pharmacology, in the treatment of malaria.

Disasters and uneven sanitary conditions are often cited as the result of negligent or discriminatory policies. This accusation against governments is to some extent correct, but over-used, and has become the source of a double illusion.

On the one hand, this characterization of the problem in terms of discrimination (“health apartheid”) or of political negligence presupposes a global authority, the equivalent of a government responsible for such inequalities – and for righting them. The growing power of “global health”, however important it has been over the last few decades, has not given transnational health institutions the power that would reside in a hypothetical “world ministry of health”.

On the other hand, the emphasis on criticizing the lack of will among political leaders assumes the knowledge and capability of medical science to achieve things governments refuse to try. Questioning possible innovations in medicine and health in developing countries challenges scientific medicine to universalize its benefits; it must therefore explore its own limits. Indeed, scientific medicine often offers to solve medical

or health problems by procedures (often with undesirable side-effects) of which the complexity and cost can themselves present serious obstacles to care and prevention for the poorest populations.

Some cultural, educational, or economic initiatives have proven far more effective in improving health than medical care or public health measures. For example, studies have shown a strong relationship between a mother's education and the health of her children.

All of this is intended to temper the enthusiasm – verging at times on intellectual overindulgence – which materializes without fail in response to the mere mention of “medical innovation” and “global health”. This article would nevertheless be meaningless if it didn't recognize that audacious research, adaptation to circumstances in limited-resource environments, and the diffusion of scientific medical products and services have saved the lives of millions each year for the last few decades. Why stop there?

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## What kind of diseases are we talking about?

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Type I diseases (such as cancer or cardio-vascular disease) affect a large number of people in all countries regardless of national income.

Type II diseases (such as tuberculosis and AIDS) affect both rich and poor countries, but occur more often in poorer countries.

Type III diseases (such as sleeping sickness and kala-azar) occur disproportionately or exclusively in poor countries.

In short, current R&D for developing countries focuses on types II and III. In fact, type I diseases are as common in rich countries as in middle- or low-income countries. Demographic and epidemiological changes mean that ubiquitous, non-transmittable diseases now cause two thirds of deaths every year.

## What are the different categories of innovation?

Medical innovation includes a number of innovations across a variety of disciplines.

Some have brought about advances in the individual treatment of patients. The introduction of artemisinin derivatives for the treatment of malaria is an example. Others, such as the use of preventative vaccines against epidemic forms of meningitis, can control morbidities at the population level.

Others involve the introduction on a large scale of recent health products (such as antiretrovirals in middle- or low-income countries), improving the formulations of older products (fixed-dose combinations) in TB treatment, or the new application of old products (using nifurtimox to treat sleeping sickness).

Another kind of innovation changes the way care is organized so as to optimize the use of existing products. For example, more than 6 million people in low- and middle-income countries would have been denied care for HIV were it not for the prescription by nurses of antiretroviral drugs which in wealthy nations are only available from doctors, in some cases only from specialists. This measure would be an innovation in so-called developed countries, whereas, in response to the challenges presented by the frequency of certain diseases, it is a common practice in resource-limited countries.

Some fields, such as rehabilitary nutrition, are not taken into account by studies. Innovations in therapeutic and supplementary nutrition are not seen as major medical innovations despite the fact that they have led to unprecedented improvements in individual care as well as improved morbidity and mortality rates at the population level.

There are several other disciplines that might contribute to this evolution, such as environmental study of the physio-chemistry of pollution (of air, water, and soil).

Other innovations would create a framework (scientific, political, economic, or administrative) favorable to innovation targeting health priorities in developing countries. The end of universal pricing in favor of sliding scales based on national revenue and the softening of intellectual property regulations by the World Trade Organization in 2001 are two examples of this kind of innovation.

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## What drives innovation in global health?

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The World Health Organization (WHO) was founded in 1948. The program to eradicate malaria, launched in the 1950s, was a failure. Success in the fight against smallpox, the eradication of which was announced in 1979, renewed hope that the threat of infection could be curbed.

Beginning in the 1970s, all health sector actors were invited to support states in their effort to turn United Nations goals into reality: the expanded vaccination program (World Health Assembly, WHA, 1974); the essential medicines list (WHA, 1977); universal access to primary care by the year 2000 (Alma-Ata International Conference on Primary Health Care, 1978); the Bamako Initiative to accelerate access to primary health care among African populations (meeting of African health ministers as part of WHO's 37th regional committee); the world initiative for the eradication of polio (WHA, 1988); the Millennium Development Goals concerning health (Millennium Summit, UN headquarters, New York, 2000), including improved nutrition, reduction of child mortality, improved maternal health, and the fight against AIDS, TB, and malaria. In 2003, the Framework Convention on Tobacco Control became the first treaty negotiated through the World Health Organization.

This list of initiatives undertaken since the Second World War should not lead us to conclude that every goal was reached. Progress in global public health cannot be that predictable or regular.

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## What were the principal pharmaceutical R&D results for developing countries over the last ten years?

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This question comes up in public debate in a post-colonial context. Multilateral actions have progressively replaced bilateral cooperation between former colonies and colonial powers. During the same period, large pharmaceutical laboratories progressively abandoned research into infectious diseases affecting the developing world, focusing instead on capturing largest market shares in richer countries. The establishment of Tropical Diseases Research (TDR) by several UN agencies (UNICEF, UNDP, and WHO) and the World Bank in 1976 indicated the willingness of international organizations to improve responses to developing



countries' research needs. This did not prevent the penury linked to the dual absence on the market of health products and medical insurance at prices compatible with the buying power of populations in developing countries.

New infectious diseases emerged in the 1990s (AIDS, hepatitis C, Ebola), while old diseases re-surfaced (cholera, dengue fever, yellow fever). States and international organizations feared pharmaceutical R&D insufficiency could have disastrous effects on security, the economy, and political stability. Deficiencies left public health actors without the means to deal with large-scale epidemics and endemic diseases.

A new institutional model, Products Development Partnerships (PDPs), was proposed to deal with the problem. Meanwhile, a new source of funding appeared, the Bill and Melinda Gates Foundation (BMGF), which has spent \$15 billion USD on global health since 1994. The goal was to create economic incentives and organizational research strategies which were likely to improve the performance of economic and scientific actors. PDPs brought private actors (pharmaceutical labs, NGOs, philanthropic organizations) and public actors (universities, research centers, government agencies, international organizations) together. Between 1999 and 2003, at least 15 PDPs were established. Each PDP focused on a specific type of product (medications, vaccines, diagnostic tests) and specific diseases (such as the Global Alliance for Tuberculosis).

What are the results of this R&D effort for developing countries as of 2011? Data are only available for medications and vaccines. Data allowing quantitative evaluation of diagnostic test development have not yet been generated. The principal sources of information on the registration of medications and vaccines have been checked, but some countries, most notably China, are not included in the analysis. Above all, a dozen years (2000–2011) is not long enough to allow us to judge the efficiency of PDPs. We can at best attempt a mid-term report.

If medical and health innovations have indeed occurred in developing countries, in the last quarter of the 20<sup>th</sup> century these were not the product of any specific R&D. The last few years confirm this tendency. Studies show five new chemical entities were introduced to the market for tropical disease and TB medicines between 2000 and 2011<sup>1</sup>, whereas there were between 16 and 32 (depending on the source!<sup>2</sup>) in the preceding 25 years.

Looking specifically at medicines for diseases primarily affecting developing countries (essentially types II and III), there are more but still insufficient available chemical entities and vaccines. Estimated at less than 3% of all such products between 1975 and 1999, the proportion reached 5.7% ten years later, while the diseases concerned are responsible for 10% of global morbidity.

A peculiar phenomenon makes the situation highlighted by a purely quantitative comparison of new products for wealthy and less wealthy nations look even worse: many of the new substances destined for the market in wealthy countries have little or no effect on the value of medical services offered to patients. While they are, strictly speaking, new chemicals, these new molecules are so similar to existing products that they may have no added therapeutic benefit. They are patented in the hopes of capturing shares in high-grossing markets. Such pseudo-innovations attest to a greed that has led them to be called “me, too” drugs, as in, “pay me, too”. Offering pharmaceutical companies short-term profits,

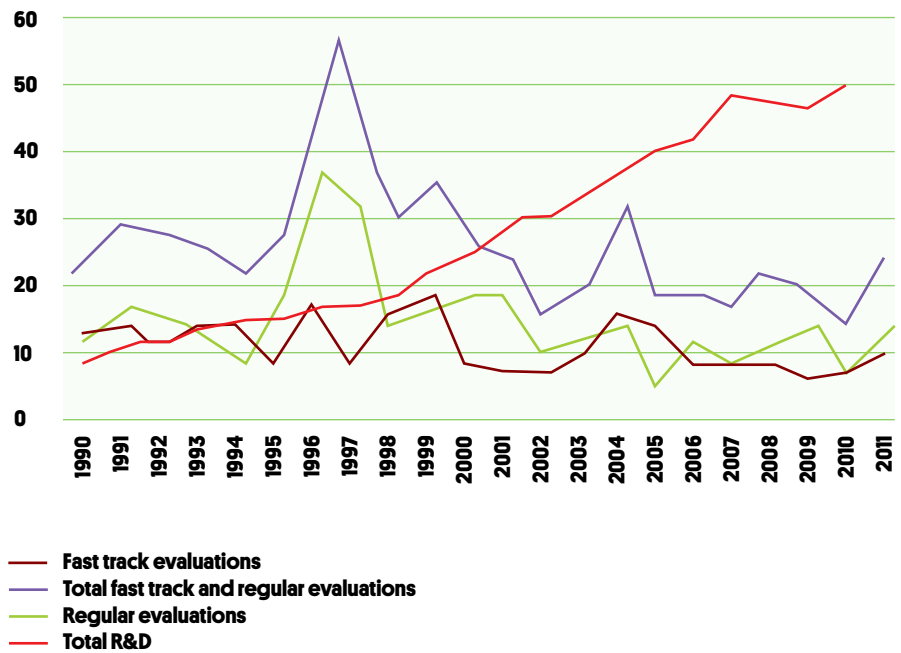
<sup>1</sup> Internal report, May 2012, on research currently underway, compiled by MSF and DNDI.

<sup>2</sup> Trouiller P, Olliaro P, Torreale E, Orbinski J, Laing R et al. Drug development for neglected diseases: deficient market and a public-health policy failure. *Lancet* 22; 359(9324):2188-94, 2002.  
 Cohen J Dibner, MS Wilson A Development of and Access to Products for Neglected Diseases. *PLoS ONE* 5(5): May 2010.

“me, too” drugs drive a cycle in which pharmaceutical multinationals spend ever-increasing amounts to bring to market drugs that are increasingly less useful in meeting the health needs of so-called developed countries (see figure 1).

**Figure 1**

**Number of news products and expenditure in R&D (millions USD) in USA.**



Source:  
 FDA and PhRMA

## What is the state of R&D for developing countries in 2011?

The introduction of so few new products in over a decade confirms the conclusion that there was a breakdown in research 10 years ago, but it doesn't tell us anything about what is going on today. In fact, over the last decade, the registration of old products for new therapeutic uses or in new forms has brought about considerable progress.

A number of projects were begun during this period, and will be registering products within a few years. To judge the importance of this on-going effort, we have databases<sup>3</sup> where researchers voluntarily record their work in progress. A snapshot of the situation in 2011 based on this shows almost 190 projects for medications and vaccines for diseases primarily affecting developing countries. A certain likely level of attrition associated with all research means that many of these projects will be unsuccessful, but for so many to have been undertaken is a sign of an historic change. As the lack of new products over the last ten years proves, the pipeline was empty at the end of the 1990s; this is no longer the case today.

<sup>3</sup> See, e.g., <http://clinicaltrials.gov/>.

If the available data suggests developing countries experienced a beneficial effect of globalized medical research, an imbalance nevertheless persists between what is done for the many and what is done for the rich. An analysis of on-going research in 2011 shows that the number of projects destined for developing countries is but a tiny percentage, despite the size of their populations. Among the 190 projects underway, around 27 are for new chemical entities with therapeutic applications, and around 77 are for vaccines. It seems that prevention is being given much more attention than treatment. The pipeline for medications remains bare, especially if we remember that not all of the projects will lead successfully to the introduction of a new medicine on the market.

The products and services resulting from research undertaken in rich countries into type I diseases are often ill adapted for use in resource-poor environments. They nevertheless benefit populations a good deal less affluent than those for whom they were created. Over the last decade, millions of AIDS patients living in developing countries have benefited from antiretroviral treatments developed in wealthy countries. Adapting these products to new social, cultural, and economic circumstances is in itself a form of R&D. This is facilitated by the research already done in so-called developed countries. We must note, however, that the development by which products and protocols created to treat type I diseases in wealthy countries are adapted to medical practice in developing countries is neglected by global health institutions.

Still, many teams are working at local level to adapt type I disease treatment protocols created in privileged environments to the less favorable conditions in developing countries. This helps to initiate care for type I diseases in countries whereas type II and III diseases are still the greatest causes of morbidity and mortality. It must be noted, however, that the business of simplifying and reducing costs will have effects on treatment in so-called developed countries, where problems with health care costs can only get worse as the population ages. Research into simpler and less costly solutions is increasingly important. The phenomenon is not new. To take one example, oral rehydration salts, created to reduce mortality caused by diarrhea in the so-called Third world, have proven extremely useful for improving dehydration care in Europe. The globalization of medical and health innovation is therefore a reality. Medical and health innovations travel in every direction: South to South and South to North, as well as North to South.

Any assessment of this effect of globalized health should nevertheless be carefully balanced. When anthropologists and sociologists observe this phenomenon at local level, they note ruptures in the implementation of models and actions defined by the organizations promoting global health. These models in fact only take into account a small fraction of practices. The discontinuities, the reconfigurations, and the inventions affect the evolution prescribed by global health models, which must always be negotiated, reinvented to meet “very local” dynamics and human relations.

## What are the basic stages of the innovation process?

The first step in innovation is the recognition of failure. Without that, why make the effort? More specifically, innovation starts when a failure occurs in a form that can be recognized by society. Today, that means presenting the problem as well as the solution according to the norms of evidence-based medicine.

The second stage is the identification of an alternative. New products and protocols are then tested on a small scale, within the privileged framework – in terms of human resources and materials – of a clinical research institution. If efficiency and lack of severe undesirable side-effects is established, the alternative therapy or prevention can be deployed on a public health scale, presuming an ad hoc financing system is established.

It is essential to note that no important global health initiative (expanded vaccination, family planning, essential medicines, introduction of new treatments such as antiretrovirals) could have succeeded under initial market conditions. Each time, a specific funding mechanism was put in place. In order to enlarge these actions to the public health scale, the initial prices of these products were reduced by 20 (vaccines), 50 (contraceptives), or 100 (antiretrovirals).

To become common practice, an innovation must pass through a series of decisive stages: finding a manufacturer who can make a quality product at reasonable cost, financing purchasing and implementation, obtaining import/export licenses, creating protocols, organizing and maintaining a network of clinicians, training and supervising personnel, collecting and analyzing data to monitor the efficiency or possible toxicity of new products.

An innovation is therefore an invention that has survived an obstacle course. Let us add that these obstacles require surmounting in a way that meets a variety of norms (scientific, political, economic, administrative, legal, etc.). These norms and the institutional procedures to enforce them could do with a major critical review in order to make them more accommodating to the survival of innovations which meet important health priorities. At the turn of the century, it was difficult to expand the use of antiretrovirals to treat AIDS because prescribers simply didn't know where to get quality products at reasonable costs, even though suppliers existed.

## How should the innovation process be managed?

Research institutions and industry provide management models for innovative projects – which is to say, projects with a high degree of uncertainty. One example is an article by Bruno Latour, *The impossible business of technical innovation*<sup>4</sup> (figure 2), which discusses a number of innovative projects. The author defines these as ever more expensive experiments carried out by researchers and decision-makers who explore various degrees of uncertainty by capitalizing on information in the hope of connecting potential users and citizens to the product or service proposed. How does the author recommend managing such a hazardous enterprise?

The author's recommendations are intended for the directors of innovative industries and are accompanied by 16 indicators across four main categories designed to help prevent what the author calls “the four pathologies of innovation”:

- The belief that an innovative project can be aimed, in the sense that all its stages and rhythms can be known in advance;
- Paranoia causing hostile and contemptuous reactions to any criticism of the project;
- Manipulation so the project will be judged by non-representative experts and irrelevant tests;
- The disappearance of the project because it was impossible to reconcile the various contradictory environments and interests that the initial phases of the project revealed.

Bruno Latour's indicators are briefly noted to underline that management models specifically designed for projects with very uncertain results can be found in other professions, such as industrial research. This is no small challenge because, as the author underlines, there are always consequences for carelessness: “It is often said at business dinners that research and innovation are the best (if perhaps most agreeable) way to go bankrupt.”

Given the risks associated with innovation, the management model proposed consists of evaluating the progress of the project according to a “learning curve” measured in stages. At each stage, resources are assigned according to the acquisition of new knowledge and know-how during the previous stages. Resources allocated are thereby transformed into new information about the different states of the world in which the innovation will be deployed and about the outlines of the innovative object, which must find a place there.

<sup>4</sup> Bruno Latour, “L'impossible métier de l'innovation technique”, in *Encyclopédie de l'innovation*, Philippe Mustar et Hervé Penan (ed.), Paris, Economica, 2003, p. 9–26.

## Figure 2

**Bruno Latour,  
“L'impossible mé-  
tier de l'innovation  
technique”, in  
*Encyclopédie de  
l'innovation*, Philip-  
pe Mustar et Hervé  
Penan (ed.), Paris,  
*Economica*, 2003,  
pp. 9-26**

“Calculations cannot be used to assess the chances of an even slightly radical innovation, because the world in which it will be introduced isn't stable enough to get reliable numbers; yet it would be futile to trust natural selection, since evolution isn't guided by any sense of efficiency. So do we just give up, extol the perils and greatness of research “that no one knows how to manage,” and support random projects while hoping for the best? This approach – while it might be gratifying to researchers – usually ends up being a colossal waste. The issue is to know whether we can evaluate without calculations. Things that can't be calculated can still be described. But how do we give a good description of an innovation that doesn't yet exist? The way research projects are usually introduced makes evaluation nearly impossible. The researcher always tends to present his discovery as the eighth wonder of the world. Without flaws, opposition or competition, it shines – according to him – with the combined light of scientific truth, technical efficiency, economic profitability, and perhaps even social justice – not to mention the inevitable progress. To hear him, shareholders, venture capitalists, colleagues and consumers need only pull out their chequebooks. This is only human... but it isn't assessable. Now let's suppose that someone asks the innovator to describe his project not as an absolute necessity, but as a perilous adventure that might well fail. We ask him to name the competitors whose products currently occupy the niche he wants to fill; we ask him to spell out the alternatives his project will have to settle for if it fails to convince; we want to know how it can be modified to incorporate opponents' objections, and so on. Instead of making his presentation watertight, we ask him to describe the risks. Why, you might ask, would that kind of description allow a better assessment than the impossible calculation? If we can't, in all fairness, ask the promoter of a radical innovation to

calculate his project's chances, we certainly can't ask him to know the answers to all of these questions about the ecology of an innovation yet to come. Nor does the evaluator's judgment apply to in-depth knowledge; to a nascent innovation we can only expect a nascent response. The evaluation is based not on a thorough knowledge of the project's environment, but only on the increasing richness of the innovator's description. The inventor can't know the future; he might fail; he might be wrong; he is feeling his way in the dark; we can't rely on any expert to judge him; we can't trust unfair natural selection. While all of this is true, there is only one thing doesn't lie – Ariadne's thread remains solidly in our grasp – is the description of the project's future world richer and more detailed now, after the project has gone through testing, than when the innovator and evaluator last met? What the evaluator can measure with some small degree of certainty is the “learning delta”, which makes it possible, between two tests or two meetings, to improve the description of the project, making it both more easily articulated and more negotiable. “Negotiable? Take it or leave it!” cries the indignant innovator. If that's the case, don't give him a penny – let the project languish on the shelf with all the other brilliant but unworkable inventions. What you're looking at is not the next great thing, but a white elephant, a labyrinthine contraption. In order to exist in ten or twenty years, the project has to be able to fit into an ecology as fragile as an Amazonian jungle; either the innovator tries to understand the environment with you, and you have to support him through his testing, or he's only interested in his project and not its ecology, and his project has no chance whatsoever of becoming reality. Demanding the description, you'll get savings the calculation wouldn't get you – and that beats counting on Darwin.”

## How are potentially successful innovations identified?

An innovation's chances of success can be seen by examining the balance between the following three variables:

- the state of scientific knowledge and available products;
- the political will and subsequent availability of possible financing;
- the nature of the behavioral changes required of patients, clinicians, and medical institutions for the proposed innovation to be achieved.

Sometimes scientific knowledge and technologies exist but are still limited. That was the situation in the fight against AIDS from the 1980s until the early 2000s, after the introduction to the market of a test for seropositivity but before the discovery of antiretroviral tritherapies. Despite the limited ability to act, political will grew, driven by fear of a widespread heterosexual epidemic. States began to treat HIV as a threat to security, the economy, and political stability. To compensate for lack of knowledge and technology in a politically charged atmosphere, there were broad calls for rapid and massive behavioral change. The inhabitants of the planet were invited to limit their number of sexual partners and to use a condom at each sexual encounter. In this case, the demand for behavioral change was so radical that it was unlikely to occur or spread.

When scientific and technological capital accrue (the introduction of effective tritherapies) to equal the level of political will, calls for behavioral change are more measured. Still using the example of AIDS, tritherapies in the form of a pill taken twice a day were introduced in poor and middle-income countries when resolutions were passed by the G8 countries in 2000 and the World Trade Organization and the UN General Assembly in 2001. Patients were able to afford the medicine and there were awareness-raising campaigns concerning the disease and its treat

**Figure 3**

<b>Period and Objectives</b> →	<b>1985 – 2000</b> <b>To curb the expansion of the HIV epidemics through preventive measures</b>	<b>After year 2000</b> <b>Treat the patients with antiretroviral treatment</b>
<b>Three variables assessment and outcomes achieved</b> ↓		
<b>Scientific knowledge and available technologies state of the art</b>	<p style="text-align: center;">+</p>	<p style="text-align: center;">+++</p>
<b>Political will</b>	<p style="text-align: center;">++</p>	<p style="text-align: center;">+++</p>
<b>Characteristics and relevance of the requested behavioral changes</b>	<p style="text-align: center;">+++</p>	<p style="text-align: center;">++</p>
<b>Outcomes</b>	<b>It can not be achieved</b>	<b>Millions of people survive thanks to the antiretroviral treatments</b>



## As examples, in which fields could medical innovations prove decisive in the next ten years?

### **Change the scientific, political, economic, administrative, and judicial environment**

Decisions about innovation in medicine and health should no longer be taken in secret by politicians, industrialists, and experts. The interests of politicians and experts are often in conflict in relation to industrialists. They should no longer make medical and health decisions by themselves behind closed doors using as their only criteria the possible effect on public health, the cost/benefit analysis and technical feasibility. Patients' representatives, representatives from associations fighting the pathologies in question, and clinicians' representatives should all be better integrated into the process. Essentially, the setting of health priorities should be a matter of democratic process in which representatives of the populations living in the most affected countries play a central role.

Improved global coordination of R&D activities is needed.

It is currently very difficult simply to know the entirety of all the activities taking place, their principle results, and their costs.

The public sector in wealthy countries provides two thirds of the financing for diseases of types I and II (see figure 4). The final third comes, in almost equal parts, from philanthropic organizations and pharmaceutical industry investment. While they already make a large contribution, states should continue to move to the forefront, as the possible consequences of inadequate research could have an affect on public security and economic and political stability which private enterprises, charitable organizations and philanthropic foundations won't have the power to fix.

New financing mechanisms are needed to give R&D for developing countries continuous and sufficient funding and to find new funding sources.

The choice of so-called open models built on cooperation rather than competition between institutions could improve R&D results, reduce costs, speed the creation of new products, and avoid the needless reproduction of labor. Such research initiatives, supported by public funding, should aim to separate the cost of development from the cost of the product, which would then be available as a public service rather than as simple merchandise.

Simplified administrative procedures should be established to assure broader and faster access to new treatments, reduce the cost of research and, above all, of development.

## Figure 4

### Main Funding Sources for Neglected and Tropical Diseases (NTD) 2010 USD \$

Source: report G-Finder 2011 ([http://www.policycures.org/downloads/g-finder\\_2011.pdf](http://www.policycures.org/downloads/g-finder_2011.pdf)) published in the report of the Consultative Expert Working Group on Research and Development: Financing and Coordination (CEWG) established by the World Health Assembly (WHA).

## Table 1

Funding Sources	2010 (US \$)	2010 (%)
US National Institutes of Health (NIH)	1 211 704 054	39,6
Bill & Melinda Gates Foundation	455 832 350	14,9
Pharmaceutical and biotechnology societies total	503 525 794	16,4
European Commission	92 529 756	3,0
United States Department of Defense	69 942 925	2,3
United States Agency for International Development (USAID)	85 975 465	2,8
Department for International Development (DFID)	97 229 720	3,2
Wellcome Trust	80 459 662	2,6
Medical Research Council (MRC)	60 857 019	2,0
Dutch Ministry of Foreign Affairs	-	-
French National Institute of Health and Medical Research (Inserm)	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
<b>Subtotal 12 Main Sources of Funding</b>	<b>2 742 875 728</b>	<b>89,6</b>
<b>Total R+D Funding</b>	<b>3 062 669 973</b>	<b>100</b>

## Table 2

Funding Sources	Montants alloués à des PDP 2010 (US \$)	Proportion du montant alloué par source de financement (%)	Proportion du financement total des PDP en 2010 (%)
Bill & Melinda Gates Foundation	235 755 901	55,7	52,5
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 Ministry of Foreign Affairs	15 833 146	92,1	3,3
Norwegian Ministry of Foreign Affairs	9 047 299	100,0	1,9
European Commission	7 941 688	8,6	1,6
The Spanish Minister of Foreign Affairs and Cooperation (MAEC)	7 159 668	100,0	1,5
Irish Aid	6 508 789	99,7	1,3
Doctors Without Borders (MSF)	4 725 479	100,0	1,0
Swedish International Development Cooperation Agency (SIDA)	4 231 695	31,9	0,9
The Swiss Agency for Development and Cooperation (SDC)	3 764 103	86,2	0,8
World Bank	2 757 154	100,0	0,6
<b>Subtotal 12 Main Sources of Funding</b>	<b>453 170 675</b>	<b>56,9</b>	<b>93,8</b>
<b>Total Funding Allocated in PDPs</b>	<b>483 166 820</b>		
<b>% of Total Funding Allocated in PDPs by the 12 Main Funding Sources</b>	<b>93,8</b>		

### Main Funding Sources of Products Development Partnerships (PDP's) 2010 US \$

## Innovate health care delivery procedures

The effect of research into better divisions, specific to each situation, of responsibilities between patients (and their entourages) and care teams is generally underestimated. Thus, in the case of nutritional rehabilitation of infants suffering from the most severe form of acute malnutrition, the new generation of therapeutic foods allowed responsibility for administering treatment to be transferred in at least three quarters of cases from paramedical personnel to a family member, generally the mother. This transfer of responsibility allowed the majority of cases to be treated at home rather than at the hospital. Once the bottleneck resulting from the need for hospitalization was relieved, the number of children receiving treatment increased tenfold.

It is important to specify that medicine cannot progress without the establishment of medical files that can be transmitted to the patient just as they would be to health professionals involved in treatment. The creation, upkeep, conservation and transmission of the medical file are vital to improving practice and practical ethics. In this case the value of innovation using contemporary information technology is clear.

Improving the quality of diagnostics is prerequisite to all other improvements in patient care. Attempts to save money by foregoing additional tests are still too common. Few clinical diagnoses are confirmed by a biological exam or scan. Malaria is a good example of the importance of diagnostic confirmation using biological testing. The creation of rapid tests that can be administered outside the clinic even in precarious situations revealed that the number of people being treated following an erroneous positive diagnosis was often as high as 50% or more.

### **Some examples of clinical and health situations in which critical innovations seem possible**

This is not exhaustive, nor is it meant to suggest that some issues should be given priority, but just offers concrete examples of critical innovations that could be achieved within a few years.

#### *The treatment of young children*

Every year, several million infant deaths can be attributed to malnutrition and infection. Given current knowledge and available products, a large number of these deaths could be avoided. Ideally, all infants visiting a doctor would be given vaccinations if these were not up to date, and an alimentary supplement if there were any imbalances. Making vaccinations available at every contact with an infant assumes overcoming two major obstacles: the need to refrigerate vaccines, and their administration by injection. Scientific and technological progress make it likely that enlarged vaccination programs (EVP) would be less temperature-sensitive, making it possible to break the cold chain. They might also be administrable by methods other than parenteral injection (transcutaneously, for example); having done away with the burden of a refrigerator, care professionals could also be free of needles and syringes.

Alimentary supplements for nutritional rehabilitation in children aged between 6 months and 3 years exist but sociocultural and economic obstacles mean they are reserved only for children who have reached the worst stages of malnutrition. Globally, the proportion of children treated for severe malnutrition is under 10%. Administration of alimentary supplements at earlier stages of malnutrition would be good for the child,

and improve morbidity and mortality at population level. More effort must be made. Why? In the first place, without adapted vaccines, recommendations and funding allowing broad access to therapeutic and supplementary food ready for use, we are incapable of controlling the number of deaths in some regions, including about 30 countries in Asia and Africa where infant and child mortality remain very high. In the second, the scientific and technological conditions exist, as does the political will. Hunger and infant and child mortality are at the center of the Millennium Development Goals. All that's missing is the funding which would allow the necessary products to be widely distributed at prices that wouldn't discourage use.

#### *Malaria*

Malaria is an infection for which there is no known vaccine. As a result, malaria weighs heavily on morbidity and mortality among infants and children. Diagnosis has been vastly improved by the introduction of rapid diagnostic tests (RDT). Combination therapies using artemisinin derivatives have improved treatment. Despite these new diagnostic and therapeutic tools, however, there is still no protocol for the reduction of high parasite transmission rates. Can we imagine crossing this barrier, for example at district level, combining vector control by insecticides and mosquito nets with new diagnostic tests and recent efficient treatments? It seems possible given the importance of recent scientific and technological developments. In addition, malaria is one of three priority infectious diseases targeted by governments and international organizations, along with AIDS and tuberculosis.

#### *Tuberculosis*

The emergence of the AIDS epidemic created a favorable environment for opportunistic infections, contributing to the spread of tuberculosis. The failure to control the disease at the population level was compounded by the difficulty of cure at individual level in a limited but increasing number of cases: some forms of the disease are resistant to the normal treatment by antibiotics. Drug-resistant tuberculosis epidemics, such as the one in New York in 1991, have been known for at least 20 years. At the beginning of the 21st century, descriptions of the previously unknown spread of multi-drug-resistant strains in the former Soviet Union and Central Asia confirmed the severity of the situation. It is rapidly becoming clear that no part of the world has been spared. In 2005, an epidemic of ultra-resistant forms – essentially incurable – were reported in South Africa. Recent epidemics of “totally resistant” tuberculosis, such as the one in Bombay in 2012, seem to be the result of our inability to control the disease.

Scientific and technological progress are now on the point of offering new weapons to actors in the battle against tuberculosis. Diagnosis has already been made easier by the introduction of a new test, GeneXpert®. While this doesn't meet the specifications devised by practitioners, it nevertheless represents real progress. New molecules, notably those created by the Tibotec and Otsuka laboratories, are reaching the final stages of clinical trials. The arrival of these new antibiotics, the first in 60 years, raises hope that the situation can be improved in the short term. They effectively allow us to predict shortened treatment times – from a few months to a few weeks – but also to foresee treatment of strains that are resistant to the current generation of antibiotics.

End