Pragmatic and Principled: DND*i*'s Approach to IP Management

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ABSTRACT

The mission of the Drugs for Neglected Diseases initiative (DND*i*) is to develop safe, effective, and affordable new drugs for patients suffering from neglected diseases and to ensure equitable access to these drugs. DND*i* believes that intellectual property (IP) rights should not pose a barrier to access to these medicines. Hence, a balanced approach to IP management is critical for effective implementation of DND*i*'s mission. The organization has written an IP policy that both encapsulates and articulates DND*i*'s approach to IP based on core principles and beliefs. The policy reflects the DND*i* philosophy, vision, and mission, ensuring that its products are accessible and affordable to patients who need them most. DND*i* recognizes the reality of IP and seeks to implement its humanitarian mission using best, pragmatic practices for IP management. Indeed, DND*i* has already demonstrated that this is feasible, having successfully negotiated with both private and public sector institutions in order to actualize its principled mission.

1. INTRODUCTION

In 1999, a need was identified for an alternative method to research and develop new drugs for infectious, tropical diseases. The doctors of Médecins Sans Frontières (MSF) gave testimony to the fact that the handful of drugs (to treat such diseases) that did exist was inaccessible to patients suffering from the diseases. Most of the drugs still have to be delivered in hospital situations, which is difficult where health care is rudimentary. In addition, the medicines are unaffordable, as a consequence of the need to recoup the supposedly high costs of researching and developing the drugs and the need for pharmaceutical companies to make a profit. These drugs were, and are, not only out of reach for individual patients but also for governments of disease-endemic countries. Intellectual property (IP) rights are among the factors driving these high prices, leaving patients in the developing world to their own limited resources and, ultimately, to undesirable outcomes with disability and death as the worst consequences.

The statistics show that hundreds and thousands of disadvantaged people in developing countries are suffering their diseases in silence. These patients are unable to afford even the (largely inadequate) existing treatments, most of which have toxic side-effects, are ineffective, and need to be delivered in hospital conditions. These patients, though they urgently need new, safe, and field-adapted medicines, do not constitute lucrative markets that the current drug R&D model targets, hence the plight of these patients remains unanswered (Figure 1). Of the 1,556 new drugs that came to the market from 1975 to 2004, only 21 (1.3%), were for tropical diseases such as human African trypanosomiasis, Chagas' disease, leishmaniasis, helminthic infections, schistosomiasis, onchocerciasis, malaria and tuberculosis – diseases that account for 12% of the global

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disease burden. Ten of the 21, including four of the five developed since 1999, were marketed for malaria and tuberculosis.[1] This fatal imbalance is responsible for the deaths of more than 35,000 people a day.

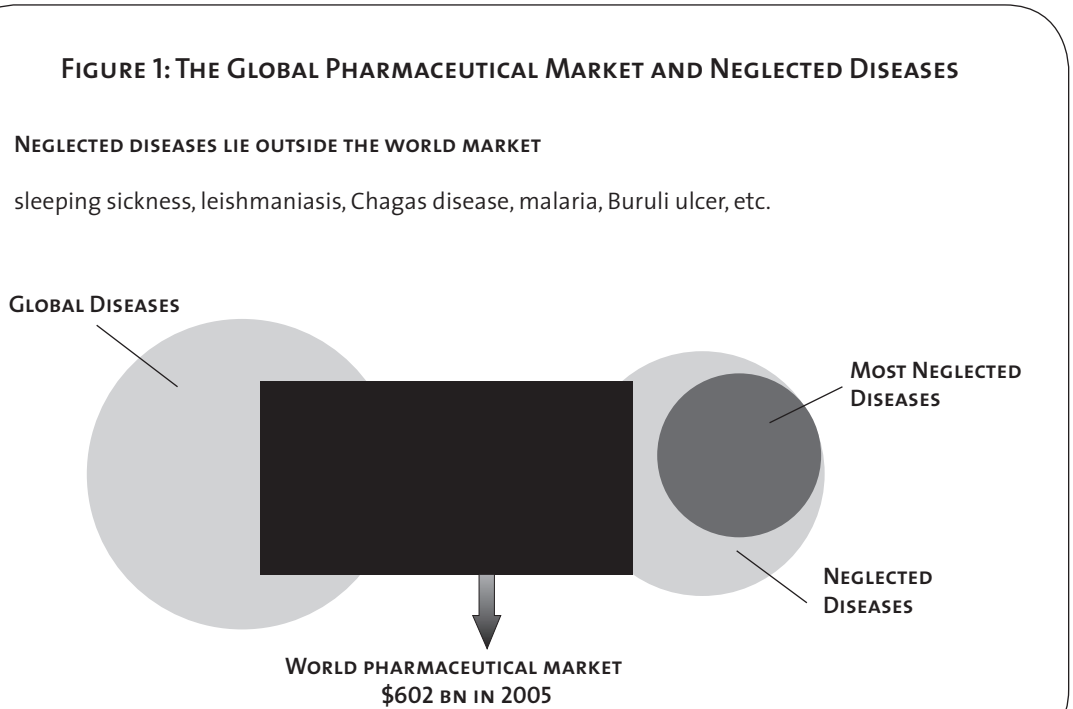
The Drugs for Neglected Diseases initiative (DND*i*) firmly believes that drug research can be an activity in the public domain that leads to the advancement of health, and recognizes that patented products do not always benefit those who need them most. DND*i* considers its products as public goods. It does not wish to profit from its new products and wants to share the knowledge it creates by transferring technology to other researchers and manufacturers when required. The R&D process requires access to knowledge from both private and public research organizations so that DND*i* can use the best available science to research and develop new drugs for neglected diseases. Based on its core principles and beliefs, DND*i* has crafted an IP policy that pragmatically captures the organization's philosophy, vision and mission, and, thereby, ensures that products offered by DND*i* are made accessible and affordable to patients who need them most (see Box 1 at the end of this chapter).

2. DND*i*'S VISION AND MISSION

DND*i* was set up to address the imbalance in access to critically needed medicines, by giving patients in developing countries the opportunity to be the direct beneficiaries of new products of drug R&D for diseases that do not represent a viable drug market. DND*i*'s mission is to develop safe, effective, and affordable new drugs for patients suffering from neglected diseases (Figure 1) and to ensure equitable access to these. By 2014, it aims to develop and make available six to eight such field-relevant treatments.

This, of course, is easier said than done, primarily because to most scientists, pharmaceutical companies, and institutions with whom DND*i* collaborates, the idea of placing a potentially commercial product, such as a drug, into the public domain is both novel and bizarre. DND*i*'s "no profit, no patents" stance calls for, and is committed to, a significant amount of long and sensitive

Figure 1: The Global Pharmaceutical Market and Neglected Diseases



negotiation, to ensure that it becomes more acceptable and widely supported.

Furthermore, whereas the response to calls, from numerous civil society groups and non-governmental organizations (NGOs), to dispense with patents for essential health tools has been met in some spheres with scorn and disregard, certain organisations are slowly beginning to agree that patents often hinder R&D. For example, the recent 2006 report from the World Health Organization (WHO) Commission on Intellectual Property, Innovation, and Public Health (CIPIH) explicitly stated, "*There is no evidence that the implementation of the TRIPS* [Trade Related Aspects of Intellectual Property] *Agreement*[2] *in developing countries will significantly boost R&D in pharmaceuticals on Type II and particularly Type III [neglected] diseases*.[3] ***Insufficient market incentives are the decisive factor***."

This assertion is echoed loud and clear in the preamble of the recently adopted (27 May 2006) World Health Assembly resolution (WHA 59.24) titled Public Health, Innovation, Essential Health Research, and Intellectual Property Rights: Towards a Global Strategy and Plan of Action which notes, "… *that intellectual property rights are an important incentive for the development of new health-care products; … however … **this incentive alone does not meet the need for the development of new products to fight diseases where the potential paying market is small or uncertain***… ."

Nevertheless, DND*i*'s approach to IP, although highly principled, is quite pragmatic (as articulated in its IP policy), and will, therefore, contribute to encouraging further innovations and, even more importantly, to ensuring that patients have access to new products. At the heart of DND*i*'s IP policy lies the belief that the lives of neglected patients are more important than the profit motive. However, convincing industrial and academic partners that this belief should influence their investment decisions continues to be a challenge. Decisions regarding the possible acquisition of patents, ownership, and licensing terms will be made on a case-by-case basis.

3. NEGOTIATING WITH INDUSTRY

DND*i*'s first opportunity to put into action its vision of IP came in October 2003 when it established preliminary contact with the French pharmaceutical giant sanofi-aventis regarding artesunate-amodiaquine, a fixed-dose artesunate-based combination therapy (FACT) for chloroquine-resistant malaria. Artesunate-combination therapies are considered an important addition to the arsenal of treatments for chloroquine-resistant malaria, especially in Africa, where more than a million children die each year from the disease. FACT was one of DND*i*'s earliest projects operating under a grant from the European Commission's International Cooperation and Development (EC-INCO DEV) programme. The terms of its contract with INCO-DEV described collaboration with an industrial partner (sanofi-aventis) for industrial validation, production, and distribution.

In keeping with these terms, DND*i* established preliminary contact with sanofi-aventis, offering them the stable artesunate/amodiaquine fixed-dose combination (AS/AQ) for completion of development and industrial scale-up and to make the registered medicine available to malaria patients. At the time, the drug company already had a combination AS/AQ on the market but it was not a fixed-dose combination (two drugs in one tablet), as was the one DND*i* had been able to develop.

Negotiations led, finally, to a contract agreeable to both parties that was signed in December 2004, and DND*i* transferred its AS/AQ dossier to sanofi-aventis. The agreement was an innovative breakthrough. Both parties wished to make this easier-to-use combination available to the poorest patients, at an affordable price and manufactured to highest international quality standards. At its own cost, sanofi-aventis took full responsibility for the drug registration, as well as for the constitution of a WHO pre-qualification file.

DND*i* was able to convince sanofi-aventis to agree to *exclusivity* of AS/AQ until first registration in a 'reference state'[4] or prequalification by WHO,[5] after which the drug would be *non-exclusive* and available for production by any generic manufacturer without paying either sanofi-aventis

or DND*i* for the right to do so. The agreement also stated that sanofi-aventis would supply the drug at cost (as a *generic*) to the public sector, NGOs (for example, MSF), and international organizations, such as WHO and the United Nations Children's Fund (UNICEF). Under the terms of the agreement, sanofi-aventis could market the product under a trade name in all territories—including disease-endemic countries where the generic product would be available—in the private sector (pharmacies) at a commercial price. For the information and the data made available to the private sector by DND*i*, sanofi-aventis would pay DND*i* a fee, amounting to 3% of net sales, for seven years after launch of the product. DND*i* has decided to use this amount to further reduce the price of AS/AQ to the public sector.

This was DND*i*'s first success. Each negotiation that followed for other projects was an equally uphill task as illustrated in the following example of a research agreement with the University of California, San Francisco.

4. NEGOTIATING WITH ACADEMIA

Following the biotechnology boom during the last couple of decades, most universities see considerable financial potential in much of their medical research. University research departments now ensure that if this research is to be licensed to outside partners, then proceeds from any commercialization flow back to the university and the inventors. Protection of IP by the university is central to this, together with ensuring that the best commercial license is negotiated with the partner if a marketed product is the likely outcome of the research.

When DND*i* first approached the University of California, San Francisco (UCSF), it sought to support research that might lead to new treatments for human African sleeping sickness. Both parties found ready agreement in the use of IP for research purposes. However the goal of DND*i* was to commercialize the product of the research in a way that makes it accessible to patients, and its marketing strategy is somewhat contrary to normally accepted practice in the United States. DND*i* aims to manufacture and sell its products for the lowest price possible. It would have been difficult for UCSF to find a less attractive partner!

At the start, major issues of contention were the requests by DND*i* for:

- a royalty-free license to develop drugs arising from the research for commercialization in all disease-endemic countries
- freedom to manufacture the drugs in any country
- freedom from the requirement to patent the research outcomes for commercialization in any of the disease-endemic countries (Patents can add several million dollars to the cost of a drug.) UCSF retains the right to patent for other uses but not in a manner that will restrict DND*i*'s use of the research.

Throughout the protracted negotiations, staff at the university's business development department were supportive of DND*i*'s IP policy and commercial goals. The main obstacle was simply the difficulty faced by the legal representatives when asked to step away from the standard pro forma protocol and negotiate an agreement that flew in the face of their obligation to negotiate the best return on IP. Fortunately, at the end, a compromise was reached that favoured DND*i* very strongly, and all its requests were met. Equally gratifying was the comment from the staff of the UCSF commercialization departments that they gained tremendous personal satisfaction from the terms of the contract and from being involved in making new treatments available for the seriously neglected disease.

DND*i* has learned some lessons from this experience. In many instances, legal opinions were drafted by third parties who were not familiar with the mission of DND*i*, which slowed the pace of negotiations. Furthermore, the people with whom DND*i* held negotiation talks agreed with the organization's goals but often did not convey them effectively to outside legal representatives and other decision makers. During the final negotiations, however, DND*i* interacted with all decision makers directly—their strong support of DND*i*'s goals is reflected in the final draft of the agreement.

4. CONCLUSIONS

As clearly articulated in its IP Policy statement, DND*i* is committed to managing IP in a manner that pragmatically and effectively advances its mission of providing the most vulnerable populations in developing countries with equitable access to critically needed medicines. Perhaps this is most clearly stated in the preamble of the DND*i* IP policy statement:

The DNDi IP approach will be pragmatic, and decisions regarding the possible acquisition of patents, ownership, and licensing terms will be made on a case-by-case basis. DNDi will put the needs of neglected patients first and will negotiate to obtain the best possible conditions for them. The DNDi's decisions regarding IP will contribute to ensuring access and encouraging further innovations.

By taking this realistic, yet creative, view of IP, DND*i* seeks to advance best practices in IP management that will directly address global public interest. More importantly, by engaging in sophisticated, successful negotiations with both the public and private sectors to fulfil its dynamic vision, DND*i* has demonstrated that this mission and policy is not simply an academic exercise. These negotiations skills, based on the foundation of the DND*i* IP Policy statement, will ultimately ensure the implementation of DNDi's mission with long-term benefits accruing to those who most need, yet can least afford, essential medicines. ■

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1 Chirac P and E Torreele. 2006. Global Framework on Essential Health R&D. *The Lancet* 367 (9522):1560–61.

2 The TRIPs Agreement of the World Trade Organization (WTO) is an agreement that addresses intellectual property concerns. It provides a set of minimum standards for intellectual property protection to which all but the poorest member countries of the WTO must conform.

3 Type II diseases are incident in both rich and poor countries, but with a substantial proportion of cases in the poor countries, for example, HIV/AIDS and tuberculosis. Type III diseases are those that are overwhelmingly or exclusively incident in the developing countries such as sleeping sickness or African river blindness. Type II diseases are often termed *neglected diseases* and Type III, *very neglected diseases*.

4 Countries that have stringent regulatory requirements are considered "reference states." Registration of a drug in a reference state facilitates its approval in other countries that do not have the regulatory infrastructure to fully assess a new registration dossier.

5 Prequalification is a rigorous process of review and approval of the quality, safety, and efficacy of drug products conducted by the World Health Organization at the request of the manufacturer. It was originally intended to give United Nations procurement agencies a guarantee of quality and now extends to other bulk purchasers, including countries and NGOs.

Box 1: DND*i*'s IP Policy

DND*i* hereby adopts the following intellectual property (IP) policy:

I. Preamble
The mission of DND*i* is to develop safe, effective, and affordable new treatments, for patients suffering from neglected diseases, and to ensure equitable access to these.

The DND*i* IP policy will be guided by the following principles as laid down in the business plan:

1. The need to ensure that drugs are affordable to and access is equitable for patients who need them
2. The desire to develop drugs as public goods when possible

The DND*i* IP approach will be pragmatic, and decisions regarding the possible acquisition of patents, ownership, and licensing terms will be made on a case by case basis. DND*i* will put the needs of neglected patients first, and will negotiate to obtain the best possible conditions for them. The DND*i*'s decisions regarding IP will contribute to ensuring access and encouraging further innovations. DND*i* regards drug research as a public good that should primarily lead to the advancement of health.

In addition to a pragmatic day-to-day approach on IP, the DND*i* is committed to contributing to the thinking and development of IP approaches in health R&D that are aimed at serving the public good.

II. Definitions
For the purpose of this policy, the term "intellectual property" includes, but is not limited to, intangibles that are protected by the principles of patents, copyrights, trademark, and trade secrets.

III. Intellectual Property and DNDi's Work
Basic Principles

In implementing the IP strategy, DND*i* will adhere to the following basic principles:

1. DND*i* will ensure that the results of the work carried out under its auspices are disseminated as widely as possible and its products made readily available and affordable in developing countries.

   Where the acquisition of IP is not necessary to promote its mission and goals, DND*i* will make all possible efforts to ensure that the results of its work are placed and remain in the public domain. However, it is possible that promoting DND*i*'s mission and goals will sometimes require outputs to be protected by IP (*see* Sections IV and V). Given the costs involved, patenting is likely to be the exception rather than the rule. Other nonpatent types of IP such as confidential information ("trade secrets") and copyrights will also need to be considered.
2. To make the results of its work useful and encourage the research community to engage in additional or follow-on research in the field of neglected diseases, DND*i* will seek—whenever possible, and without undermining its rationale for acquiring IP—to disseminate its research through publications, presentations, the Internet (emulating the Human Genome Project) and other appropriate channels.
3. DND*i* does not seek to finance its research and operations through IP rent revenues. Although they will constitute an exception rather than the rule, patents might be sought to strengthen DND*i*'s ability to ensure control of the development process and to negotiate with partners.

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Box 1 (continued)

4. IP is generated through DND*i*-sponsored research projects, it should be used to achieve DND*i*'s mission. To this end, DND*i* will pursue creative and innovative strategies to make the fruits of research projects readily available to patients affected by neglected diseases. This will require avoiding prohibitively costly approaches, restrictive IP strategies, or other issues that may inhibit or delay the rapid adoption of the invention to the benefit of developing countries.

IV. Rationale for Acquiring or Otherwise Dealing with Intellectual Property

DND*i* recognizes that in pursuing its mission it may find it necessary to acquire or otherwise manage and enforce IP. In this regard, DND*i* acknowledges that it will have to deal with IP to:

1. conclude contracts and undertake research with its research partners, contractors, collaborators and founders;
2. obtain rights to work on and develop molecules, including facilitating DND*i*'s or its partners' access to proprietary research materials;
3. ensure equitable access to, and affordability of, the end products of its research for patients.

V. Acquisition, Management, and Enforcement of Intellectual Property

Where it is considered necessary to acquire or otherwise manage IP, DND*i* will put in place measures to ensure the timely acquisition of IP by itself or its project partners, collaborators or founders for and on behalf of DND*i*. When necessary to achieve DND*i*'s objectives, enforcement may include legal actions to protect the DND*i* IP.

DND*i* will ensure that IP, however acquired, allows the initiative full freedom to operate, including retaining the right to use the inventions on which IP is obtained for DND*i*'s further research, including with other partners. To this end, DND*i* will use various mechanisms such as assignment of the IP to DND*i*, exclusive licenses and licenses of right. It will negotiate terms with partners to ensure that they will not use the acquired and/or held IP in a manner that impedes equitable and affordable access to the products of the research, or that impedes additional or follow-on research by DND*i*, its partners and other researchers, especially those undertaking research on neglected diseases.

DND*i* will not accept projects in which IP is obviously going to be an insurmountable barrier to follow-up research on behalf of DND*i* and/or equitable and affordable access. Either at the onset of a project or when problems arise, it will be important that negotiations with the public and/or private sector are backed with advocacy support.

VI. Transfer and Licensing of Intellectual Property

DND*i* seeks to enhance R&D activities for neglected disease therapeutics and may wish to in-license technologies developed by others that would help bring such products to the public. To ensure the availability and affordability of neglected disease therapeutics, it will transfer or out-license its technologies to facilitate manufacturing and distribution of its products. As a general policy:

1. DND*i* will ensure that the terms of each transfer or licensing agreement take into consideration the impact of the technology on research in medicine, and more broadly, public health; the level of support provided by DND*i*; the stage of scientific and clinical development of the technology; DND*i*'s portfolio and drug pipeline requirements; and timing and other business and economic considerations;
2. DND*i* will ensure that the terms and conditions of any licensing or transfer agreement allow the continuing availability of technology that supports further research in the field of neglected diseases;

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Box 1 (continued)

3. DND*i* will ensure that technologies developed under DND*i* sponsorship are brought to practical application in a timely manner and made affordable and accessible to the public;
4. DND*i* will negotiate and award licenses which may be exclusive, for specific indications, fields of use, or geographic areas, and other terms as circumstances allow;
5. DND*i* will monitor the performance of licensees and ensure that licensed technology is fully developed;
6. DND*i* will develop and use model agreements, where appropriate, to enable alternative forms of dispute resolution and therefore avoid litigation.

VII. Communities' Involvement in DNDi's Research and Benefit Sharing

When DND*i* will consider patenting an invention resulting from work with communities on traditional medicine or on community genetics, that community will be assured of receiving all eventual benefits from this work.

VIII. Amendments and Changes to the Policy

DND*i* retains the right to review, revise and/or amend this policy or any of its terms at its discretion, at any time. When warranted and in agreement with the Chair of the Board, the Executive Director will recommend the review, revision or amendment of this policy for further approval of the DND*i* Board of Directors.

IX. Administration and Implementation of the Policy

The Executive Director will ensure the full implementation of this policy and put in place, subject to Board approval, administrative, financial, technical, and other mechanisms and procedures to ensure its full implementation.