

Submission on Drug Innovative Research for Infectious Diseases of the Poor to the Intergovernmental Working Group On Public Health, Innovation And Intellectual Property

Section 2 Proposals in Response to Resolution WHA60.30

A Concerted Effort on Innovative Drug Discovery For the Production of Lead Compounds for Neglected Diseases

This submission is based on the need to build a Consortium for drug discovery research for infectious diseases of the poor. Currently, greater efforts are required and should focus on the early phases of drug research and advancing the development of lead compounds. The submission further points to the need to associate all key players – The Special Programme for Research and Training in Tropical Diseases (TDR), academia (from both developed and Innovative Developing Countries), the pharmaceutical industry, and Product Development Partnerships (PDPs) – and increase the coherence between the important efforts each have undertaken. Building such a consortium will make better use of the financial contributions made by governments and the few private foundations funding drug research and development for infectious diseases of the poor.

Prevention, vaccines and drugs are efficient health tools; they have changed, and continue to change, the course of diseases and have progressively improved the health status in all countries. Drug research has produced, through the efforts of both academic and private institutions, a wealth of drugs to fight cancer and address cardiovascular, psychiatric, rheumatologic, and orphan diseases. Almost every other field of medicine, except infectious diseases, and more specifically those that primarily affect the poor, such as malaria, tuberculosis, kinetoplastids, helminths parasitoses, and other neglected diseases,¹ have seen the development of numerous treatments.

The last ten years have seen a mounting consciousness of the need to change the situation for neglected diseases. The 2000 G8 Okinawa Summit took the subject under consideration; it was decided to promote greater involvement of all countries and international organizations. Progress is notable and has been made possible through a series of studies and organizations².

1 Four drug research and development public/private partnerships have been formed³ and have, in a few years, built an interesting portfolio for malaria, tuberculosis, human African trypanosomiasis, visceral leishmaniasis and Chagas disease. A consortium organized by the University of North Carolina is developing drugs for human African trypanosomiasis and visceral leishmaniasis. Several other less visible initiatives are also active in this field of drug research and development for neglected diseases. This endeavour will most probably bring an

¹ Other infectious diseases, such as cosmopolitan bacterial, viral and fungal infections have been successfully targeted by modern R&D efforts.

² Commission on Public Health Innovation and Intellectual Property Rights, Intergovernmental Working Group on Public health, Innovation and Intellectual Property, The Special Programme for Research and Training in Tropical Diseases (TDR) new strategy.

³ Drugs for Neglected Diseases Initiative (DNDi), Medicines for Malaria Venture (MMV), TB Alliance, Institute for One World Health (IOWH).

immediate answer to the need for new treatments by using old drugs, known compounds or families of compounds for new indications, or by producing new fixed dose combinations. However, none of these organizations is in the position, on its own, to mobilize the resources of modern drug innovation science and technology. None of these organizations is in the position, alone, to give access to drug innovation to patients like industry does for type 1 diseases⁴. None has had nor presently has, the human and financial resources to organize full drug discovery programs. Building this capacity will make it possible to provide new drugs with fewer limitations than those of the currently available compounds, in regards to efficacy and tolerance. Drug discovery is a complex activity, which requires the association of several sciences and technologies under a single leadership to advance well-conceived and funded programmes.

2 A small number of large pharmaceutical companies⁵ have committed resources to neglected diseases. Two of them, among others, GlaxoSmithKline and Novartis⁶ have invested in drug discovery activities with sufficient resources to hopefully be in a position to bringing new chemical entities to development. Entering into those activities implies having access to the numerous and powerful databases on genomics and all the “omics” of man and infectious agents. It implies that there is efficient and constant cooperation between medicinal chemists, biologists and pharmacologists, so that early, iterative exchanges take place on the pharmacologic activity and potential toxicity of a given compound. This iterative exchange, which takes place on a very large number of compounds from the company library, allows the optimisation⁷ of compounds with the goal of advancing the leads into early pre-clinical development. This is the most difficult part of drug research: it has to be conceived and championed for neglected diseases with the same input in terms of human competence, programme quality and funding as industry devotes to any drug development programme. Such activities mobilize hundreds of specialized scientists in a wide array of disciplines, focused specifically in the production of lead compounds in each of the several research centres that specific companies often manage worldwide. Such activities are costly; success in the production of innovative lead compounds and later in the development of innovative drugs is not frequent for any given company, even when final cost to social security systems is not a stumbling point for a therapeutic indication. Thus, it is unlikely that industry, large, medium size or small companies will devote large drug discovery programmes to neglected diseases, most of which are represented by patients having no buying capacity, in countries which have little buying power. What industry has done in this context is to undertake drug research programmes on a limited number of diseases⁸. They have also shown willingness to give access to their expertise and tools, including their compound libraries, when conditions are clearly set, in particular with respect to intellectual property rights.

3 Pharmaceutical research activities are not to the exclusivity of North America, Western Europe and Japan anymore. Countries like China, India, Brazil, Korea, Singapore, Malaysia,

⁴ Diseases that are incident in both rich and poor countries with a large number of vulnerable populations in each. It is represented by communicable diseases, measles, hepatitis B...and non-communicable diseases (cardio-vascular diseases, metabolic or tobacco-related illnesses).

⁵ MSD, GSK, Novartis, Sanofi-Aventis, Astra-Zeneca, Pfizer...

⁶ Mainly through a not-for-profit entity, the Novartis Institute for Tropical Diseases in Singapore

⁷ Screening for new compounds goes from screening collections of chemical entities on a target which can be a protein, an enzyme, or the whole organism. This produces hits of various efficacy and potency. A few with sufficient potency are chosen for optimisation. The successful result of this phase provides a lead compound with efficacy against the tested target at very low concentrations, and toxicity profile that has been assessed and found acceptable.

⁸ Malaria, tuberculosis, dengue.

and South Africa,⁹ among others, are concentrating their efforts on drug production, as well as on drug research and development. Powerful public and private drug research centres exist in China and India. Drug innovation and translational research centres are being built in India and Brazil and a cooperative agreement on drug research has been established between South Korea and Institut Pasteur. In addition, all Innovative Developing Countries have traditionally undertaken sophisticated research on natural substances¹⁰. Unlike countries of the North, most of these countries are confronted with the presence of parasitic diseases in large segments of their populations. However, the resources that are being invested by individual countries in these areas are still clearly insufficient to properly answer the need for new drugs.

4 Currently available funds to the entire field of neglected diseases are significantly greater than those that were available ten years ago. Countries like the USA, the United Kingdom and other countries of the North are now starting to spend sizable amounts on biomedical research on neglected diseases, especially on malaria and tuberculosis. The presence of the Bill and Melinda Gates Foundation in the last five years has radically changed the perspective of drug research and development. All PDPs and TDR are now or will likely soon have the benefit of substantial Bill and Melinda Gates Foundation grants. This funding enables the most interesting drug development programmes now in place at the five not-for-profit entities to be taken forward¹¹. A different present and future allocation of resources, a stronger presence of countries of the North, as well as the financial presence of countries from the South, and especially of the Innovative Developing Countries, could provide the necessary funding for a serious and sustained effort.

5 One of the specific missions of TDR, as outlined under its strategic plan approved by the organization's Joint Coordinating Board (JCB) in June 2007, is to organize networks and partnerships with the aim of feeding the various PDPs with solid lead compounds¹². JCB, under the aegis of WHO, have committed TDR to rapidly implementing and finding the resources and the right approach to reach that objective in the two years to come.

A Concerted Action for a Consortium Devoted to Drug Discovery Research

Well-conducted drug discovery research is essential to fostering innovation in the field of infectious neglected diseases. New tools, drugs and vaccines are urgently required to effectively control the most important, and hopefully all, neglected diseases in the next two decades, and thus also contribute to the alleviation of poverty.

Substantial scientific knowledge exists, is well-used by the industry, and now needs to become available for the discovery and development of new drugs for neglected diseases.

Sizable funding is available, either as actual research activities already in place or through funding of research and development activities by governments or private foundations/charities.

⁹ Now described under the Innovative Developing Countries denomination.

¹⁰ Natural substances, from vegetal or marine origin are often the source of complex chemical structures, which are used by modern chemistry in conceiving new drug chemical structures.

¹¹ In addition to funding drug research and development, large sums are now committed to buying drug for treating patients with neglected diseases by the Global Fund, UNITAID, the Clinton Foundation, and the UK International Finance Facility. In addition, the Advanced Market Commitment scheme is being implemented for vaccines.

¹² TDR Business Plan: Business Line N°3, Lead Discovery for Drugs.

It would then be warranted for the International Working Group on Public Health, Innovation and Intellectual Property (IGWG) to consider exploring and finally keeping as one of its recommendations to form a concerted action in building drug discovery capacity for the benefit of the control of neglected diseases.

Organization and Governance

The concerted-action, the proposed consortium, should be largely virtual in its organization based on agreements passed between the founders and all public or private organizations willing to offer drug discovery capacity up to produce valid lead compounds. Building laboratory facilities and recruiting scientists will be avoided, unless it becomes crucially necessary during the course of developing the Consortium. Recruitments will only be needed for effectively managing the projects and programmes of the Consortium.

The mission of the drug discovery consortium will be to build capacity capable of giving access to science and technology for the production of new compounds. These compounds could then be offered to PDPs, such as DNDi, MMV, and TDR-R&D¹³ and not-for profit pharmaceutical industry entities to further develop them into viable therapeutics for neglected infectious diseases. That mission will be fulfilled by conceiving programmes based on the most accurate knowledge on the science of drug targets and medicinal chemistry.

The governing body will associate the minimum number of partners likely to bring science and technology, as well as funds, in order to hope a reasonable output in term of lead compounds to be offered for further development. A careful assessment is required to decide if an existing organization/body can coordinate such a consortium or if a new organization needs to be created. Both options will require new resources and the capacity to produce lead compound through partnership.

The next steps will entail detailing the objectives including the initial, most feasible programmes¹⁴, the operational processes to be established and the resources required. These tasks will be undertaken by the governing body.

Funding could be secured from national entities from developed and transition countries, complemented by contributions from important philanthropic foundations.

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¹³ TDR for its Business Line N°6: Drug Development and Evaluation for Helminths and other Neglected Tropical Diseases.

¹⁴ In particular, the choice of diseases and the consortium's priorities, to ensure that the organization does not initially take on too broad of objectives. The ability to properly organize the consortium and the speed of at which it is built will dictate decisions to expand its focus and partner base..