

Intellectual Property and Product Development Public/Private Partnerships

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This is the final report of an interview study of US-based product development public/private partnerships (PDPPPs) focused on the development of new drugs, vaccines, and other products for diseases that disproportionately affect developing countries. PDPPPs are nonprofit entities that sponsor others to perform or directly perform themselves at least one of the following R&D activities: basic research (such as target identification, validation and proof of concept), animal, preclinical and clinical testing, licensing, and manufacturing. The successful PDPPP may also be responsible for distribution. PDPPPs are distinguished from Access PPPs, which are nonprofit entities concerned primarily with expanding access by pulling together manufacturers, funding agencies (such as GAVI, USAID) and developing countries to enable the purchase and distribution of existing drugs, vaccines, and other medical products.

The roles of PPPs are depicted in Figure 1. Access PPPs typically function to bring existing drugs to underserved markets. PDPPPs, in contrast, serve to defray some of the costs and risks of product development, thereby motivating firms to provide necessary capital and technology to provide new products to the developing world. As shown in Figure 1, this is only necessary for diseases for which there is no or only limited developed world private or “payer” markets from which pharmaceutical firms would typically expect to recoup and profit from their investments in R&D. If there is a limited payer market, then push strategies may be sufficient to entice firm investments by minimizing the risk of development. If there is no effective payer market, push strategies would be inadequate, and purchase guarantees or other pull strategies would be called for. If there is profit to be made, then firms will take the risks themselves, and would likely be unwilling to partner at the development stage because of what they would be asked to give up (IP rights and, perhaps more problematically, proprietary know-how). This

study does not include Access PPPs, except to the extent an Access PPP also engages in or sponsors research that facilitate the entry of products into developing countries.

Disease / Market Characteristics	Products needed	Existing product(s)
Large developed countries markets	Pharma will develop drugs at own expense	
Payer markets not adequate to support R&D; large public market demand	PDPPPs	Access PPPs
No payer market; large public market demand	PDPPPs	Access PPPs

Figure 1 The roles of PDPPPs and Access PPPs in helping to develop and provide drugs, vaccines, and other products to developing countries. Note that the shaded area may be a null set, because products would not have been purposively developed unless there was an advanced economies market.

The aim of this study is to describe: 1) the range of models used to organize and fund each effort; 2) the nature and comprehensiveness of intellectual property (IP) faced in an area, and the strategies and experiences of PDPPPs in addressing IP issues; 3) the number and nature of collaborative and licensing arrangements used to gain access to necessary IP and technological know-how; and 4) any problems faced and solutions developed to ensure freedom to use. One aim of this study is to place intellectual property issues into the larger context of

development and distribution of products in an environment that is technologically and fiscally challenging, highly regulated, and subject to international trade conditions.

METHODS

The method used in this study was to: 1) develop a census of US-based PDPPPs; 2) examine publicly available information (e.g., websites, news accounts, and published case studies (1,2)) about the founding, goals, funding, and strategic planning of the organizations; and 3) use semi-structured interviews of top managers, attorneys, and consultants to examine experiences with the use of and problems raised by intellectual property.

The interview guide is included as Appendix A. The study was approved by the University of Pennsylvania Institutional Review Board. Interviews were planned to be taped and transcribed, and all data was to be recorded for attribution, unless specifically requested otherwise by a respondent.

To begin the study, the author attended a workshop of PPP executives, attorneys, and others, entitled Dealmaking and Intellectual Property Management for Public Interest, held at Aeras Global TB Vaccine Foundation, Bethesda, Maryland, USA, on November 29-30, 2004. This meeting proved quite useful, as attendees aired many of the common issues they face in negotiating agreements with commercial firms, universities, and others (3). The interview guide was modified to address some of the issues raised at the meeting.

It became clear from the meeting, in which speakers uniformly asked that their comments be held in confidence and not discussed outside the group, that the details of the contractual issues to be addressed in this study were considered proprietary and that it was highly unlikely that interview respondents would be willing to speak openly for attribution. Thus, it was decided to hold interviews in confidence, without taping, to assure respondents that no results would be

reported in a way that would identify them or their institutions. Even with this change, respondents clearly avoided discussing specific details of existing contracts and, even more so, of ongoing negotiations.

It also became clear that the sample of institutions that could be examined are the relative “success stories.” Inquiries of attendees suggested that there were 2 cases in which efforts to start a development venture foundered, attributable to inability to gain access to necessary intellectual property from industry. It was suggested that the firms were unconvinced of the value of the relationship and what the proposed organization would offer them. Unfortunately, we were unable to get any leads to individuals involved in these efforts from whom we might have learned more.

The beginning sample of US-based PDPPPs was generated from the list compiled by the Initiative on Public-Private Partnerships for Health (4). Several listed organizations were found to be filling advocacy and facilitation roles, and were not actually *funding or performing research and product development*; several of these groups were interviewed to gain their insights to the relevant IP issues. One organization bridged development with access of forthcoming products, and was retained in the sample because it was performing product development research in developing countries.

Snowball sampling identified 2 other PDPPPs: Global Vaccines Inc. was added to the sample, yielding a total of 14 PDPPPs. The Population Council was identified too late in the process to be included in the interview sample. It was planned to include about 3 non-US based institutions in the sample for comparison purposes, but this was determined to be of little potential value, because the broad range of practices revealed by the US-based institutions suggested that no useful comparisons could be drawn from a small number of non-US PDPPPs.

Finally, we attempted to identify and interview individuals from relevant nongovernmental funding agencies as well as individuals in a handful of firms that have contracted with subject PDPPPs to gain some insight to their perceptions and experiences with IP issues.

With the assistance of Celia Goetzl (UPenn) and David Chokshi (Oxford), web-based searches were performed to describe the history, management, and institutional goals; sponsorship, partnership and licensing relationships; and IP policies and patent ownership of the PDPPPs. This information is summarized in Appendix B.

RESULTS

Between December 2004 and mid-May, 2005, interviews were sought with a total of 30 individuals, using phone calls and email, and 24 interviews were held with representatives of all 14 PDPPPs in the census as well as 5 other organizations. There were no express refusals.

Models of Organization

There is no single model being pursued for situating, structuring, or managing PDPPPs. This holds true as well for IP management. Nonetheless, there are several common threads. First, the organizations are nearly uniformly run as small businesses that happen to be nonprofits. As one Respondent put it, a PDPPP “needs a sound business model” to be successful, and another noted that they intended to apply “biotech type discipline to developing world diseases.” Second, these PDPPPs are highly goal oriented; they are narrowly focused, “laser like,” on generating the necessary science and technology in order to move products towards commercialization. The means by which these organizations pursue this common goal vary widely.

PDPPPs vary in their in-house specific competencies, ranging from the purely “virtual” – where all research, development, and manufacturing capacity is contracted from universities or firms – to those having substantial scientific and other resources and expertise needed for carrying out discovery, running clinical trials, securing regulatory approvals, and manufacturing. For most organizations, FDA licensing of new drugs and vaccines is left to commercial partners that have the necessary expertise. Most PDPPPs are early in the discovery and development processes, and have not yet addressed regulatory requirements, much less manufacturing and distribution, leaving these issues for future resolution.

Contractual Relationships

PDPPPs report using all types of relationships with businesses and universities, including giving grants and loans, creating partnerships and consortia, and using collaboration agreements, sponsored research agreements, and in- and out-licensing (on exclusive and nonexclusive bases). This reflects the wide spectrum of development efforts being pursued, from basic discovery of new agents to all phases of preclinical and clinical trials. Two recent successful clinical trials were reported in the press for the Malarial Vaccine Initiative and the Institute for OneWorld Health, both of which organizations must now move toward manufacturing and distribution.

Respondents were asked about the contracting terms that presented the most difficult issues for them. First, many stated that in-license pricing presented a hurdle. According to several respondents, negotiations with academic institutions were often hard, reflecting rigidity and overvaluation. One respondent mentioned 2 cases of protracted negotiations in which a university demanded royalties (on gross revenues) for licenses covering developing world markets. Others mentioned the perceived preference of university technology managers and faculty to secure up-front licensing fees in lieu of downstream royalties to cover their costs of

patent prosecution and reward the inventors. One Respondent reported that licensing from universities was getting worse in time, but several respondents contradicted this, noting that things are improving with universities being more flexible and creative. This may reflect the effort by the Technology Managers for Global Health, an interest group within the Association of University Technology Managers (AUTM) to raise awareness of licensing opportunities to benefit the developing world.

Regarding licensing with others, several respondents reported that negotiations with biotechs were difficult for them, because the firms tended to look at the PPP as a source of funds without concomitant duties or rights in resulting IP. On the contrary, one respondent stated a preference for working with biotechs because of the ability to secure favorable terms, in contrast to large pharmaceutical firms. Finally, another respondent was of the opinion that licensing from the NIH was trickier than from universities or firms because of “strict” practices and difficulty extracting commitments. Despite these difficulties, there were only a small number of cases reported by Respondents in which license negotiations broke down; given that these PDPPPs had entered a large number of contracts (ranging from a handful to more than 20 different agreements for each institution) suggests that most of the time deals can be struck.

Second, many respondents noted that contracts related to R&D left many issues related to manufacturing and distribution to future resolution. Rights or options for manufacturing held by a commercial partner appeared to be common in sponsored research and codevelopment agreements. These rights are typically subject to quantity and pricing targets. Only if those targets are not met would rights vest in the PDPPP, giving it the ability to seek alternative manufacturing and distribution partners or licensees. A sticking point in resolving such contingencies involved the transfer of know-how; this was particularly sensitive for vaccine

manufacturers, where proprietary know-how may be much more important than any patented technologies. This nonetheless was often resolved explicitly in contracts, by granting rights to know-how, defining know-how in great detail in contractual documents, and in one case, requiring that know-how be reduced to writing and deposited in escrow.

A third major contracting issue involved target pricing. As discussed above, all PDPPPs seek to develop products that will be provided into developing countries at a low cost, to assure broadest access. Of course, since most development efforts are relatively nascent, there is a lot of uncertainty about pricing of any potential products. Thus, price negotiations typically call for drugs for the developing country markets to be provided at “reasonable” or “affordable” prices, or providing a stated markup over costs. The latter results in complex negotiations over how cost will be calculated (5).

Finally, the fourth common negotiation issue is market segmentation. Negotiations over markets typically differentiate between countries with sizeable private or payer markets and those with small private markets and sizeable or overwhelming public markets. A commonly relied upon starting point was use of the so-called GAVI countries, a list of (currently 71) countries eligible for funding from the Global Alliance for Vaccines and Immunization and the Vaccine Fund to buy vaccines (6). Other Respondents mentioned using the WHO’s list of advanced economies as well as World Bank income data.

The difference in markets is depicted in the demand curves shown in Figure 2. There is general agreement about the wealthy countries (depicted by curve A) and poor developing countries (B), and negotiation often focuses on dividing rights in those mixed market countries that have sizeable payer markets as well as large public markets (C) (typically focusing on

Brazil, India, and China). For some communicable diseases such as Malaria, the only demand in developed countries is for the “traveler’s market” and the military.

For mixed market countries, one respondent mentioned the difficulty of getting some governments to accept tiered (discriminant) pricing. An open question regards what types of discriminant pricing models are available, how effective they are at maintaining market differentiation and their long-term political viability.

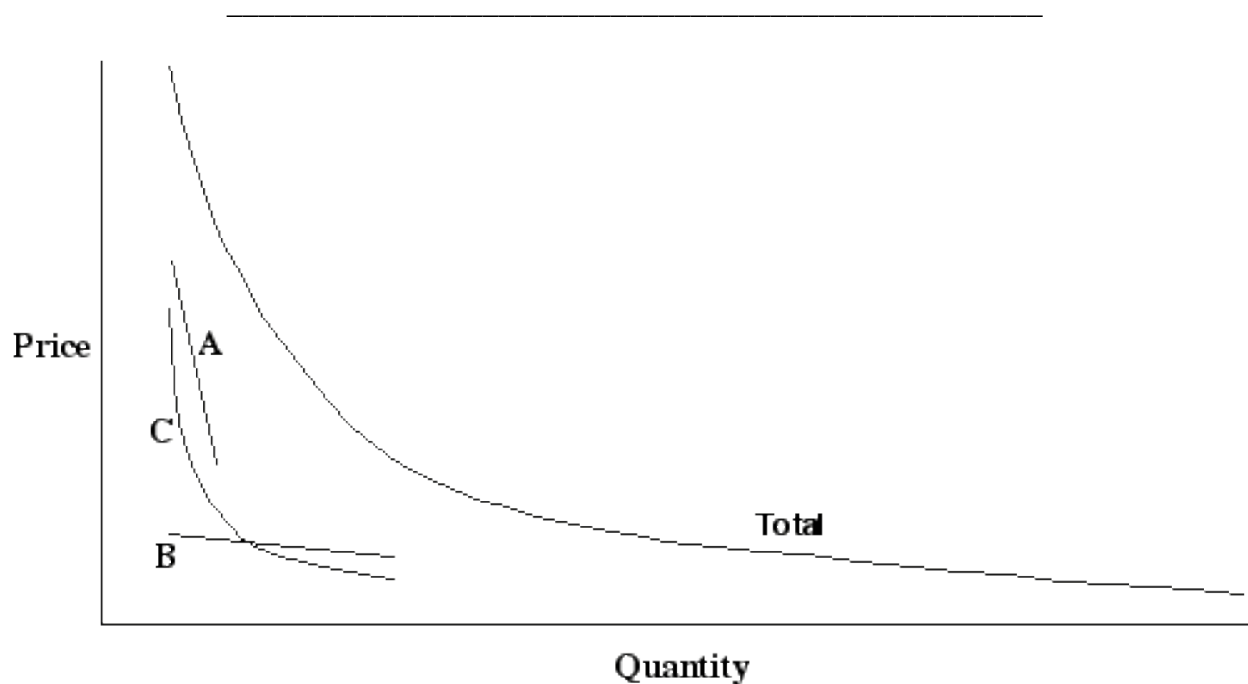


Figure 2 Hypothetical demand in a small rich country (A), a large poor country (B), and a large mixed income country (C). The Total aggregates demand across all markets. PDPPPs are one mechanism for addressing the need for drugs by large numbers of persons across the world, where the profits to be earned in potential payer markets do not justify the financial risks of product development for the firm.

Intellectual Property Issues

All Respondents were duly respectful of patents and intellectual property generally, recognizing that patents are necessary to ensure an exclusive period during which the patent holder can profit and recover the substantial costs of R&D. As one Respondent put it, “Our

success depends on treating IP just like a company handles it.” This was viewed by some as true even for developing country markets. One Respondent related that lack of patents on a hepatitis B vaccine had allowed 6 different firms to develop products in India, where the market could not justify and support this oligopoly. In the long term, the firms will undoubtedly adapt, but the fear of excess competition could suppress product development and innovation in the future. Others felt that the exclusivity assured by patents was inconsistent with the underlying goal of broad and inexpensive product access. One Respondent also commented that ownership and profiting from developed world sales could be a conflict of interest that would bias them in making judgments about which products would be best to support in developing countries.

All PDPPPs perform due diligence on intellectual property, typified by prior art searches and freedom to operate (FTO) analyses. Nonetheless, the extensive “landscape” analysis performed by MVI (7) was unusual; most Respondents noted that such studies are simply too expensive (costing upwards of U.S.\$50,000) and that their money is better spent elsewhere. Only one Respondent reported knowingly infringing patents after having difficulty getting a license, asserting that by the time a product was developed, the patents would have expired. In all other cases, Respondents reported that they would seek licenses or work around existing patents. One respondent reported several instances in which licenses on acceptable terms could not be negotiated, and in each case the PPP was successful in developing and patenting new and improved technologies. The development of a portfolio of patents assured the PDPPP the freedom to operate, and also provided it with negotiating power and intellectual assets.

The respect shown for intellectual property may be explained by the fact that PDPPPs view themselves as nonprofit companies and many PDPPP executives have corporate biotechnology and pharmaceutical company backgrounds.

PDPPPs have adopted markedly different strategies regarding ownership of IP, ranging from outright ownership (or at least coassignment of patents resulting from sponsored or collaborative efforts) of all IP in order to control its use, to not wanting to own any IP as long as rights (ranging from letters of intent and memoranda of understanding to outright licenses) sufficient to meet the organization's goals are obtained. Some PDPPPs reported being assigned patents by universities and companies at which they sponsored research; others allowed the partners to retain ownership of any resulting patents, subject to licenses for developing world uses.

The organizations seeking broadest rights recognize the value of those rights if they can be translated into products that can be sold in developed countries (and payer markets in mixed market countries). As one Respondent stated, ownership yields "something to sell," that can be leveraged to entice commercial partners as well as to generate revenues from royalties to support the main, charitable goals of the organization. Another Respondent called this a "Robin Hood" strategy. For all PDPPPs adopting this stance, no royalties are collected on licenses covering developing country markets.

Some organizations reported being assigned patents by collaborators despite a general policy opposing ownership. The costs of patenting led others to be careful about what they would patent, and where they would seek protection. One Respondent noted that worldwide patent rights could cost U.S.\$500,000, and maintenance fees on their patents were close to U.S.\$100,000 per year. A search of the US Patent and Trademark Office database (<http://www.uspto.gov/patft/index.html>) found that many PDPPPs in the sample have been assigned patents, as shown in Appendix B. This data likely understates ownership because it

may fail to capture secondary assignments, and no data on licensing rights to patents were collected.

We asked Respondents about problems they have had related to IP, and several related cases in which patents presented problems, both for the science as well as the business of their organizations. One Respondent stated that “a few times” patent holders have refused to license patents on key antigens or antibodies, where the PDPPP was compelled to either focus development efforts on countries where no patents had been secured or to use alternative, “less effective” targets. A different Respondent associated with the same organization reported a case, perhaps one of those discussed above, of an affiliated academic scientist who avoided use of a patented antigen, choosing instead a less scientifically preferred alternative.

One major concern about patents is that they may block development of products for use in markets that can not afford to pay patent rents. Few Respondents reported cases in which they were unable to secure licenses. Two Respondents reported that their organizations had approached firms that held exclusive NIH licenses on, in one case, a potentially blocking patent, and in another, a desirable technology, and in each case licenses were outright refused. In the latter case, the PDPPP was able to invent around the technology. A third Respondent reported that a company had refused to grant a license for an “enabling technology” even though it was for a different field of use, and the PDPPP was able to use other technologies to fill the gap. A fourth Respondent related a case in which a vaccine was exclusively licensed by the NIH with worldwide rights to a large pharmaceutical firm, which had no intention to market in the developing world; the NIH was heavily – and successfully -- lobbied to get them to alter their licensing strategy in subsequent technology transfer agreements.

Challenges Faced

To place the problems of IP in context, Respondents were asked what hurdles had been faced in achieving their goals, and what challenges they anticipated in the future. Not surprisingly, many Respondents discussed the complexity of the science, particularly in early stage drug discovery and vaccine development. Several others mentioned the broad range of issues involved in simply establishing and running what, in effect, is a small, international pharmaceutical company.

Nearly all Respondents raised the concern about the sustainability of their efforts; that is, ensuring continuity of funding and collaborative relationships to maintain progress and avoiding what one Respondent called “donor fatigue.” As one Respondent put it, funders must be “willing to stay the course.” For another, it was sustaining the “political will” to prioritize treatment of their target disease. Several Respondents stated that sponsors had unreasonable expectations about the duration of the effort, and that they had to work hard at keeping interest up for the requisite 5 to 15 years it could take to bring their various products to market.

On a related point, several Respondents noted that there is limited money available to support PDPPP efforts, largely from the Gates, Rockefeller and a number of other foundations, USAID, and various foreign governments. There is a tension between diversifying the portfolio of R&D efforts and ensuring the most promising efforts are funded adequately. The growth in the number of PDPPPs will spread those limited funds, limiting what’s available to any one effort. There may also be too little diversity in potential funders, translating in too great a reliance on the Gates Foundation. As one Respondent put it, “but for Gates, we’d be dead.”

Finally, one Respondent discussed the problems of demonstrating sufficient and credible demand to justify risk-taking by corporate partners; this Respondent stated that IP is but one

piece of the larger economic and market puzzle, and that given adequate market pull, the economic incentive would ensure that the IP issues would be resolved. Consistent with this, another Respondent noted that for some early stage discovery of product development targets, “push didn’t work,” compelling the PDPPP to take products further down the pipeline, through clinical trials, before they could “reengage industry” to pick up and run with a product.

Overall, most Respondents did not perceive IP issues to be insurmountable, but they clearly are requiring substantial efforts in time and money to manage. As one Respondent put it, his “day job is to work around tough IP issues.” Several Respondents mentioned the high costs of patents, maintenance fees, freedom to operate studies, and legal services related to contract negotiations, the costs of which they would prefer to spend on their science.

DISCUSSION

The results reported here suggest that the environment in which these PDPPPs are operating is changing rapidly. Several Respondents noted that universities and others are more open now to innovative licensing strategies than they had been in the past. It was also noted that the NIH has been moving from basic science funding towards sponsoring development. Indeed, numerous Respondents noted that what they are doing really is a no-brainer. There are substantial potential benefits of facilitating product development for use everywhere, with a focus on ensuring access in developing countries. There are also few downsides, and the approaches being pursued should appeal to everyone, including industry. Several Respondents noted that they have the “moral high ground” that can be used, if necessary, to publicly pressure corporations, universities, and governments to license on reasonable terms. It was acknowledged, however, that this card should not be played often, or lightly.

From a critical perspective, a health policy colleague, Don Light, suggested that, because of the primacy of corporate interests served in PPP arrangements, PPPs should be called private/public partnerships (8). We find that in most partnerships, corporate partners retain substantial rights for manufacturing, subject to meeting developing country demand. Pricing would be set to provide some profit. By externalizing for the firm at least some R&D costs and otherwise helping to facilitate the overall process, PDPPPs aim to bring value to their corporate partners while retaining rights to markets that cannot afford patent rents. Interestingly, the best price in these (as a matter of fact, all) markets would arguably be achieved by pure competition for manufacturing and distribution, as this would drive prices toward their marginal costs of production. Nonetheless, only one Respondent explicitly mentioned pursuing this model. Instead, only if the corporate partner fails to meet demand or otherwise breaches production targets would the PDPPP be free to look for alternative manufacturers. It does seem that IP ownership or exclusive rights in developing country markets unburdened by contingent manufacturing rights of partners would be a dominant strategy for a PDPPP to pursue. Nonetheless, that PDPPPs have not secured broader rights may reflect their lack of market power or perceived value added for firms. Consistent with this, one Respondent noted that they are more likely to retain rights in deals with small biotechnology firms because of their greater leverage, and several other Respondents noted that it is simply easier to contract with smaller firms for the same reason.

Respondents voiced 2 potential downsides of partnering for firms. First is the issue of technology transfer and know-how, where firms do not want to put their proprietary technology at risk of disclosure, especially to rival firms. This may be the biggest reason firms seek to retain manufacturing rights. Indeed, one corporate Respondent noted that they will not license know-

how, saying they “guard that very very closely.” Second is the concern, often voiced by big Pharma, about the political viability of price discriminant practices. This can (and has) led to calls for legislation to permit parallel importation of drugs. The potential political fallout is said to be one reason drug companies give away drugs for use in developing world markets in lieu of selling them at deep discounts.

Conclusion

The PDPPPs studied here can be characterized as a fledgling “industry”; just over half of the organizations are less than 5 years old, and only 2 predate 1990. On a microscale, these entities are dealing with fundamental questions about the relationship between intellectual property and drug and vaccine development and access that face policy makers at national and international levels. From all of this experimentation may emerge new models for addressing public health needs in the developing world, as well as new insights about patents and pharmaceuticals. It is too early to tell which, if any, models work better than others, and particularly whether aggressive patenting and ownership strategies will help PDPPPs achieve their charitable goals more effectively than alternative strategies.

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