Intellectual Property Management Approaches to Promoting Access to New Therapies in Developing Countries

Dr. Cathy Garner,
Chief Executive Officer,
Centre for the Management of Intellectual Property
in Health Research and Development

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Introduction

Intellectual property (IP) plays a role in the delivery of medicines for those in developing countries, but the author contends that its role in controlling the affordability and availability of medicines for the poorest has been overstated in the past. Nonetheless, the paper concludes that as barriers to access to medicines are tackled and as funds increase through new models for drug development, using IP creatively to ensure that the benefits of investment are differentially targeted to the poor in developing countries makes IP management a force of positive intervention.

In the past polarised positions have been taken. On the one hand the R&D based pharmaceutical industry has asserted the need for strong IP protection to enable the development of new drugs, while on the other campaigning organisations have blamed strong IP protection for the high cost of existing medicines and the lack of their availability to treat neglected diseases. The actuality lies somewhere between. IP is a tool providing a means to deliver an end result. Much can be gained by understanding the practicalities of that role, addressing contentions and becoming more skilful in using the tool to deliver humanitarian outcomes.

This paper seeks to make a contribution to the better understanding of the practical role which IP and its management can play in access to medicines for the poor in developing countries. It describes the background to the polarisation of the debate, the part played by IP in a number of case studies and the approach which a new organisation – MIHR – is taking.

The Polarisation of Views on IP:

In any discussion of the role of IP in medicines for the poor in developing countries it is useful to understand that views about IP and its management have become polarised and contentious over the past decade.

"Since the early 1990's Intellectual Property policy has become one of the most economically and politically contentious issues in the international arena ..."[1]

These are the opening words of a major United Nations Conference on Trade and Development (UNCTAD) report published in 2003.

[1] UNCTAD-ICTSD, "Intellectual Property Rights: Implications for Development", Project on IPRs and Sustainable Development, Geneva, August, 2003.

When the pharmaceutical industry challenged the right of the South African government in 1998 to use its powers to access medicines by compulsory licensing or parallel importation[2], there was a considerable backlash. The AIDS pandemic in sub-Saharan Africa has drawn stark attention to the failure of provision of health care for the poorest. Although the fact that the weight of the disease burden falls most on those who cannot afford treatment is not new, the magnitude of the AIDS epidemic which took the lives of 2.4 m Africans in 2002 brought the facts into clear focus. The realisation that treatment regimes were controlled by multinational corporations rather than public institutions, gave rise to a serious backlash in public opinion. Those who sought to challenge the trend of globalisation used the South African challenge as an illustration of the dangers in private hegemony and the weakening of the power of the nation state. The streets of Seattle became a focus for heated debate and protest. The World Trade Organisation (WTO) and its treaties were challenged. In particular, the Uruguay round of the General Agreement on Tariffs and Trade (GATT) in 1994 and its introduction of TRIPS (Agreement on Trade-Related Aspects of Intellectual Property Rights) which had set out to establish minimum standards on all types of IP rights was seen to have been promoted by the corporations of advanced economies. At that time, multi-national corporations were beginning to see their competitive edge being eroded by counterfeiting and piracy.[3] The US based pharmaceutical industry was amongst the leaders of the movement to protect their position through the introduction of TRIPS.

The events of the 1990's and early 2000's, therefore brought IP rights into focus as an international issue of contention and division. For some, the debate became centred on the rights and wrongs of the monopolistic position which the IP system conferred on the multi-national pharmaceutical giants. For others it was an issue of human rights. Inevitably in such an emotionally charged and polarised debate, the actual role which IP rights played became obscured. The IP system itself was challenged as being a negative force[4]. However as over time and as much has been done by the pharmaceutical industry and public and philanthropic institutions to begin to address Africa's AIDS pandemic a more constructive debate has developed. More creative approaches have been developed[5] including a clarification on the WTO rules through the Doha

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[2] On 18th February 1998, 28 pharmaceutical companies and the Pharmaceutical Manufacturers Association challenged the right of the South African Government to include a clause (15c) in its Medicines and Related Substances Act to permit compulsory licensing or parallel importation. The challenge was withdrawn on the 20th April 2001 and a joint working party was established including the pharmaceutical companies.

[3] de Koning, 1997 – quoted in Correa, C. M. "Intellectual Property Rights, the WTO and Developing Countries", Zed Books, London, 2000

[4] http://www.cptech.org

[5] Attaran, A and Gillespie-White, L. " Do Patents for Antiretroviral Drugs Constrain Access to AIDS Treatment in Africa?, JAMA, October 17th, Vol. 286, 2001

declaration.[6] However, much remains to be done to clarify the role of the IP system, for example, the UNCTAD paper[7] not only states the issue of contentiousness surrounding IP rights but also highlights the fact that:

"... for policy makers working in the international development arena, IP policy is an entirely new subject"

IP rights are an arcane area dominated by legal professionals and few developing countries have a wealth of experience in their use. Experience which does exist has tended to be isolated from and marginal to, the discussions on national development. There is therefore a need to ensure that this situation can be addressed in a practical and de-mystifying fashion. It is hoped that the examples in this paper will help to contribute to a clearer view of the role of IP in access to medicines in developing countries.

The IP and Drug Development Systems

Understanding the role of IP in drug development is an important step to placing IP in context. An understanding of the complexities of modern drug development and the role of patent protection therefore is essential to a better understanding. The IP system provides incentives for private sector investment. If the effort to produce all new medicines could be undertaken by public funds and all risks could be borne by taxpayers, then there would be no need to patent. However, where the risk of development is passed to the private sector as companies and/or investors (pension funds or individuals) there is a need to provide a security of return.

As patent protection is the predominant form of IP protection used in the pharmaceutical industry patents are the focus of this paper. The UK Patent Office describes a patent in the following manner:

"A patent for an invention is granted by government to the inventor, giving the inventor the right for a limited period to stop others from making, using or selling the invention without the permission of the inventor. When a patent is granted, the invention becomes the property of the inventor, which - like any other form of property or business asset - can be bought, sold, rented or hired. Patents are territorial rights.[8]

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[6] http://www.cptech.org

[7] UNCTAD-ICTSD, "Intellectual Property Rights: Implications for Development", Project on IPRs and Sustainable Development, Geneva, August, 2003.

[8] http://www.patent.gov.uk/patent/definition.htm

Importantly, when a patent is issued, details of the invention are published. This contrasts for example, with trade secrets which allow the invention to remain private - such as the recipe for Coca Cola. In the context of the pharmaceutical industry, a patent is a mechanism which allows the codification of knowledge of an invention whereby it can be reduced to practice and can be passed from the inventor "under licence" to others for production while retaining ownership and the benefits of ownership to the inventor(s). However, as patenting results in publication, others can then access the information to also make the invention. In countries where the inventor has not obtained patent coverage and in countries where there is no recognition of the rights conferred by patents, there is scope for re-engineering and copying of the original. This is why the extension of the patenting system under TRIPS has become an issue of contention.

Patents have a greater importance in R&D based pharmaceutical industries than in other industries. Mansfield[9] estimated that some 65% of new drugs would not have been produced had no patents been in place. This compares with only 30% of products in the chemical industry and 4% of electrical equipment. The investment risk is high with an estimated level of attrition of 99 out of 100 new compounds failing to be developed into products.[10] The cost of the development of new drugs is estimated to be as high as $800 m. Although the actual costs of development as compared with the costs of development and sales and marketing are often debated, estimates suggest that even under models of public-private partnerships (PPPs) where marketing and sales are not involved, the costs remain considerable. Towse, of the Office of Health Economics in the UK quotes the estimates in Table 1.[11]

Table 1: Estimated Costs of the Development of New Drugs in the Private Sector and Two Public-Private Partnerships ($ US m)

	Capitalised $m	Out of Pocket $m
Private Sector	802	403
MMV	409	164
GATB	345	171

The lower costs projected by the Medicines for Malaria Venture (MMV) and the Global Alliance for TB (GATB) may arise from the difference in costs of Phase III

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9 Mansfield , E, Patents and Innovation: An Empirical Study", Management Science, February,1986

10 Kettler, H., White, K. and Jordon, S., "Valuing Industry Contributions to Public-Private Partnerships for Health Product Development, Initiative on Public-Private Partnerships for Health(IPPPH),Global Forum for Health Research, Geneva, 2003

11 Towse, A, Presentation to the Royal Institute of International Affairs, November, 2003.

clinical trials and the fact that there is an intention to out-license products before the conclusion of the drug development process.

The pharmaceutical industry's reliance on strong patent protection is also a consequence of the nature of the drug development process where many players are involved in a chain of relationships which require to be governed by contractual obligations and mutual trust and shared risk. The patent system provides security and the ability to contract. The need for strong patent protection in the pharmaceutical industry has developed as a corollary of the R&D paradigm which has emerged with the ever increasing complexity of science and the need for specialist contractors in different parts of the process.

Table 2: Multiple Players in the Stages of Drug Development

	Target Identification	Drug Discovery	Drug Dev(1)	Drug Dev(2)
Process	Discovery of the biological mechanisms implicated in the cause of a disease	Use of enabling technologies to screen millions of potential drug candidates or rationale design to produce new therapeutics	The creation of a pharmacologically effective means of formulating and delivering the new therapeutic agent to its site of action	Demonstration of efficacy and safety to gain regulatory approval
Organisations & Technologies Involved	Universities Hospitals Large Pharma Biotech companies Bio Informatics	Universities Large Pharma Biotech Companies Contract analysis Contract manufacture Chemical Synthesis Animal Models BioInformatics	Drug Delivery Large Pharma Biotech Companies GMP Animal Models BioStatistics Toxicology Pharmacokinetics CRO's Phase I Trials	Large Pharma Hospitals GMP BioStatistics Phase II Trials Phase III Trials Packaging Companies Regulatory Bodies (eg FDA) Consulting Organisations
In Support	**Patent Agents, Lawyers, Business Support Agencies, NGO's,**			

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In addition to the many organisations and the complex web of interrelationships which comprise this process, it must be recognised also that contractual relationships must pertain over a period of many years. On average a new drug takes 8-10 years from potential lead compound to entering the market. The time frame for vaccines is dramatically higher – an average of 35years. The reality is therefore that either the entire process has to be held within the same company and governed by corporate responsibility (and/or trade-secrets) or by strong contractual and propriety rights.

While this system has been relatively successful in the delivery of new drugs for which there is a profitable market, the system has two limiting consequences for the provision of drugs for the poorest[12]. This is can be characterised as presenting on the one hand an affordability problem and on the other hand an availability problem.

Affordability and Availability of Medicines for the Poorest

There are essentially two dimensions of concern in the provision of medicines for the poorest:

- ♦ Affordability of existing medicines;
- ♦ Availability of medicines developed for diseases of the poor in developing countries.

First, there is the issue of the affordability of existing medicines which can be procured by individuals or by health systems on behalf of their populations. In a world where 1.2bn people live on less than 1$ US per day and health spending in total on medicines in countries like Uganda now stand at US$1.2 per head of population in 2003,[13] even the cheapest of medicines are frequently too expensive.

Second, for diseases where no market or only a small market exists, the investment in drug discovery and development is unlikely to be recovered. Private sector pharmaceutical companies which remain responsible to their shareholders cannot justify the up-front and high-risk investment. Such diseases have come to be known as *neglected diseases*.[14]

Neglected diseases mainly affect people in developing countries. Public research institutions in the industrialised world traditionally have not viewed these diseases as either a priority or as a major threat to their populations and research-based drug companies do not pursue promising compounds for drugs to treat those illnesses because of inadequate returns on investment.[15] Only the recent developments in *bio terrorism* and the rapid spread of SARS may have begun to change these positions in recent times.

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[12] Kettler, H. and Towse, A. Public- Private Partnerships for Research and Development: Medicines and Vaccines for Diseases of Poverty, Office for Health Economics, London, 2002.

[13] Caines, K et al. "Impact of Public-Private Partnerships Addressing Access to Pharmaceuticals in Low Income Countries: Uganda Pilot Study", IPPPH, Geneva, 2003.

[14] Medecins Sans Frontieres Access to Essential Medicines and the Drugs for Neglected Diseases Working Group, "Fatal Imbalance – The Crisis in Research and Development for Neglected Diseases", Geneva, 2001.

[15] Ibid.

In addition, developing countries may not give the highest priority to spending on health products and for many countries with the lowest income there is neither the scientific capability nor the manufacturing infrastructure to undertake self-provision. It is estimated that over 84% of global R&D expenditures are concentrated in ten of the OECD countries alone and some 94% of patents are granted in the USA.[16]

Table 3: Two Dimensions of concern in the provision of medicines for the poorest – novel approaches being tried.

Affordability of available Drugs: Mechanisms being used	**Drugs for Neglected Diseases: Mechanisms being used**
Tiered/ preferential pricing with market segmentation	Public Private Partnerships (PPP)
Donation programmes	Creating social markets
Voluntary Licences	Philanthropy
Compulsory Licences	Orphan Drug Approach
Generic Alternatives	Global Fund Purchasing

Table 3 illustrates that there are a number of new initiatives being undertaken to address both affordability and availability issues. Only a limited number of these initiatives address matters related to IP rights. Likewise, these do not begin to consider the problem of accessibility because of poor health infrastructures or the appropriateness of treatments for the way of life in developing countries. Such topics are beyond the scope of this paper.

It is likely that many, if not all of the initiatives in Table 3, will have to deal with IP rights at some point in their operation, but given the political will and the availability of public or philanthropic funds, IP rights *per se* can be managed to deliver the outcome which is desired. The existence of privately- held IP rights will impose transaction costs and may take time to negotiate access but they do not in themselves present an insuperable barrier. Many lessons can be learned from the actions that have been taken by the pharmaceutical industry to date and from the emergence of new models of the PPPs and public sector ventures. The following section will summarise a number of these initiatives to illustrate how IP rights have been and are being managed to deliver improved access to medicines for the poorest and those suffering from neglected diseases.

[16] Pedro Roffe, *IPRs and access to technologies – a developing country perspective,* WIPO-WTO Workshop, November 2003.

Initiatives to Improve Affordability and to Address Neglected Diseases

The pharmaceutical industry has undertaken considerable action in recent years to address its critics and to make major contributions towards the issues of affordability of existing medicines especially for AIDS sufferers in developing countries and to begin to use their resources to tackle neglected diseases.

Private Sector Initiatives

A leading company in this has been GlaxoSmithKline (GSK) plc. Dr. JP Garnier, GSK's Executive Director was recently honoured for his efforts in this field by The American Society of Tropical Medicine and Hygiene (ASTMH)[17]. GSK was cited for its vital contribution to healthcare in developing countries through action in three areas: investing in research and development that target infectious disease particularly affecting the developing world; preferential pricing of antiretrovirals (ARVs), antimalarials and vaccines; and for community investment activities and partnerships that foster effective health care. In June 2001, GSK published a document setting out their commitment and contribution to improving healthcare in the developing world. In 2001, the company issued a progress report[18] in which it cited a number of important IP related initiatives in addition to their approach to preferential pricing for ARVs in 31 countries worldwide.

> One example is a voluntary licensing deal on GSK patents for the ARVs *Retrovir, Epivir and Combivir* to Aspen Pharmacare in South Africa. The license enables Aspen to manufacture the products and sell them to the South African government and others in the not-for–profit sector. GSK waived the right to a royalty fee and instead a 30% fee on net sales will have to be paid to NGO's that manage care programmes related to HIV/AIDS in South Africa. This deal also involved the patent holders of lamivudine (Shire Pharmaceuticals Group plc) who have waived their rights to royalty payments on these products. [18]

The above example illustrates that with political and corporate commitment, IP rights do not necessarily provide a barrier to access. Indeed, the fact that GSK holds the rights enabled them and their commercial partners (Shire) to place conditions on the use of the IP that directs fees from sales toward the delivery of improved healthcare infrastructures in the local domain. This is an example

[17] GSK , Philadelphia April 12th ,2003 ; http://www.gsk.com
[18] GSK, "Facing the Challenge One Year On", Brentford, UK, July 2002.

where, IP control is being used assertively for wider public benefit. Without the existence of IP and the direction of the IP licensor, monies from the purchase of drugs might have been channeled out of the South African healthcare sector.

There are a number of business-initiated HIV / AIDS efforts beginning to roll out in Africa. Extensive discussions and planning over the past year has formed a partnership between The Coca-Cola Africa Foundation, GlaxoSmithKline, PharmAccess International and Population Services International of between US $4m and $5m per year.

> Coca-Cola Africa has provided its 1,200 employees in Africa with comprehensive healthcare benefits, including full antiretroviral drug coverage since June 2001. Since June 2001, The Coca-Cola Africa Foundation has worked in partnership with UNAIDS and focused on three aspects of the fight against AIDS: developing AIDS prevention, education and treatment programmes in local communities; employing Coca-Cola's marketing expertise to develop public awareness and information campaigns; and implementing model human resource practices for employees of Coca-Cola Africa.

It is interesting to note that this initiative does not involve IP rights directly but both multinational companies involved have strong IP policies in relation to their own business. It demonstrates that access to medicines in developing countries is a complex and multifaceted problem with no simple solutions. In general, IP *per se* does not present an insuperable barrier. It is the manner of its use which determines the impact.

In addition to efforts to address the affordability issue by the private sector, the introduction of purchasing mechanisms such as those being developed through the Global Fund[19] can begin to make a difference in attacking the disease burden of the poorest in the world.

In relation to neglected diseases, a number of private sector initiatives are underway. The effort by the pharmaceutical industry is summarised in Table 4.

[19] http://www.theglobalfund.org

Table 4. Major Initiatives Targeting Diseases of the Poor by the Pharmaceutical Companies

DISEASE	INITIATIVE	COMPANY
Blinding Trachoma	International Trachoma Initiative	Pfizer
Guinea Worm	Guinea Worm Eradication Programme	Johnson & Johnson
Leprosy	Global Alliance to Eliminate Leprosy	Novartis
Lymphatic Filariasis	Global Alliance to Eliminate Lymphatic Filariasis	GlaxoSmithKline Merck
Polio	Global Polio Eradication Initiative	Aventis Pasteur Wyeth Chiron
Onchocerciasis	MECTIZAN® Donation Programme Onchocerciaisis Control Programme	Merck
African trypanosomiasis	Sleeping Sickness Partnership	Aventis Bayer Bristol-Myers Squibb

Source: Neglected Diseases and the Pharmaceutical Industry, International Federation of Pharmaceutical Manufacturers Associations, DECEMBER 2003.

The MECTIZAN® programme to tackle onchocerciasis (river blindness) by Merck is probably the best known donation programme for one of the world's neglected diseases. The programme was established in 1987 and now reaches some 30 million people every year in over 30 countries and has donated some 250 million treatments.

Similarly, GSK is working with the World Health Organization in the Global Programme to Eliminate Lymphatic Filariasis (LF). Also known as elephantiasis, LF is one of the world's leading causes of disability and disfigurement. GSK has pledged to donate as much *albendazole* medicines as is required to eliminate the disease from the world by 2020. To date, the company has donated 240 million treatments to 38 countries. It is estimated that some 90-100 million people have been reached, and several countries (including Egypt and several Pacific Islands) are seeing sharp declines in infection levels.

These are important contributions and yet the statistics of suffering continue. For example it is estimated that one child dies every three minutes from Malaria. In Uganda alone, Malaria is responsible for the death of 70,000 to 100,000 children under five years of age annually. When the toll from TB, Chagas disease, Human African Trypanosomaisis, Leishmaniaisis and others are calculated, the lack of effective drugs and the lack of the development of new treatments justify grave concern.

Few of the multi-national pharmaceutical companies have existing programmes of drug discovery for neglected diseases. In 2001, the top 20 pharmaceutical companies in the world were surveyed and while the survey demonstrated activity in the area of neglected diseases, the private sector investment was limited. None of the companies surveyed had brought a drug to market in the last five years for any of the most neglected diseases included in the survey. [20] Indeed, it has been shown[21] that of the 1233 new chemical entities registered between 1975 and 1997 only 11 were for tropical diseases of poverty and half of the latter were for veterinary purposes.

It is accepted that IP *per se* is not an issue in relation to neglected diseases indeed it could be argued that the lack of IP development is part of the problem. As stated above the problem is one of insufficient return to interest private sector investors and a lack of focus by public sector R&D institutions to tackle these problems.

Public-Private Partnership (PPP) Initiatives

This situation has led to the instigation of a number of disease-focused, product-development Public-Private Partnerships being established. The numbers of PPPs which currently exist in the field of global health initiatives are numerous. Many are in relation to "access" in the field – i.e. the delivery of healthcare through national infrastructures. Those PPPs which have an interest in IP management are limited in number.

A number of the PPP's were instigated by the Rockefeller Foundation, including the International Aids Vaccine Initiative (IAVI), Medicines for Malaria Venture (MMV), the Global Alliance for TB (GATB), the International Partnership for Microbicides (IPM) and the Pediatric Dengue Vaccine Initiative (PDVI). These partnerships are based "virtual" models of production and as such operate with extensive use of IP development and partnership licensing. The approach to the

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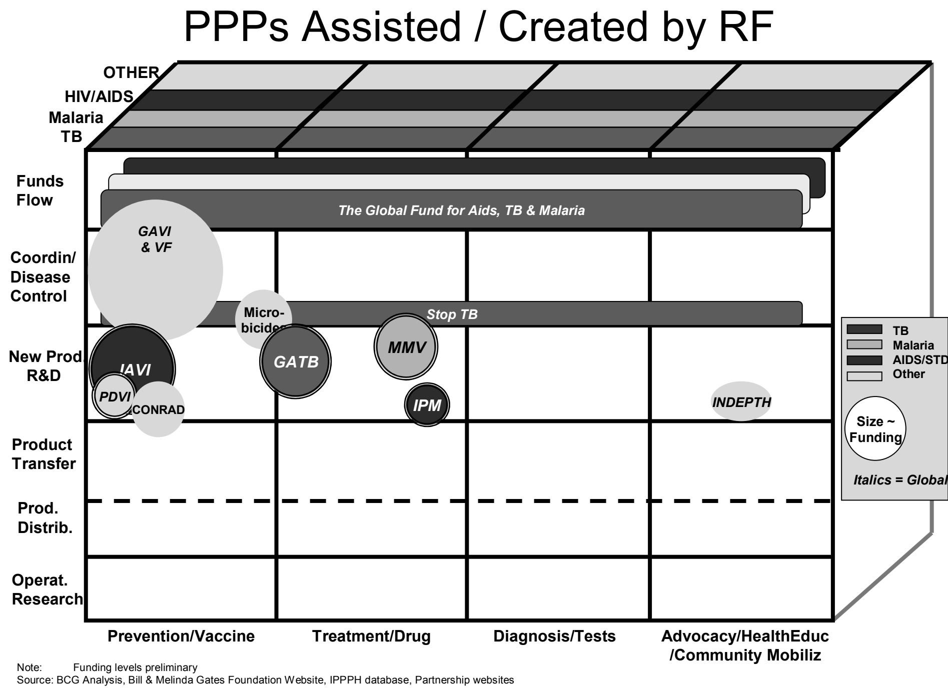
[20] MSF/ DNDi, Op Cit.

[21] Trouiller, P., Olliaro, P., Torreele, E., Orbinski, J., Laing, R. and Ford, N. "Drug Development for Neglected Diseases a deficient market and public health failure", The Lancet, 2002.

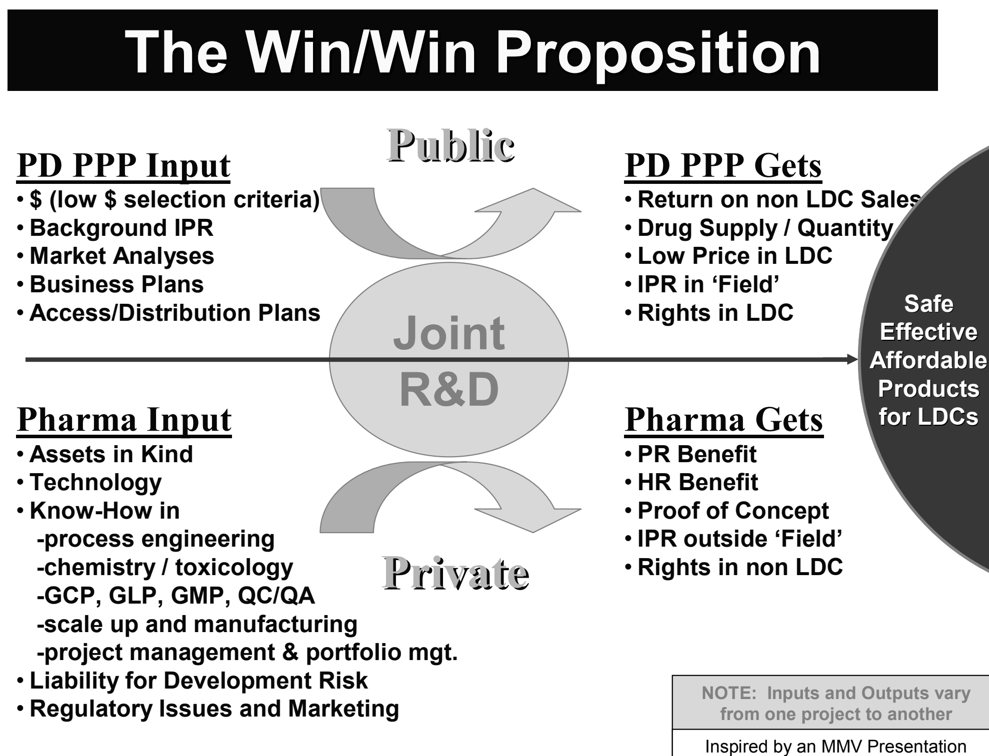
development and ownership of IP varies across the PPPs but none operate without the anticipation that product development will need to be undertaken by license to the private sector.

Table 5: PPPs Involved in Global Health Initiatives



Source: By permission, Rockefeller Foundation, 2003

Table 6: Product-Development PPP's Approach to Partnership



Source: By Permission, Rockefeller Foundation, 2003

A number of the PPP's do not seek to take ownership of the IP which they developing but their partnership agreements are clear about the conditions of access and the approach to limiting the price at sale to "cost plus". In instances where the PPPs may create products which have potential developed markets, all reserve the rights for developing countries. The basis of the PPPs rests on the development of a win/win proposition as illustrated in Table 6 above with the private and public sectors bringing distinctive contributions and receiving appropriate benefits. This includes *inter alia,* IP rights and know-how both as background and its use in the relation to the final distribution of the product which is developed. Two examples illustrate the creative use of IP rights in the PPPs.

Medicines for Malaria Venture (MMV)

Medicines for Malaria Venture (MMV) is a public-private partnership [22] established in 1999 to tackle this major global disease by developing new drugs. In just three years since its establishment. MMV has managed to create what is widely viewed as 'the largest antimalarial drug research portfolio since World War II' comprising of 15 projects at different stages of development. The

[22] http://www.mmv.org

objective of MMV is to introduce an inexpensive antimalarial drug designed for developing countries' conditions every five years. Thus, the founders of MMV hope to address both the problem of resistance and the need for affordable drugs for the populations most affected by malaria – i.e. pregnant women and children. Malaria has become one of the priority diseases targeted by various international organisations, and MMV and other attempts to develop new antimalarial medicines fill in an important gap in the antimalarial value chain (e.g. GlaxoSmithKline work with Malaria Vaccine Initiative on Phase III clinical trials of a malaria vaccine candidate).

Medicines for Malaria Venture (MMV) works only on malaria drugs and seeks to balance a portfolio in terms of risk and opportunity by investing in early discovery, preclinical and development projects. The challenge in this area of neglected disease is great and affordable and appropriate treatments could have dramatic impact. MMV works with both academic research groups and with large pharmaceutical companies. Its approach to the management of IP rights varies but it does not necessarily seek to own the IP or to have exclusive rights. MMV has focused on retaining exclusive marketing rights for any malaria product produced in low-income countries where the disease is endemic.

Global Alliance for TB Drug Development

The Global Alliance for TB Drug Development is a public-private partnership driven to halt the rise and reverse the spread of the world's oldest infectious disease by developing new, faster-acting and affordable tuberculosis medicines[23]. It is estimated that there are currently some 1.9bn people worldwide infected by TB, and while one person dies every 15 seconds, there have been no new drugs developed in the past 30 years. The Alliance sets out to accelerate research and development in the field and to ensure affordability of the drugs developed, especially in the more impoverished countries with a high burden of TB. A not-for-profit venture, it seeks to connect the best practices and drive of the private sector with the resources and health equity needs of the public sector, designing new ways to leverage worldwide science and market forces for public good.

The TB Alliance pursues intellectual property rights with the sole focus of ensuring the availability of novel technologies for public benefit. This approach allows the balance of affordability and health equity with effective incentives for collaboration and win-win agreements. For example, PA-824 was acquired through an exclusive license deal with Chiron Corporation in June 2002. PA-824 has moved briskly through the R&D pipeline, passing several important milestones in preclinical development. Key issues of compound synthesis,

[23] http://www.tballiance.org

toxicology and preclinical efficacy have been addressed. Early research during the discovery stage showed that PA-824 and its analogs demonstrated activity against both drug-sensitive and multi-drug resistant strains of TB, signaling possible improvements in TB treatment. Development is being undertaken with support provided by the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health.

Other Initiatives

Other initiatives which characterize themselves as not-for- profit pharmaceutical companies, such as One World Health[24] and DNDi[25] have also been established to develop drugs for selected neglected areas.

One World Health

The Institute for One World Health advances global health by developing new medicines for infectious diseases that disproportionately affect the developing world. Launched in 2000, the Institute for OneWorld Health is the first non-profit pharmaceutical company formed in the United States to bridge the gap between medical science and its application to the urgent health needs of the developing world. Using an entrepreneurial business model, OneWorld Health fuses the rigors of pharmaceutical science with the dedication of a social mission.

OneWorld Health's experienced team of pharmaceutical scientists uncover the most promising drug and vaccine candidates to develop effective and affordable medicines for those most in need. OneWorld Health directs the preclinical and clinical development of drugs and vaccines and then seeks regulatory approval of these new medicines in the most affected developing countries. OneWorld Health targets infectious diseases in the developing world that lack adequate therapies, such as leishmaniasis, Chagas disease, diarrheal diseases, and malaria. Each year these neglected diseases threaten more than four billion people worldwide.

In one of the first deals of its kind, Celera gave the San Francisco-based Institute for OneWorld Health an exclusive license to develop a treatment for parasitic infections in people. Celera will not receive any royalties or cash payments in exchange for the license to the drug, known as CRA-3316. The company made the deal because of the lack of commercial opportunity. Celera may benefit if the group's research proves that the concept behind the drug works, opening potential opportunities for similar medicines.

[24] http://www.oneworldhealth.org
[25] http://www.dndi.org/

The group is working with the National Institutes of Health (NIH) to test CRA-3316 for treating Chagas disease, a parasitic infection that afflicts an estimated 16 million to 18 million people in Central and South America and kills about 50,000 annually.

Most people with Chagas disease are poor. The infection is spread by insects that live in cracks and holes of poorly constructed homes, or by blood transfusions. Current therapies, developed in the 1940s, treat only the early, acute phase and can have severe side effects. There is nothing to treat the chronic phase, in which parasites multiply, weaken the heart and eventually cause fatal heart failure. CRA-3316 drug targets an enzyme that the Chagas disease parasite needs to survive, and scientists hope it will prove to be a safe, effective oral treatment. The NIH is conducting animal studies, and the Institute for OneWorld Health hopes to start the first human tests this year. The institute believes CRA-3316 could be made affordable for developing countries.

Drugs for Neglected Diseases (DNDi)

DNDi which is the brainchild of MSF was established as a not-for-profit foundation in 2003. It is working specifically with the public sector and recognizes that while the commercial sector can contribute to such developments that it cannot be expected to take the lead. DNDi is stated to have three core objectives:

- Developing a needs-driven portfolio which will undertake projects which in the short term will seek to make better use of existing drugs and compounds and in the longer term will organize research on new leads;
- Raising awareness about the need for R&D for neglected diseases;
- Use and strengthen existing capacity in and technology transfer to disease-endemic countries.

DNDi has initial core funding from MSF for five years while it hopes to raise a mixture of public and private funding of up to $250m over a period of 12 years and in that time deliver 6-7 registered drugs. The initiative aims to attract over half of its funding from public sector sources.

Early Stage R&D licensing and example from Yale University

In February 2001, MSF, sought permission from Yale University in the USA to use a generic version of the AIDS drug, *stavudine* in South Africa[26]. The licence to the drug candidate had been licensed exclusively to Bristol Myers Squibb and although the request was directed to the University, because of the nature of the license it was the decision of the drug company which agreed to supply in South Africa. The University opened discussion with the pharmaceutical company regarding its position on patent protection in South Africa. Although the negotiation had in fact little to do with the IP rights which existed and much more to do with the long-term business relationship between the University and the company, two excellent examples arise from the action that was taken.

First, the potential for licenses from publicly funded research to determine access to drugs for those most in need and second, the fact that access arrangements could be developed that would neither abrogate the University's responsibility under the Bayh-Dole Act nor financially disadvantage the licensor.

Following the action taken by Yale University, the development of good practice procedures has grown momentum and can be seen to have important potential for the future availability of new drug leads arising from US (and other) university research. US universities file over 3,000 patents per annum[27]; therefore the potential for creating a more positive patent position in bio-life in the future has significant potential.

Yale itself has adopted a charter of good practice in licensing and has a recent example of innovative licensing by subdividing the rights for fields of use between a private sector company and a non-profit drug development initiative in relation to a compound which may have commercial return in one field of use and be a potential candidate for a new treatment for one of the world's neglected diseases.[28]

The Concept Foundation

The Concept Foundation[29] is a not-for profit organisation for the Management of Intellectual Property through Public-Private-Partnerships with Pharmaceutical Industry for Maximizing Public Sector Benefits. It was established in 1989 in

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[26] Kapczynski, A. Crone, T.E. and Merson, M, "Global Health and University Patents", Science, Vol.301, 19th September, 2003.
[27] AUTM Annual Survey 2002.
[28] Personal correspondence.
[29] www.conceptfoundation.org

Bangkok, Thailand. The Foundation is focused on increasing product availability and product choices for reproductive health care services in developing countries. It was established initially for the purpose of managing existing intellectual property.

An example of creative licensing can be seen in the work which the Concept Foundation has undertaken in relation to access to the once-a-month injectable contraceptive Cyclofem®. IP rights covering Cyclofem® were transferred to the World Health Organisation and licenses to produce the contraceptive were granted with non-exclusive global rights in the public sector and strict price controls. As a result, hundreds of thousands of women in developing countries who could otherwise not afford this product now have access to it.

The IP owned by the Concept Foundation is primarily in the form of:

- Data from medical research and clinical trials,
- Data from pharmacological studies
- Manufacturing instructions

In other cases, the IP owned by organisations such as the WHO which may have been received through donations from pharmaceutical companies for use in public sector applications in the developing world. The Concept Foundation then enters into license agreements with the private sector for the manufacture and marketing of the products worldwide. In its licence agreements the Foundation sets out the terms and conditions. All licensees are bound to public sector distribution in developing countries as their top marketing priority over the sales into private markets.

The Contribution of Creative IP Management

As can be seen from the discussion above, IP management may be an essential tool in the delivery of medicines in developing countries. In other cases however, it is the lack of developed IP which is the problem. In 2002 an organisation was established to work specifically in this area. The Centre for the Management of Intellectual Property in Health Research and Development (MIHR) [30] was established as a not-for-profit organisation with UK charitable status. Based in Oxford, England the organisation was founded by the Rockefeller Foundation and has drawn additional support from the UK Department for International Development and the Wellcome Trust among others. MIHR has as its vision

[30] http://www.mihr.org

"To contribute to a world in which creative management of intellectual property leads to better health in developing countries."

Important objectives for MIHR are to improve the understanding of the role which IP management can play in the availability of medicines for those in need in developing countries and to work with partners in developing and developed countries to find ways to use IP and its management for this purpose. MIHR has a group of twelve international experts as its Board of Trustees and in addition draws on the expertise of members of its Committee of Interested Parties who come from over 48 organisations worldwide. In addition to the publication of a Handbook of Best Practices in Intellectual Property Management in Health research and Development, MIHR has led a number of workshops and training conferences in places such as South Africa, Egypt, India and Mexico, to assist the development of IP policies for public sector R&D institutions and to help promote their capability to utilise intellectual property for local applications for those in need. As part of this work, MIHR uses a portfolio of case study examples to demonstrate the potential for the more creative management and licensing of IP in health R&D. The examples used here come form that portfolio.

Conclusions

As has been demonstrated by a number of the case studies presented here, IP and its creative management can make a vital contribution to the development and availability of new therapies to treat the diseases of the poor in developing countries. As the funding for Global Health initiatives increase and as new models are established for drug development, the positive and imaginative management of IP becomes a tool which can ensure that the outcomes of that increased investment are directed to the poor in developing countries.