BIAG

BIOMEDICAL INDUSTRY ADVISORY GROUP

The Biomedical Industry's Commitment to Diseases of the Developing World

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The Biomedical Industry Advisory Group (BIAG) was formed to help the World Health Organization's Commission on Intellectual Property Rights, Innovation and Public Health (CIPIH) better understand the role the biomedical industry plays in combating Diseases of the Developing World (DDW). BIAG includes representatives from pharmaceutical, biotechnology, medical devices, vaccines and diagnostic industries.

Since its formation, BIAG has provided its expertise, insights and relevant supporting data on the impact of intellectual property rights on research and development for disease disproportionately affecting the developing world.

In May 2005, BIAG provided its submission to CIPIH, which can be found at www.biag.org. This is a summary of BIAG's submission.

BIAG drew on the expertise of individuals from the following institutions:

GE Med Systems
GlaxoSmithKline
International Federation of Pharmaceutical Manufacturers & Associations
Interpharma
Merck & Co. Inc.
Nicholas Piramal India Limited
Novartis International AG
Pfizer Inc
Sankyo Co. Ltd
sanofi-aventis
Serono International S.A.
Tufts University School of Medicine
Wyeth Pharmaceuticals

INNOVATION IS KEY TO TREATING DISEASES OF THE DEVELOPING WORLD

Since only a few diseases lack effective treatment options, why is it that less than a third of those afflicted are effectively treated?

Failure to adequately treat Diseases of the Developing World (DDW) results from multiple factors that are described in this booklet.

Biomedical companies – through their research and development organizations – can help address the need for improved therapies through a series of initiatives. To achieve this and other sustainable solutions will require public policy incentives that support innovation. Given the high cost of research and development (R&D) and the sophisticated technical skills required to effectively treat DDW, encouraging innovation is the key to the solution, and intellectual property rights fuel innovation.

The biomedical industry is committed to strengthening its already substantial role in discovering, developing and delivering new treatments to save and improve lives around the world. While much has been done, the biomedical industry is committed to working in partnership with all interested parties to help ease the burden of disease in the developing world.

Today's effective therapeutics – typically off patent products – exist for almost all DDW, yet less than a third of the people afflicted receive effective treatment. Most of the DDW either have effective therapies that are not reaching patients in need due in part to lack of medical infrastructure and/or there are multiple therapies in active R&D programs with biomedical companies, or together with companies in Public-Private Partnerships (PPPs).

ADDRESSING THE BURDEN OF DISEASE

Off-Patent Therapeutics are Available But Not Deployed

Many treatments are simply not reaching the disease populations in need. Why? Poor or non-existent medical infrastructure, a lack of health professionals in resource-poor areas, under-diagnosis, insufficient education and inadequate delivery methods in local markets are the core issues.

Off-Patent or "At Cost" Therapeutics Exist But Are Not Procured

Even off-patent or at-cost treatment – often offered at just pennies per regimen – are beyond the means of many developing countries. Moreover, there is inadequate support to purchase or set aside sufficient quantities of workable treatments for populations in need.

R&D Hurdles for Existing Pipelines

While efforts are underway to discover and develop new treatments for the few diseases where no treatment currently exists or where increasing resistance has diminished the efficacy of current therapies, there are potential hurdles that could slow progress. They range from inadequate local infrastructure for late stage clinical trials to cumbersome regulatory processes in the developing world.

Incentives for Innovation Are Essential

Creating any new treatment is a lengthy, costly and risky endeavor. Existing incentives and measures to protect investments – including intellectual property rights – are necessary to ensure the risk-reward balance for innovation. It is worth noting that incentives in the form of effective IP rights protection are often lacking in developing countries.

Insufficient Political Will and Lack of Sustained Funding

All sectors must make a firm and ongoing commitment to provide funding that will spur new solutions. Even Public-Private Partnerships (PPPs) face the prospects of having to cut programs because of a lack of funding. In fact, five of the largest PPPs – Global Alliance for TB Drug Development, Medicines for Malaria Ventures, Drugs for Neglected Disease Initiative, International Partnership for Microbicides, International AIDS Vaccine Initiative – face a shortfall of 75% of their cumulative budgets between now and 2007.

PATENTS PLAY AN ESSENTIAL ROLE IN THE BIOMEDICAL INDUSTRY

Patent laws lay down exacting requirements for approval of a patent. A patented drug must be proven to have a chemical structure sufficiently different from others in its class, or it must provide new or unexpected therapeutic effects or benefits.

In the long journey from idea to laboratory to patient, biomedical companies must prove the new medicine is stable, that medicinal content doesn't degrade in the environment, that it can be safely stored and that it can be uniformly manufactured in acceptable quantities.

At the same time, a patent covering an improvement to an existing patented product does not prohibit generic competition against the existing product after the patents protecting the original product have expired.

With this calibrated system of protections, products must prove that they are legitimately innovative, yet allow generic competitors to enter the market once patents expire.

R&D FOR TRULY NEGLECTED DISEASES

Therapeutic progress on Diseases of the Developing World (DDW) will require a global coordinated effort to overcome the many hurdles faced. Only by focusing on the underlying issues can we expect to make steady and long-lasting progress. The key elements are:

- **Funding:** Increased financial resources are needed in a sustainable way to create and maintain a strong pipeline of drug candidates, and to ensure that these therapies will reach patients in need. Despite the generosity of donors and the ongoing involvement of the pharmaceutical industry, more funds need to be made available within the global public health community to secure, accelerate and sustain important R&D efforts that are showing promise.
- **Basic research:** Fundamental research on new biologic mechanisms is needed to form the basis for new therapeutics. Substantial additional research is needed to gather detailed epidemiological information to help shape research and development efforts.
- **Drug development infrastructure:** Capacity building in developing countries to facilitate early and late stage clinical trials, swift product registration and post approval evaluation of medicines, including systems for assessment of adverse events.
- **Drug delivery infrastructure:** The global health community needs to make sure that new medicines are actually delivered to patients in need, such as building on successful disease control programs.

Without implementing these steps, discovering and developing new therapeutics will be a futile exercise to overcome the challenges of diseases affecting developing countries.

CURRENT STATUS OF DRUGS FOR NEGLECTED DISEASES

Disease	Existing Medicines	Limitations of Current Medicines	Need for Specific Uses
African trypanosomiasis	Yes	• Efficacy and safety • Dosage form (injectable) • Cost • Potential drug resistance	No
Chagas disease	Yes	• Activity only in acute stage of disease • Safety	No
Leishmaniasis	Yes	• Safety • Dosage form (injectable) • Cost • Potential drug resistance	No
Dengue fever	No	N.A.	HIV co-infection
Malaria	Yes	• Compliance • Cost • Partially safe • Drug resistance	Pregnant women Paediatric formulations
Tuberculosis	Yes	• 6-9 month course of treatment • Compliance • Drug resistance	HIV co-infection

Source: UNICEF/UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Disease (TDR)

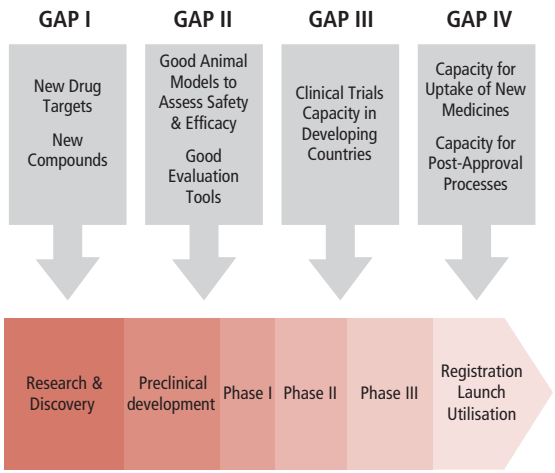
SUCCESSFUL DISEASES CONTROL PROGRAMS

Disease/Program	Pharmaceutical Industry's Contributions	Impact on Society
Onchocerciasis Mectizan Donation Program	**Merck** donates Mectizan® (ivermectin) to all who need it and as long as necessary. To date, the company has donated over **one billion tablets**, with more than **350 million** cumulative treatments distributed.	In West Africa alone, approximately **18 million** children have been protected against onchocerciasis, and **600,000 people have been saved** from blindness. Some **62 million** acres of previously infested areas has been resettled and is now being cultivated through Mectizan treatment and vector control. Currently, Mectizan treatments are preventing **40,000 cases** of blindness annually in Africa.
Leprosy Global Alliance to Eliminate Leprosy	**Novartis** donates $37 million in multi-drug treatment for leprosy, and works with WHO and other partners to improve delivery and care.	Over **14 million** people have been cured of leprosy and the prevalence rate has dropped by over **90 percent** since 1985, and the number of countries considered endemic has been **reduced from 122 to 15**.
Lymphatic Filariasis Global Alliance to Eliminate Lymphatic Filariasis	**GlaxoSmithKline** donates albendazole, and **Merck** donates ivermectin (Mectizan®). To date 250 million treatments of albendazole and 20 million treatments of Mectizan® have been donated.	By the end of 2004 almost **250 million** people in **39 countries** had received treatment for lymphatic filariasis. This is a marked increase compared to the year 2000 when only 25 million people at risk were covered.
Guinea Worm Guinea Worm Eradication Program	**Johnson&Johnson** has donated enough medical supplies such as Tylenol®, foceps and gauze, to treat more than 5,000 villages in the endemic countries.	The number of people suffering from guinea worm has dropped from **3.5 million** in 1986 to **16,026** in 2004. Globally, over **150 countries** and territories have been certified free of parasite transmission.
Blinding Trachoma International Trachoma Initiative	**Pfizer** has donated more than $225 million in product donations (Zithromax®) and health educational grants.	**Over 9.5 million** people have been rid of active trachoma infection through antibiotic treatment and more than **85,000 cases** of blindness have been prevented through surgeries.
African trypanosomiasis WHO Program to Eliminate Sleeping Sickness	**Sanofi-Aventis** has supplied some 1.2 million drug ampoules of three medicines used in treatment, as well as financially supported the work of mobile medical teams and research activities of WHO on a new formulation of a drug for African trypanosomiasis.	During the past three years, more than **60,000 people** have benefited from this initiative, receiving medical counsel, screening and treatment.

EXAMPLES OF PRODUCT DEVELOPMENT PUBLIC-PRIVATE PARTNERSHIPS FOR NEGLECTED DISEASES

Malaria	Medicines for Malaria Venture (MMV) Malaria Vaccine Initiative (MVI) European Malaria Vaccine Initiative (MMV) Japanese Pharmaceutical, Ministry of Health, WHO Malaria Drug Partnership (JPMW) Lapdap™ Antimalarial Product Development (Lapdap)
Tuberculosis	Global Alliance for TB Drug Development (TB Alliance) Global TB Vaccine Foundation (Aeras) Foundation for Innovative New Diagnostics (FIND)
African trypanosomiasis **Leishmaniasis** **Chagas disease**	Drugs for Neglected Diseases Initiative (DNDi) Gates Foundation/University of Carolina Partnership (GFUNC) Infectious Disease Research Institute (IDRI) Institute for One World Health (IOWH)

CRITICAL GAPS IN DRUG R&D FOR NEGLECTED DISEASES



THE COST TO DEVELOP A NEW THERAPEUTIC

In a given year, only about 30 new therapeutics make it through an increasingly expensive, complex and lengthy process before finally reaching patients, though thousands of compounds exist at various stages of research and development. R&D costs vary, but various studies cite costs over $800 million to more than $1.7 billion. Those costs represent the sum of the costs involved at each stage of discovery (excluding basic research) and development, including what is spent on candidates that fail. The mean cost for both discovering and developing a new therapeutic is $881 million.

Such a costly process presents sizeable financial risks. In the late 1990s, for instance, 240 products were launched with $230 billion spent on all R&D by the top 25 biopharmaceutical companies. That works out to $900 million per drug.

While the industry's R&D investments continue to grow, the process to bring a compound to market is becoming more difficult, largely because of increased complexity in science and expanded regulatory requirements. In addition, attrition during development due to lack of efficacy or concerns regarding safety continues to climb. Also, technical advances in the discovery phase have not been sufficiently transferred into clinical development.

The cost of R&D is staggering and growing as attrition rates increase. Only by supporting current incentives for R&D can industry innovation help reverse and treat the DDW.

PHARMACOEVOLUTION: ADVANTAGES OF INCREMENTAL INNOVATION

Drugs based on incremental improvements almost always bring significant advances in safety, efficacy, and/or dosing refinements that can improve patient compliance. The result: reduced hospital stays, fewer physician visits and increased worker (patient) productivity.

The fact is that people respond differently to different versions of a particular class of medicine, in ways that often are not predictable. Therefore, multiple versions benefit more people than a single product. Newer versions also assure supply of needed medications if for any reason, the lead drug in a certain class is removed from the market or often never makes it to market due to safety and/or efficacy issues.

What's more, expanding drugs within a class spark price competition, with new drugs entering existing classes often priced at a discount from the first-in-class product.

THE ECONOMICS OF FOLLOW-ON DRUG R&D

Despite prevalent misconceptions, "follow-on" or "me-too" drugs are, in fact, needed therapeutic options. Over the past 30 years, for instance, market exclusivity for breakthrough drugs (i.e., only drug in a class) has fallen dramatically: from an average of 10.2 years in the 1970s to only 1.2 years in the 1990s.

As the idea-to-market development cycle usually runs from 10 to 15 years, the vast majority of the follow-on drugs created in the last decade were already in clinical development before the class breakthrough or "innovator" drug was approved. Accordingly, it must be understood that new drug discovery and development tends to be a race between candidates, rather than a quick imitation.

A GLOBAL FRAMEWORK FOR INTELLECTUAL PROPERTY RIGHTS

Many consumer activists and representatives of international organizations allege that provisions within national patent laws and bilateral free trade agreements impose so called "TRIPS-Plus" obligations that extend beyond those expressly outlined in the World Trade Organization Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS). In fact, the TRIPS agreement provides a minimum standard of intellectual property protection, and serves as a general framework to allow countries significant flexibility in setting IP protection.

National governments are within their sovereign right to enhance intellectual protections within this framework.

Characterizing provisions in national laws or bilateral free trade agreements as "TRIPS-Plus" is inaccurate, as these provisions are completely compliant within the established TRIPS framework.

PROPOSALS TO INCREASE R&D FOR NEGLECTED DISEASES

Additional incentives or initiatives could significantly improve the R&D pipeline environment for neglected diseases. But as a crucial first step, political leaders must set a public health agenda that addresses the underlying core issues. With these in place, biomedical companies – through their individual R&D organizations – can help address the need for improved therapies through a series of initiatives:

- **Product Development Public-Private Partnerships (PPPs):** These independent organizations can attract public and private funding to finance applied research, development and delivery of new medicines for neglected diseases.
- **Advanced Purchasing Commitments (APC)/ Advanced Market Commitments (AMC):** Such agreements compensate for inadequate market size by specifying price and volume requirements for the development of a certain drug.
- **Global Fund for Tropical Diseases:** Such a fund makes necessary finances available to countries and communities, so they can purchase new and existing drugs for neglected diseases.
- **Tropical Diseases Drug Act:** Similar to the Orphan Drug Act, this legislative package would provide incentives to increase R&D for neglected diseases. Key features would include a combination of "push/ pull" mechanisms such as R&D tax credits, grants, reduced regulatory fees, fast track regulatory approval, combined with advanced purchasing commitments to provide a market where none exists. Likewise, much better therapies are required for TB and malaria. These are being actively pursued in many biomedical research companies and with PPPs.

A CALL FOR A HOLISTIC APPROACH

Any solution must include steadfast political will and funding. Governments from both industrialized and developing countries must recognize the colossal cost of inaction and therefore join with industry, academia and Non-Governmental Organizations to find and implement practical solutions.

In the end, relieving the burden of developing world disease requires contributions from every stakeholder, strengthened by favorable public policy and harmonized regulatory policies. To achieve a sustainable solution, a successful approach must be holistic, from R&D incentives to building a better health care infrastructure throughout the developing world. A cross-sector approach drawing on the inherent strengthens of each is the most promising solution to meet the critical needs of patients suffering from the burden of disease in the developing world.

"TRULY NEGLECTED" DDWS

While most of the diseases of the developing world have effective therapies that are not reaching patients, the following four diseases still require significant R&D:

- Human African Trypanosomiasis
- Chagas Disease
- Dengue Fever
- Leishmaniasis

In each case research efforts are now underway to help find new therapies.