

# Patent Buy-Outs for Global Disease Innovations for Low- and Middle-Income Countries

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## I. INTRODUCTION

The World Health Organization's CHOICE program analyzes the cost effectiveness of various health interventions related to the Millennium Development Goals.<sup>1</sup> The program identifies the best strategies for improving health in low-income countries, using a standard set of methodological assumptions.<sup>2</sup> These studies evaluate interventions in many areas, including child health<sup>3</sup> and HIV/AIDS.<sup>4</sup>

For some of these treatments, drug costs are a significant variable: if the drug price doubles, the intervention becomes less cost effective. But if the drug price is reduced by 90%, then more therapies become affordable.<sup>5</sup>

Drug prices are uniquely susceptible to radical price reductions through generic competition. Patented pharmaceuticals may be priced at more than 30 times the

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<sup>1</sup> WORLD HEALTH ORG., CHOOSING INTERVENTIONS THAT ARE COST EFFECTIVE, available at <http://www.who.int/choice/en/> (last visited Apr. 6, 2006).

<sup>2</sup> David B. Evans et al., *Time to Reassess Strategies for Improving Health in Developing Countries*, 331 BRIT. MED. J. 1133, 1135 (2005).

<sup>3</sup> Tessa Tan-Torres Edejer et al., *Cost Effectiveness Analysis of Strategies for Child Health in Developing Countries*, 331 BRIT. MED. J. 1177 (2005).

<sup>4</sup> Daniel R. Hogan et al., *Cost Effectiveness Analysis of Strategies to Combat HIV/AIDS in Developing Countries*, 331 BRIT. MED. J. 1431 (2005). The most cost effective interventions are mass media campaigns for safer sex, peer education and treatment of sex workers, prevention of mother to child transmission (PMCT), treatment of sexually transmitted infections, voluntary counseling and testing, and ARV therapy. *Id.* at Tables 3 & 4.

<sup>5</sup> Critics such as Amir Attaran question whether patents are important barriers to essential medicines. Amir Attaran & Lee Gillespie-White, *Do Patents for Antiretroviral Drugs Constrain Access to AIDS Treatment in Africa?*, 286 JAMA 1886 (2001); see also Amir Attaran, *How Do Patents and Economic Policies Affect Access to Essential Medicines in Developing Countries?; Poverty, Not Patent Policies More Often Inhibits Access to Essential Medicines in the Developing World*, HEALTH AFF. 155 (Nov./Dec. 1994). One cannot have it both ways; if patents are indeed unimportant in developing countries, then the drug industry wouldn't be hurt by giving up those patent rents. For a more expansive rebuttal to Attaran's more nuanced position, see Kevin Outterson, *Pharmaceutical Arbitrage: Balancing Access and Innovation in International Prescription Drug Markets*, 5 YALE J. HEALTH POL'Y L. & ETHICS 193, 255-58 (2005) [hereinafter *Pharmaceutical Arbitrage*].

marginal cost of production;<sup>6</sup> the excess is the *patent rent* collected by the drug company while the patent and exclusive marketing periods remain.<sup>7</sup> Patent rents are significant. AIDS drugs which sell for US\$10,000 per person per year in the US are sold generically for less than US\$200.<sup>8</sup> If patented drugs could be sold at the marginal cost of production, cost effective treatments would become even more attractive, and other interventions would become affordable.

This Article proposes marginal cost (generic) pricing<sup>9</sup> for most essential medicines used in the developing world. Global collection of patent rents must be relaxed in order to achieve this objective. Some damage to the profits of pharmaceutical companies would ordinarily be expected, but a properly designed buy-out mechanism can ensure adequate incentives for pharmaceutical innovation.

Two case studies are examined to illustrate the proposal: the recently-developed Human Papillomavirus (HPV) vaccines for cervical cancer and second-line antiretroviral (ARV) treatments for AIDS.

Global pharmaceutical markets and global disease burdens are mismatched, making this proposal uniquely attractive. Some 80% to 90% of the global sales of patented pharmaceuticals occur in the 30 wealthy countries which are members of the Organization for Economic Cooperation and Development (OECD), roughly similar to the World Bank's definition of 29 high-income countries.<sup>10</sup> Pharmaceutical markets for patented products largely follow the money.

But the vast majority of patients needing treatment for global chronic and infectious diseases reside in non-OECD (middle- and low-income) countries. These countries include more than 84% of the world's people, and they are disproportionately sick.<sup>11</sup> The global burden of disease falls most heavily where the market is least attractive.

This mismatch between global pharmaceutical markets and global disease burdens leads to an interesting opportunity. Patented pharmaceuticals could be offered to more than 84% of the world's population at generic prices. (Only high-income country patients would continue to bear pharmaceutical patent rents). The gain in health from increasingly affordable pharmaceuticals would be considerable. The primary disadvantage of this plan would be a quite small reduction in global R&D cost recovery; but even this small deficit could be restored to the companies

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<sup>6</sup> Outterson, *supra* note 5, at 253-55 (demonstrating a differential pricing ratio exceeding 30:1 on 1<sup>st</sup> line ARVs, and a ratio of 264:1 on Ciprofloxacin).

<sup>7</sup> Kevin Outterson, *The Vanishing Public Domain: Antibiotic Resistance, Pharmaceutical Innovation and Intellectual Property Law*, 67 U. PITT. L. REV. 67, 86-89 (2005) [hereinafter Outterson, *Vanishing Public Domain*].

<sup>8</sup> Outterson, *supra* note 5, at 253. When generic AIDS drugs were introduced in Malaysia in 2004, the prices dropped by 90%. Meraiah Foley, *WHO Urges Nations to Bypass Patent Laws*, NEWSDAY, Sept. 22, 2005. When generic AIDS drugs were introduced in Malaysia in 2004, the prices dropped by 90%. *Id.*

<sup>9</sup> Under conditions of robust competition, generic pricing should approach marginal cost pricing.

<sup>10</sup> The official World Bank definition of high-income country is: "High-income country. A country having an annual gross national product (GNP) per capita equivalent to \$9,361 or greater in 1998. Most high-income countries have an industrial economy. There are currently about 29 high-income countries in the world with populations of one million people or more. Their combined population is about 0.9 billion, less than one-sixth of the world's population. In 2003, the cutoff for high-income countries was adjusted to \$9,206 or more." World Bank Group, DEPweb, <http://www.worldbank.org/depweb/english/modules/glossary.html#h> (last visited Apr. 5, 2006).

<sup>11</sup> *See id.*; see also ANDRÉS DE FRANCISCO, THE 10/90 REPORT ON HEALTH RESEARCH: 2001-2002, 91-92 (Sheila Davey ed., Global Forum for Health Research, 2002) (discussing neglected and very neglected diseases).

through a carefully designed patent buy-out mechanism. The World Health Organization recently agreed to appoint an intergovernmental working group to address issues of public health and innovation.<sup>12</sup> This article illustrates some of the concepts which could be useful in that process.

## II. GLOBAL DISEASES: BEYOND NEGLECTED DISEASES

Much attention has been focused over the past decade upon ‘neglected’ or ‘tropical’ diseases, conditions largely overlooked by global pharmaceutical research companies.<sup>13</sup> Examples include onchocerciasis (river blindness),<sup>14</sup> leishmaniasis (kala-azar), Chagas disease, and African sleeping sickness.<sup>15</sup> In the past few years, donors have created some initiatives to direct R&D towards neglected diseases.<sup>16</sup>

The neglected disease programme tends to overlook the fact that chronic conditions in the high-income and low-income worlds are converging.<sup>17</sup> It is the poor themselves who are neglected, rather than just their diseases. *Global diseases* are conditions which affect patients in both rich and poor countries, but disproportionately affect the poor.<sup>18</sup> The global disease list includes many of the

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<sup>12</sup> World Health Organization, 59<sup>th</sup> World Health Assembly, PUBLIC HEALTH, INNOVATION, ESSENTIAL HEALTH RESEARCH AND INTELLECTUAL PROPERTY RIGHTS: TOWARDS A GLOBAL STRATEGY AND PLAN OF ACTION (Agenda Item 11.11; A59/A/Conf.Paper No.8) (May 27, 2006) (hereinafter WHO GLOBAL R&D RESOLUTION).

<sup>13</sup> E.g., DE FRANCISCO, *supra* note 11; Bernard Pécoul et al., *Access to Essential Drugs in Poor Countries: A Lost Battle?*, 281 JAMA 361 (1999); David B. Ridley et al., *Developing Drugs For Developing Countries*, 25 HEALTH AFF. 313 (2006); COMMISSION ON HEALTH RESEARCH FOR DEVELOPMENT, HEALTH RESEARCH: ESSENTIAL LINK TO EQUITY IN DEVELOPMENT 3 (Commission on Health Research for Development ed., Oxford University Press, 1990). The WHO GLOBAL R&D RESOLUTION was not limited to tropical or neglected diseases, although it does focus on “diseases and conditions disproportionately affecting developing countries.” WHO GLOBAL R&D RESOLUTION, *supra* note 12. The case studies in this article concern AIDS and cervical cancer, both of which disproportionately affect people in developing countries.

<sup>14</sup> For a voluntary Merck program to address onchocerciasis, see Jeffrey L. Sturchio & Brenda D. Colatrella, *Successful Public-Private Partnerships in Global Health: Lessons from the MECTIZAN Donation Program*, in THE ECONOMICS OF ESSENTIAL MEDICINES 255 (Brigitte Granville ed., Royal Institute of International Affairs, 2002).

<sup>15</sup> MÉDECINS SANS FRONTIÈRES, FATAL IMBALANCE: THE CRISIS IN RESEARCH AND DEVELOPMENT FOR DRUGS FOR NEGLECTED DISEASES 11 (Médecins Sans Frontières Access to Essential Medicines Campaign, Sept. 2001), *available at* <http://www.msf.org/source/access/2001/fatal/fatalshort.pdf>.

<sup>16</sup> The Drugs for Neglected Diseases Initiative, founded by a group of seven organizations, focuses research and development efforts on 3 truly neglected diseases -- visceral leishmaniasis (Kala-azar), Human African Trypanosomiasis (Sleeping Sickness), and American Trypanosomiasis (Chagas disease). See DNDi: Drugs for Neglected Diseases Initiative, <http://www.dndi.org> (last visited Apr. 18, 2006).

<sup>17</sup> Non-communicable disease accounted for 47% of the global burden of disease in 2001. World Health Org., WHO GLOBAL STRATEGY ON DIET, PHYSICAL ACTIVITY AND HEALTH 2 (May 2004), *available at* [http://www.who.int/dietphysicalactivity/strategy/eb11344/strategy\\_english\\_web.pdf](http://www.who.int/dietphysicalactivity/strategy/eb11344/strategy_english_web.pdf). Cardiovascular disease (CVD) and cancer (malignant neoplasms) are the first and second most common causes of death respectively in developing countries. World Health Org., WORLD HEALTH REPORT 2003 81 (2003), *available at* [http://www.who.int/whr/2003/en/whr03\\_en.pdf](http://www.who.int/whr/2003/en/whr03_en.pdf). “In 1998, non-communicable diseases were responsible for 59% of total global mortality and 43% of the global burden of disease. Importantly, 78% of NCD [non-communicable disease] deaths were borne by low- and middle-income countries, as was 85% of the NCD burden of disease . . . nearly 50% of deaths worldwide were due to CVD, diabetes, cancer and chronic lung disease.” STEPHEN LEEDER ET AL., A RACE AGAINST TIME: THE CHALLENGE OF CARDIOVASCULAR DISEASE IN DEVELOPING ECONOMIES 13-14 (2004).

<sup>18</sup> Herein, the term global disease refers to conditions for which a therapeutic market exists in high-income countries, and the condition is also endemic to the low or middle income world. The

major chronic conditions associated with wealthy countries — including cardiovascular disease, stroke, mental illness, diabetes, and arthritis. These diseases are the leading causes of adult disease burdens throughout the world:

Figure 1.  
Top 10 Global Disease Burdens in DALYs,  
(Men 15 Years and Older)<sup>19</sup>

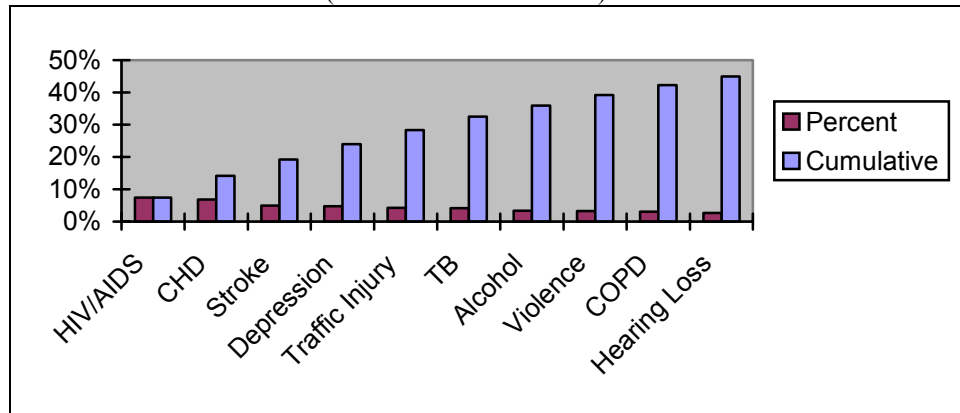
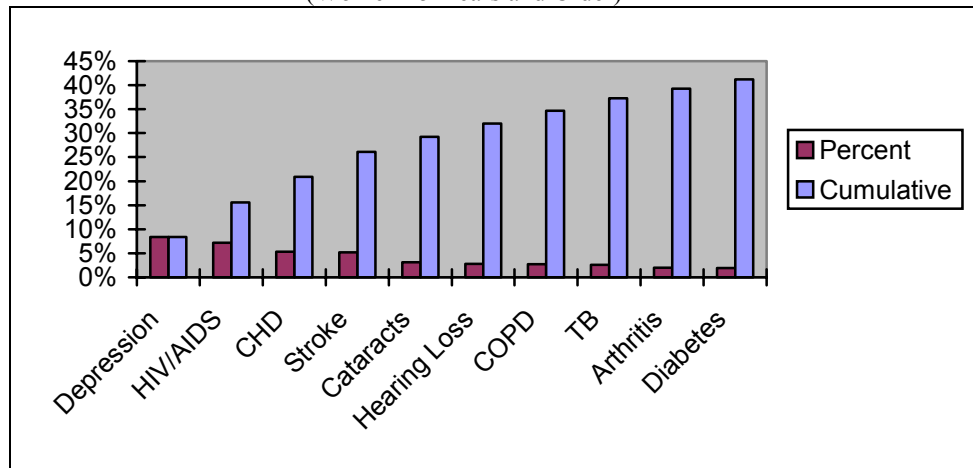


Figure 2.  
Top 10 Global Disease Burdens in DALYs,  
(Women 15 Years and Older)<sup>20</sup>



definition of global disease is not static. Malaria was once a global disease, but is now largely eradicated in high-income countries, rendering it potentially neglected were it not for research for military and tourist markets. Tuberculosis remains a significant condition in OECD markets, even though its disease burden falls heavily on the poor. For a fuller discussion on global diseases in this context, see Bradley Condon & Tapen Sinha, *Global Diseases, Global Patents and Differential Treatment in WTO Law: Criteria for Suspending Patent Obligations in Developing Countries*, NW. J. INT'L L. & BUS. 1, 25-28 (2005); Outtersson, *supra* note 5, at 244-250.

<sup>19</sup> The graph depicts DALYs lost due to various conditions in men aged 15 and above in 2002. JUDITH MACKAAY & GEORGE A. MENSAH, WORLD HEALTH ORG. & CENTER FOR DISEASE CONTROL (CDC), ATLAS OF HEART DISEASE AND STROKE 46 (2004).

<sup>20</sup> Depicting DALYs lost due to these conditions in women aged 15 and above in 2002. *Id.* at 47.

The first characteristic of global diseases is that a robust level of research is assured by high-income markets alone. Anticipated R&D cost recovery from low- and middle-income countries carry little or no weight in the decision to commit resources to R&D concerning global diseases. The powerful lure of high-income markets—particularly the US, the EU, and Japan—draw R&D funds to global diseases, without much regard for the market potential in countries like Brazil or Costa Rica.<sup>21</sup>

AIDS is a paradigmatic case of a global disease. Several thousand early AIDS cases in the United States and Europe were sufficient to trigger an avalanche of science.<sup>22</sup> The global aspects of the epidemic were either unknown or relatively unimportant to the decision to allocate research resources. ARV drugs would have been invented on the same timetable even if no African or Asian had ever been infected. High-income markets alone were sufficient incentive for discovery.

Cancer is another global disease. Development of HPV vaccines was prompted by the multi-billion dollar market to prevent less than 17,000 cervical cancer deaths per year in high-income countries,<sup>23</sup> even though more than 90% of cervical cancer deaths occur in low- and medium-income countries.<sup>24</sup> Similar global disease profiles exist for other cancers: one recent study listed the 12 major types of cancer for which the global burden of disease largely falls in the low- and middle-income countries.<sup>25</sup> In every category the majority of the global cancer disease burden fell in low- and middle-income countries.<sup>26</sup> Only cancers of the lungs, pancreas, colon and rectum were disproportionately found in high-income countries, but nevertheless the majority of the burden remained in low- and middle-income countries.<sup>27</sup>

Global diseases have a second important characteristic: global disease innovation can be shared without damaging innovation. Knowledge is

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<sup>21</sup> Some observers claim that the incentive deficit in these countries is the lack of adequate IP laws. See, e.g., Alan O. Sykes, *TRIPS, Pharmaceuticals, Developing Countries, and the Doha "Solution,"* 3 CHL. J. INT'L L. 47, 58-62 (2002). As I have argued elsewhere at length, it is the poverty of the people, rather than the lack of IP laws, which makes the collection of pharmaceutical patent rents problematic in these countries. See Outterson, *Pharmaceutical Arbitrage*, *supra* note 5, at § I.D.4.viii (arguing that global and neglected diseases do not require additional IP laws in developing countries).

<sup>22</sup> Many early AIDS-related drugs qualified for orphan drug status in the United States when the expected U.S. market was fewer than 200,000 persons. Steven R. Salbu, *AIDS and Drug Policy: In Search of a Policy*, 71 WASH. U. L.Q. 691, 703-707 (1993) (noting that the FDA designated AZT as an orphan drug in 1987 and half of AIDS drugs as of August 1991 were designated as orphans). North America and Western Europe account for less than two million of the thirty-four to forty-six million people living with HIV/AIDS in 2003. UNAIDS/WORLD HEALTH ORG., AIDS EPIDEMIC UPDATE 37 (2003), available at [http://www.who.int/hiv/pub/epidemiology/en/epiupdate2003\\_III\\_en.pdf](http://www.who.int/hiv/pub/epidemiology/en/epiupdate2003_III_en.pdf) [hereinafter AIDS EPIDEMIC UPDATE].

<sup>23</sup> Goodarz Danaei et al., *Causes of Cancer in the World: A Comparative Risk Assessment of Nine Behavioral and Environmental Risk Factors*, 366 *The Lancet* 1784, 1787 (Table 2) (Nov. 19, 2005). See Ruth Mayne, United Nations Dev. Programme, Regionalism, Bilateralism, and "TRIP Plus" Agreements: The Threat to Developing Countries 21 (2005), [http://hdr.undp.org/docs/publications/background\\_papers/2005/HDR2005\\_Mayne\\_Ruth\\_18.pdf](http://hdr.undp.org/docs/publications/background_papers/2005/HDR2005_Mayne_Ruth_18.pdf).

<sup>24</sup> K. Shibuya et al., *Global and Regional Estimates of Cancer Mortality and Incidence by Site: II. Results for the Global Burden of Disease 2000*, 2 *BMC CANCER* 37 (2002) (table 7, excluding regions AMRO A, EURO A, and EURO B1).

<sup>25</sup> Danaei et al., *supra* note 23, at 1789 (Figure 2).

<sup>26</sup> *Id.*

<sup>27</sup> *Id.*

nonrivalrous.<sup>28</sup> Global disease innovation can be offered to low- and medium-income countries without damaging patent rents from high-income countries. While diversion, theft and arbitrage from low-income to high-income markets is a potential threat, companies and governments possess many tools to block pharmaceutical arbitrage, and empirical evidence of significant dysfunctional arbitrage is limited.<sup>29</sup>

The much more significant threat to high-income country patent rents – and to public health – comes from counterfeit pharmaceuticals, which are greatly encouraged by the high price discrimination ratios made possible by IP law.<sup>30</sup> Counterfeit pharmaceuticals are a grave threat to health in the developing world,<sup>31</sup> and the US drug supply chain itself appears remarkably vulnerable.<sup>32</sup> One important ancillary advantage of generic pricing is the virtual elimination of the incentive to counterfeit drugs in low- and medium-income countries: with artificial price discrimination stripped away, the vast majority of the economic incentive to create a counterfeit disappears.<sup>33</sup>

With innovation assured, the further collection of patent rents can stand aside and permit generic-priced access for the majority of humanity. The fruits of OECD global disease innovation can be freely shared with the low- and middle-income world through marginal cost pricing without harming innovation incentives.

We now turn to two case studies to examine in more depth the potential for generic pricing in low- and middle-income countries.

### III. CASE STUDIES

#### A. HPV VACCINES TO PREVENT CERVICAL CANCER

Cervical cancer is a significant cause of cancer death for women worldwide. More than 470,000 cases are diagnosed each year,<sup>34</sup> resulting in approximately 230,000 annual deaths globally.<sup>35</sup> Cervical cancer exemplifies the split between global disease burdens and markets: about 92% of cervical cancer deaths occur in

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<sup>28</sup> Kevin Outterson, *Fair Followers: Expanding Access to Generic Pharmaceuticals for Low-Income Populations*, in *THE POWER OF PILLS* (P. Illingworth & J. Clare, eds.) (forthcoming 2006) [hereinafter Outterson, *Fair Followers*]; Outterson, *The Vanishing Public Domain*, *supra* 7, at 89-92 (2005); Outterson, *Pharmaceutical Arbitrage*, *supra* note 5, at 197, 217-19, 222-30; and the sources cited therein.

<sup>29</sup> These issues have been discussed at significant length in Outterson, *Pharmaceutical Arbitrage*, *supra* note 5, at 231-35, 261-68, 284-90.

<sup>30</sup> Outterson, *Pharmaceutical Arbitrage*, *supra* 5, at 268-71; Kevin Outterson, *Counterfeit Drugs: The Good, the Bad, and the Ugly*, 16 ALBANY L. J. SCI. & TECH. (forthcoming 2006).

<sup>31</sup> WORLD HEALTH ORG., COUNTERFEIT MEDICINES, FACT SHEET NO. 275 (2006), available at <http://www.who.int/mediacentre/factsheets/fs275/en/>.

<sup>32</sup> See generally KATHERINE EBAN, DANGEROUS DOSES: HOW COUNTERFEITERS ARE CONTAMINATING AMERICA'S DRUG SUPPLY (Harcourt 2005).

<sup>33</sup> Outterson, *Pharmaceutical Arbitrage*, *supra* note 5, at 268-71.

<sup>34</sup> See Dianne M. Harper et al., *Efficacy of a Bivalent L1 Virus-like Particle Vaccine in Prevention of Infection With Human Papillomavirus Types 16 and 18 in Young Women: A Randomised Controlled Trial*, 364 THE LANCET 1757, 1757 (2004) (estimating 470,000 as of 2004); Christopher P. Crum, *Editorial, The Beginning of the End for Cervical Cancer?*, 347 NEW ENG. J. MED. 1703, 1703 (2002) (estimating 450,000 as of 2002).

<sup>35</sup> See Danaei et al., *supra* note 23, at 1787 (Table 2)(234,728); Paul D. Blumenthal & Lynne Gaffikin, *Cervical Cancer Prevention: Making Programs More Appropriate and Pragmatic*, 294 JAMA 2225, 2225 (2005) (more than 230,000).

low- and middle-income countries,<sup>36</sup> while perhaps 90% of the revenue market for cervical cancer treatments will be in high-income countries.<sup>37</sup>

The first HPV vaccine to prevent cervical cancer was recently approved by the US FDA.<sup>38</sup> In 2002, Merck's vaccine for Human Papillomavirus Type 16 (HPV-16) demonstrated significant efficacy against cervical cancer in a controlled trial.<sup>39</sup> Merck has also tested a quadrivalent HPV-6, -11, -16 and -18 vaccine, Gardasil.<sup>40</sup> In November 2004, GlaxoSmithKline (GSK) published its positive results for a bivalent HPV-16 and -18 vaccine (Cervarix), based on trials in the US and Brazil.<sup>41</sup> In May 2006, an FDA Advisory Committee unanimously recommended approval of Gardasil for the US market,<sup>42</sup> and the FDA approved the vaccine on June 8, 2006.<sup>43</sup>

The health potential for a generic priced HPV vaccine in low- and middle-income countries is significant. Within a generation of widespread vaccination, the most dangerous types of HPV could be largely eradicated. GSK projects that its vaccine will be cost effective "in both screened and unscreened populations, with important long-term implications for cervical cancer prevention, especially in countries where screening is limited or unavailable."<sup>44</sup>

In the US, GSK's Cervarix HPV vaccine is projected to cost between US\$20,600 to US\$60,000 per quality-adjusted life year (QALY), amounts which are considered cost effective in the US market.<sup>45</sup> The GSK study does not disclose the anticipated US sales price of Cervarix in this model,<sup>46</sup> but these estimates suggest that GSK could raise the vaccine price significantly in the US market while still keeping the QALY cost below US\$75,000.<sup>47</sup> Indeed, the study modeled total vaccination costs up to US\$1000 per patient, at which point vaccination becomes

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<sup>36</sup> There were 218,064 deaths in low- and middle-income countries compared to 234,728 deaths worldwide. Danaei et al., *supra* note 23, at 1787 tbl.2. The GlaxoSmithKline (GSK) study noted that "almost 80% of the cases occur in developing countries." Harper et al., *supra* note 34, at 1757. The difference derives from GSK using "developing countries" rather than "low- and middle-income countries."

<sup>37</sup> See MAYNE, *supra* note 23, at 26 (estimates of GSK's global market for ARVs).

<sup>38</sup> Gardiner Harris, *U.S. Approves Use of Vaccine for Cervical Cancer*, NY TIMES, June 9, 2006.

<sup>39</sup> Laura A. Koutsky et al., *A Controlled Trial of a Human Papillomavirus Type 16 Vaccine*, 347 NEW ENG. J. MED. 1645, 1649 (2002).

<sup>40</sup> Press Release, Merck, Merck's Investigational Vaccine GARDASIL™ Prevented 100 Percent of Cervical Pre-cancers and Non-invasive Cervical Cancers Associated with HPV Types 16 and 18 in New Clinical Study (Oct. 6, 2005), available at [http://www.merck.com/newsroom/press\\_releases/research\\_and\\_development/2005\\_1006.html](http://www.merck.com/newsroom/press_releases/research_and_development/2005_1006.html).

<sup>41</sup> Harper et al., *supra* note 34, at 1760 tbl.1 (somewhat less than half of the study participants were in Brazil).

<sup>42</sup> US FDA Vaccines and Related Biological Products Advisory Committee, May 18, 2006.

<sup>43</sup> Harris, *supra* note 38.

<sup>44</sup> Harper et al., *supra* note 34, at 1764.

<sup>45</sup> Sue J. Goldie et al., *Projected Clinical Benefits and Cost-Effectiveness of a Human Papillomavirus 16/18 Vaccine*, 96 J. NAT'L CANCER INST. 604, 608-609 (2004), available at <http://jncicancerspectrum.oxfordjournals.org/cgi/reprint/jnci;96/8/604.pdf>.

<sup>46</sup> The model identifies 'vaccination costs' of US\$377 (base case), with a range of US\$188 to US\$565, but Table 1 does not identify how much is allocated to the "three brief clinic visits, surveillance and education costs" and how much derives from the cost of the vaccine itself. *Id.* at 607 tbl.1. The model assumes 100% coverage of all 12-year old females in the U.S., a market of almost two million girls per year. See U.S. CENSUS BUREAU, ANNUAL ESTIMATES OF THE POPULATION BY SELECTED AGE GROUPS AND SEX FOR THE UNITED STATES: APRIL 1, 2000 TO JULY 1, 2004 tbl.2 (2005), available at <http://www.census.gov/popest/national/asrh/NC-EST2004-sa.html>.

<sup>47</sup> Goldie et al., *supra* note 45, at 609 tbl.3, 613 n.14.

less cost effective than screening alone.<sup>48</sup> This data suggests an upper limit price of the Cervarix vaccine series at approximately US\$623.<sup>49</sup>

GSK projects annual sales of Cervarix to exceed £1 billion,<sup>50</sup> a blockbuster drug. While we do not know GSK's anticipated unit price, the total female population aged 12 in all high-income countries is approximately 6 million persons.<sup>51</sup> If GSK anticipates meeting half of that volume,<sup>52</sup> then their Cervarix price in high-income countries must be approximately £333 per person, or about US\$570.<sup>53</sup> Merck recently announced that the wholesale price for Gardasil will be \$360 per person in the US.<sup>54</sup>

These calculations assume that only adolescent females are vaccinated, but the FDA Advisory Committee briefing package for Merck's Gardasil included some discussions about vaccinating boys as well. Apparently, Merck plans to market the HPV vaccine for both male and female adolescents.<sup>55</sup> Doubling the vaccinated population would increase profits but reduce the cost-effectiveness threshold for HPV vaccines. It should be noted that the clinical trials cited above only reported efficacy for vaccination of females.

A cervical cancer vaccine which is affordable and just marginally cost effective in the US market will be too expensive and cost ineffective for the average family in a low- or middle-income market where health expenditures per capita average US\$73.40.<sup>56</sup> Even a vaccine priced at 10% of the high-income price (say, US\$36) is completely unaffordable. If we use proportion of per capita health expenditures as a guide, the price outside of the OECD should not exceed \$3.30 per patient and the price in low-income countries should not exceed \$1.35.<sup>57</sup>

The amount of money needed to purchase the low- and middle-income country IP rights to Cervarix or Gardasil are modest. The lost market for GSK is approximately US\$172 million per year, of which the lost R&D cost recovery is only US\$29.2 million per year until patent expiration.<sup>58</sup>

<sup>48</sup> *Id.*

<sup>49</sup> Taking the US\$1000 as an upper limit, and subtracting the US\$377 base case. If costs of the vaccine itself are already included in the base case, the upper limit would be somewhat higher.

<sup>50</sup> Ben Hirschler, *Glaxo Says Cervarix to Transform the Vaccine Business*, REUTERS, May 27, 2005, available at <http://www.signonsandiego.com/news/business/biotech/20050527-0200-health-glaxo-vaccines.html>. See MAYNE, *supra* note 23, at 21.

<sup>51</sup> HNP Summary Profile, <http://devdata.worldbank.org/hnpstats/HNPSummary/groupData/GetShowData.asp?sCtry=HIC> (last visited May 9, 2006) (2002 data).

<sup>52</sup> Merck's vaccine was granted FDA on June 8, 2006. Harris, *supra* note 38.

<sup>53</sup> The exchange rate on Nov. 28, 2005 was 1 GBP = 1.72 USD. One can find the current exchange rate at <http://www.xe.com> (the author used <http://www.xe.com> to deduce the figure in the text using the relevant exchange rate on Nov. 28, 2005).

<sup>54</sup> Harris, *supra* note 38; see also *Panel Backs Vaccine for Cervical Cancer*, New York Times, May 19, 2006.

<sup>55</sup> Patrick Brill-Edwards, Gardasil Human Papillomavirus (Types 6, 11, 16, 18) Recombinant Vaccine 10, 14, 61-66 (April 19, 2006) (final briefing document filed by Merck to the US FDA for the May 18, 2006 meeting of the FDA Vaccines and Related Biological Products Advisory Committee).

<sup>56</sup> HNP Summary Profile, <http://devdata.worldbank.org/hnpstats/HNPSummary/groupData/GetShowData.asp?sCtry=LMY> (last visited May 9, 2006) (2002 data).

<sup>57</sup> Kevin Outterson, *HPV Vaccines to Prevent Cervical Cancer: Do Patients or Shareholders Come First?* (working paper) (June 10, 2006).

<sup>58</sup> Kevin Outterson, NONRIVAL ACCESS TO PHARMACEUTICAL KNOWLEDGE, Global Forum 8, WHO/United Nations Global Forum for Health Research conference on the Millennial Development Agenda (Mexico City) (presented Nov. 18, 2004). This calculation assumes a global market for Cervarix of £1 billion per year, with 10% falling in low- and medium-income countries. See MAYNE, *supra* note 23, at 21. The R&D cost recovery percentage is estimated using the 17% number touted by



For a patent buy-out price of less than US\$30 million per year, Cervarix or Gardasil could instantly become a generic medicine in all low- and middle-income countries. The bulk of the world's women would enjoy much greater access to a cervical cancer vaccine through generic pricing. The companies would be fully rewarded for their lost sales in low- and middle-income markets. The proposal is a bargain for global public health and good business for the companies.

As this article was going to press, the Bill and Melinda Gates Foundation announced a \$27.8 million dollar grant to study the use of the HPV vaccines in the developing world; this study will focus on "the goal of informing regional and global vaccine introduction efforts and international financing plans."<sup>59</sup> This study should evaluate the merits of this patent buy-out proposal as an alternative to the oft-criticized voluntary programs recently proffered by global drug companies. The end point for such studies should be the greatest possible vaccination coverage for women. Generic pricing outside the OECD is one important component in that program.

### 1. Diagnostic tests for cervical cancer

Diagnostic tests present special cost effectiveness issues. Cheaper diagnostics for AIDS (such as CD4 counts) or microbial infections (identifying susceptibility to enable better targeting of antibiotics) could lead to more cost effective treatment with less potential for developing resistance.<sup>60</sup> But diagnostic tests might also inappropriately drive up health care costs. For example, Digene Corporation has developed a diagnostic test for HPV.<sup>61</sup> What is not known at present is whether a cheaper diagnostic would be cost effective from a societal view. In the US, routine Pap screening leads to several billion dollars of clinical intervention of doubtful efficacy and cost effectiveness since most HPV infections regress on their own.<sup>62</sup> The wasteful use of clinical resources following abnormal Pap screening is well known; indeed, GSK's HPV-16/18 vaccine derives a significant portion of its projected cost effectiveness from avoiding "more than US\$6 billion ... spent each year on the evaluation and management of low-grade lesions, the majority of which would regress without intervention."<sup>63</sup>

Of more immediate importance to the developing world, Digene has also created a streamlined version of the HPV test for use in resource-limited settings.<sup>64</sup> It is quite possible that more effective detection of HPV might lead to clinical interventions with very unfavorable cost effectiveness profiles, inappropriately expanding profligate US practices to resource constrained settings. Nevertheless,

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PhRMA, which probably represents an upper limit estimate. Patrica Barry, *Drug Profits vs. Research*, AARP BULLETIN (June 2002), available at [http://www.carlmcmillan.com/drug\\_profits\\_vs.htm](http://www.carlmcmillan.com/drug_profits_vs.htm).

<sup>59</sup> PATH Press Release, *Path to Pave the Way for Cervical Cancer Vaccines in the Developing World* (June 5, 2006), available at [http://www.path.org/news/pr060606-cervical\\_cancer\\_vaccine.php](http://www.path.org/news/pr060606-cervical_cancer_vaccine.php).

<sup>60</sup> Outterson, *The Vanishing Public Domain*, *supra* note 7, at § III.A.1.d.

<sup>61</sup> Michael Barbaro, *Digene to Adapt Cancer Test For Use in Developing World*, WASH. POST, Feb. 18, 2004, at E 05.

<sup>62</sup> DEP'T OF HEALTH AND HUMAN SERV., CTR. FOR DISEASE CONTROL & PREVENTION, DIV. OF STD PREVENTION, PREVENTION OF GENITAL HPV INFECTION AND SEQUELAE: REPORT OF AN EXTERNAL CONSULTANTS' MEETING, available at [http://www.cdc.gov/nchstp/dstd/Reports\\_Publications/HPVSupplement%20.pdf](http://www.cdc.gov/nchstp/dstd/Reports_Publications/HPVSupplement%20.pdf) cited in Harper et al., *supra* note 34 at 1764 n. 38 (2004). See also Sue J. Goldie et al., *Policy Analysis of Cervical Cancer Screening Strategies in Low-Resource Settings: Clinical Benefits and Cost-Effectiveness*, 285 JAMA 3107-3115 (2001).

<sup>63</sup> Sue J. Goldie et al., *supra* note 45, at 604 n.4, 612.

<sup>64</sup> Barbaro, *supra* note 61, at E 05.

the patent holder for the HPV test is engaged in a global campaign to promote the adoption of its test as the global standard of care, utilizing clinical sales representatives, direct to consumer advertising, and strategic relationships with women's groups and providers.<sup>65</sup>

#### B. SECOND-LINE HAART DRUGS FOR AIDS

When the Millennium Development Goals were first articulated in 2000,<sup>66</sup> treatment of AIDS with antiretroviral drugs was not considered cost effective for low-income populations. Annual costs per patient exceeded US\$7,000 for first-line Highly Active Antiretroviral Therapy (HAART) in drug costs alone.<sup>67</sup> In the world's low-income countries, per capita health expenditures are only US\$29.<sup>68</sup> As recently as December 2000, HAART prices were so high that the World Bank still considered ARV treatment in poor countries to be not cost effective.<sup>69</sup> HAART was simply too expensive.

Médecins Sans Frontières (MSF) and Partners In Health refused to listen to conventional wisdom and began treating some of the world's poorest AIDS patients with HAART.<sup>70</sup> In the days before the global implementation of the World Trade Organization TRIPS Agreement,<sup>71</sup> several Indian and Thai companies produced and exported HAART drugs generically, even though the patent remained valid in OECD countries.<sup>72</sup> The combination of public outcry and generic competition forced the prices down to less than US\$200 per patient per year.<sup>73</sup>

With these dramatic cost reductions, HAART therapy is now deemed cost effective worldwide. One recent study evaluated several strategies regarding HIV/AIDS in sub-Saharan Africa (WHO region: Afr-E) and South East Asia (Sear-D). The study recommends a range of HIV/AIDS interventions which are highly cost effective in low-income countries, with a cost per disability adjusted life year

<sup>65</sup> DIGENE CORPORATION 2005 ANNUAL REPORT (2005), <http://ccbn.mobular.net/ccbn/7/1155/1214/print/print.pdf>.

<sup>66</sup> United Nations Millennium Declaration, G.A. Res. 55/2, U.N. GAOR, 55<sup>th</sup> Sess., 8<sup>th</sup> plen. Mtg., U.N. Doc. A/Res/55/L.2 (Sept. 18, 2000).

<sup>67</sup> Outterson, *Pharmaceutical Arbitrage*, *supra* note 5, at 250-52.

<sup>68</sup> HNP Summary Profile (2002 data), *available at* <http://devdata.worldbank.org/hnpstats/HNPsummary/groupData/GetShowData.asp?sCtry=LIC>.

<sup>69</sup> See Barton Gellman, *An Unequal Calculus of Life and Death; As Millions Perished in Pandemic, Firms Debated Access to Drugs*, WASH. POST, Dec. 27, 2000, at A1.

<sup>70</sup> MÉDECINS SANS FRONTIÈRES', SURMOUNTING CHALLENGES: PROCUREMENT OF ANTIRETROVIRAL MEDICINES IN LOW- AND MIDDLE-INCOME COUNTRIES (2003), <http://www.accessmed-msf.org/documents/procurementreport.pdf> (report prepared by MSF at the request of the WHO).

<sup>71</sup> See Agreement on Trade-Related Aspects of Intellectual Property Rights, Apr. 15, 1994, Marrakesh Agreement Establishing the World Trade Organization, Annex 1C, art. 27.1, Legal Instruments—Results of the Uruguay Round vol. 31, 33 I.L.M. 81 (1994) [hereinafter TRIPS or TRIPS Agreement]. The United States implemented the WTO agreements in the Uruguay Round Agreements Act, Pub. L. No. 103-465, 108 Stat. 4809 (1994).

<sup>72</sup> This narrative has been told by many. See, e.g., Outterson, *Pharmaceutical Arbitrage*, *supra* note 5, at 250-58.

<sup>73</sup> MÉDECINS SANS FRONTIÈRES, UNTANGLING THE WEB OF PRICE REDUCTIONS: A PRICING GUIDE FOR THE PURCHASE OF ARV'S FOR DEVELOPING COUNTRIES (8th Ed., June 2005), *available at* <http://www.accessmed-msf.org/documents/untanglingtheweb%208.pdf> [hereinafter MSF, PRICING GUIDE]; Marleen Boelaert et al., Letter to the Editor, 287 JAMA 840, 840 (2002) ("This impressive discount offered by the companies to developing countries was not merely due to public outcry, but mostly as a response to competition by generic drugs.")

(DALY) ranging from Int\$3 to Int\$1144 in Afr-E.<sup>74</sup> The study assumes the annual drug cost of first-line HAART to be Int\$177.80,<sup>75</sup> following the data gathered by MSF.<sup>76</sup>

Most patients cannot remain on first-line HAART drugs indefinitely. Whether due to resistance or intolerance to specific drugs, after a number of years an increasing number of surviving patients require second-line therapy.<sup>77</sup> Second-line drugs such as protease inhibitors are not generally available at generic prices in the developing world.<sup>78</sup> Patented second-line therapies are very expensive in low-income countries. Even with voluntary discount programs, second-line therapies cost ten to twenty-six times more than the first-line drugs.<sup>79</sup> The world is stumbling towards a second AIDS holocaust, even while we struggle to make first-line therapies affordable and available to the millions who lack treatment access.<sup>80</sup>

The non-OECD buy-out price for HAART first- and second-line treatments would be modest, given the scale of the epidemic. Pharmaceutical companies will not suffer significant lost profit if all sales of HAART products dropped to zero in every low- and middle- income country. GSK is the largest global seller of HAART drugs.<sup>81</sup> GSK reports its sales to the SEC in three geographic regions: the United States, Europe, and "International."<sup>82</sup> This latter category includes high- income countries such as Japan, Canada and Australia, as well as low- and middle-income countries in Latin America, Asia, Africa and the Middle East.<sup>83</sup> Even so, total International HAART drug sales in 2003 were only £155 million,<sup>84</sup> in a year in which gross profit was £17.2 billion and selling, general, and administrative (SG&A) expenses were £7.5 billion.<sup>85</sup> Actual profits from HAART sales in both low- and middle- income markets are likely to be negligible to GSK's global profits and R&D, particularly if OECD markets in these countries remain commercial. The

<sup>74</sup> See generally Hogan et al., *supra* note 4. The most cost effective interventions are mass media campaigns for safer sex, peer education and treatment of sex workers, prevention of mother to child transmission (PMCT), treatment of sexually transmitted infections, voluntary counseling and testing, and ARV therapy. *Id.* at Tables 3 & 4.

<sup>75</sup> *Id.* at Table A (supplement).

<sup>76</sup> See MSF, PRICING GUIDE, *supra* note 73, at Table A (supplement) n. 5.

<sup>77</sup> Otterson, *Vanishing Public Domain*, *supra* note 7, at 74-75.

<sup>78</sup> A recommended second-line regime is TDF+ddI+LPV/r. MEDECINS SANS FRONTIERES, EUROPEAN PARLIAMENT COMMITTEE ON INTERNATIONAL TRADE HEARING ON TRIPS AND ACCESS TO MEDICINES 6 (Jan. 2005), available at <http://europaport.eerstekamer.nl/cgi-bin/as.cgi/0345000/c/start/file=9345000/1/j9vvyg6i0ydh7th/vgbwr4k8ocw2/f=/vgz6mnudecs3.pdf>. [hereinafter HEARING]. Second-line treatments also are important in conservation of resistance, and there is no FDC available for second-line treatment as a result of the patents; see Wanla Kulwicht, *First-line and Second-line Antiretroviral Therapy*, 364 THE LANCET 329, 329-330 (2004), available at [http://www.thelancet.com/journal/vol364/iss9431/full/lan.364.9431.analysis\\_and\\_interpretation.30311.1](http://www.thelancet.com/journal/vol364/iss9431/full/lan.364.9431.analysis_and_interpretation.30311.1).

<sup>79</sup> HEARING, *supra* note 78, at 5-6 (second-line treatment in low income countries costs about US\$3,950 per year, and as high as US\$ 5,000 per year). N. Kumarasamy, Comment, *Generic Antiretroviral Drugs – Will They Be The Answer to HIV in the Developing World?*, 364 THE LANCET (July 3, 2004), available at <http://www.accessmed-msf.org/documents/Lancet2JulycommentaryFDC.pdf>. See also MSF, PRICING GUIDE, *supra* note 73 at 9.

<sup>80</sup> WORLD HEALTH ORG., 3 X 5 PROGRESS REPORT (Dec. 2004), <http://www.who.int/3by5/ProgressReportfinal.pdf>.

<sup>81</sup> GLAXOSMITHKLINE PLC, 2003 ANNUAL REPORT 61-63, available at [http://www.gsk.com/investors/reps03/annual\\_report2003.pdf](http://www.gsk.com/investors/reps03/annual_report2003.pdf).

<sup>82</sup> *Id.*

<sup>83</sup> *Id.*

<sup>84</sup> *Id.*

<sup>85</sup> *Id.*

estimated non-OECD buy-out price for all of GSK's HAART portfolio is just US\$11.3 million per year in lost R&D cost recovery.<sup>86</sup> The annual budget of the Global AIDS Conference exceeds this amount with millions to spare.<sup>87</sup> With the lives of millions at risk, and billions being spent on AIDS programs, the buy-out price is stunning in its modesty.

### C. THE WEAKNESS OF VOLUNTARY PRICING PROGRAMS

Voluntary programs undoubtedly assist some patients. Novartis makes Glivec (imatinib) available to 346 chronic myeloid leukemia patients in Malaysia through a patient-based assistance program.<sup>88</sup> Voluntary donations of ARVs reach some AIDS patients, and many donor programs are under way, but 90% of the global need is unmet.<sup>89</sup> Pfizer's limited donation of Diflucan (fluconazole) (an anti-fungal agent useful for many purposes, including opportunistic infections in AIDS patients) was a public relations triumph in December 2000,<sup>90</sup> and yet complaints persist that Pfizer only permits a miniscule amount to reach patients.<sup>91</sup> In November 2005, Merck and Bristol Myers Squibb granted royalty-free licenses to the International Partnership for Microbicides for an anti-HIV vaginal gel.<sup>92</sup> The grants are laudable steps, but are limited to a very specific product.<sup>93</sup> In the most notable cases, significant voluntary price reductions were triggered by unlicensed generic production or the threat of compulsory licensure.<sup>94</sup> No one should mistake voluntary programs for a systematic, sustainable solution.<sup>95</sup>

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<sup>86</sup> Assuming that 75% of the International sales are to Canada, Australia, Japan and other high-income countries (i.e., low- and middle-income global HAART sales by GSK of approximately £38.75 million per year). At an exchange rate of 1 GBP = 1.72 USD, and again assuming 17% of sales are reinvested into R&D, the annual buy-out price until patent expiration is just US\$11.3 million per year. As a rough test of the Canada assumption, I checked IMS data for all sales of ARVs in the Canadian market in 2004 for all companies. The total for the year ending October 2004 was US\$130 million. (IMS Data, Canada, series J5C1, J5C2 and J5C3). If GSK's ARV market share in Canada is 40%, then GSK's Canadian sales were approximately £30 million in 2004, about 20% of the "International" total. *See id.*

<sup>87</sup> The budget for the 2004 Bangkok Conference was US\$17 million. Press Release, Communications Department, XV International AIDS Conference (July 16, 2004), available at [http://www.kaisernet.org/health\\_cast/uploaded\\_files/ias\\_pressrelease.pdf](http://www.kaisernet.org/health_cast/uploaded_files/ias_pressrelease.pdf).

<sup>88</sup> Tee Shiao Eek, *Making Treatment Affordable*, STAR ONLINE (Malaysia), July 3, 2005, available at <http://202.186.86.35/health/story.asp?file=/2005/7/3/health/11352481&sec=health>

<sup>89</sup> WORLD HEALTH ORG., "3 X 5" PROGRESS REPORT 49 (Dec. 2004), available at [http://www.who.int/3by5/pr\\_en.pdf](http://www.who.int/3by5/pr_en.pdf).

<sup>90</sup> The Diflucan® Partnership Programme, <http://www.diflucanpartnership.com> (last visited May 9, 2006).

<sup>91</sup> *See* AEGIS-TAGline: Stern Words For Pfizer, <http://www.aegis.com/pubs/tag/2004/TAG041107-04.html> (last visited May 9, 2006).

<sup>92</sup> Press Release, The International Partnership for Microbicides, IPM Signs Drug Licensing Agreements with Merck and Bristol-Myers Squibb (Oct. 31, 2005), available at <http://www.ipm-microbicides.org/>.

<sup>93</sup> *See* Justin Gillis, *AIDS Gel on a Faster Track; Merck, Bristol to License Drugs for Use in Poor Countries*, WASH. POST, Nov. 1, 2005, at A04.

<sup>94</sup> Outterson, *Pharmaceutical Arbitrage*, *supra* note 5, at 223-30.

<sup>95</sup> *See* Tihana Bicanic et al., *Antiretroviral Roll-Out Access To Treatment for Cryptococcal Meningitis*, 5 THE LANCET INFECTIOUS DISEASES 530, 530 (Sept. 2005) ("a system that relies on philanthropic initiatives by the pharmaceutical industry and the pressure of lobby groups cannot result in sustainable access to medicines.").

#### IV. THE PATENT BUY-OUT PROPOSAL

This Article proposes marginal cost (generic) pricing of patented pharmaceuticals for low- and middle-income populations (more than 84% of the world's population). Innovation is assured by reimbursing the companies for all lost R&D cost recoveries in those markets. Risks are minimized because the present IP system is retained for more than 80% of the global patent-based cash flow of the pharmaceutical companies. The following steps are proposed:

1. The purchaser acquires the patent and exclusive marketing rights for a patented global medicine from the patent owner, limited to a particular geographic market. (Example: the Global Fund purchases from GSK the global non-OECD rights to GSK's new cervical cancer vaccine. GSK retains the rights to the vaccine in all OECD countries).
2. The purchaser offers an open, non-exclusive, no royalty license to any legitimate generic manufacturer, but only for sale in the target markets. (Normal patent-based pricing remains in all OECD countries; generic pricing through multiple manufacturers prevails in all non-OECD countries).
3. The patent owner is compensated under a buy-out formula which mimics the lost R&D cost recovery from the foregone sales. (Example: GSK is paid for the lost R&D cost recovery from cervical cancer vaccine sales in non-OECD countries).

##### A. THE PURCHASER

The purchaser could be a government (the US or the EU), inter-governmental organization (WHO, UN, WTO, or the Global Fund), or a foundation donor (Gates). Governments can exercise compulsory licensure powers within their territories, but this proposal cannot rely solely on the current scope of compulsory licensure. The transaction costs and political opposition to negotiating compulsory licenses for each market country have proven to be almost insurmountable. In the five years since the much-hyped 'Doha Solution' to compulsory licenses for export, not a single pill has been produced under that protocol.<sup>96</sup> By offering compensation in exchange for the non-OECD license, it is hoped that pharmaceutical companies will embrace this proposal rather than force governments to pursue parallel compulsory licensure processes.

##### B. THE TARGET MARKET

The simplest formulation would divide the world in two: the thirty relatively richer countries that are members of the OECD<sup>97</sup>, and all other countries. Simplicity means rough justice, but surely rough justice is better than no justice. Poverty does not strictly follow political boundaries. Some elites in poor countries will gain access to generic-priced medicines when they could have afforded full price. Some poor people in OECD countries may not be able to afford their prescriptions, and

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<sup>96</sup> The Fourth Ministerial Conference was held in 2001. As of June 1, 2006, no country had provided notice of intent to export under the Paragraph 6 statement. *See Trips and Public Health*, WORLD TRADE ORG., available at [http://www.wto.int/english/tratop\\_e/trips\\_e/public\\_health\\_e.htm](http://www.wto.int/english/tratop_e/trips_e/public_health_e.htm).

<sup>97</sup> Australia, Austria, Belgium, Canada, Czech Republic, Denmark, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Japan, Korea, Luxembourg, Mexico, Netherlands, New Zealand, Norway, Poland, Portugal, Slovak Republic, Spain, Sweden, Switzerland, Turkey, United Kingdom, United States.

could have benefited from generic pricing.<sup>98</sup> Perhaps the latter group can be left to the care of their relatively-affluent governments (although in the US, approximately 27% of the population lacked prescription drug insurance in 2005 prior to the introduction of Medicare Part D).<sup>99</sup> Over-inclusion of developing-country elites is more likely to attract controversy.

Over-inclusion results in lost patent rents, particularly in countries like China, India and Brazil with millions of middle class consumers. If simplicity is desired, this over-inclusion will simply be tolerated. It will increase the buy-out price, so the companies still receive their due rewards. If anything, the inequity is between the donor and the target country government. Perhaps China, Brazil or India (or similar countries) could compensate the donor for this inappropriate subsidy.

Alternatively, PhRMA companies have demonstrated remarkable skill in segmenting markets with tiered differential pricing within particular countries.<sup>100</sup> The persistence of domestic differential pricing within the US, even in the face of extensive donor programs, is a testament to the effectiveness of market segmentation by PhRMA companies and the apparent weakness of actual pharmaceutical arbitrage pressure. Possible mechanisms are brand campaigns with trademarks, differential pricing by payor, and domestic legal restrictions on arbitrage.<sup>101</sup>

#### C. THE GENERIC LICENSE

The purchaser will offer a non-exclusive, no-royalty license to all legitimate pharmaceutical manufacturers. Negotiations will not be required, and transaction costs will remain very minimal.

In order to maximize the geographic reach of the generic licenses, and to ensure competition in each country, drugs licensed under this system which are pre-qualified by the WHO should be granted automatic marketing approval in all of the target countries, a form of reference approval in lieu of a country by country ANDA process.<sup>102</sup>

#### D. SETTING THE BUY-OUT PRICE<sup>103</sup>

The buy-out price must be set high enough to optimize global pharmaceutical innovation and low enough to be affordable for all global diseases. Lanjouw and Jack effectively set the price at zero by requiring drug companies to choose between patents in rich countries or poor countries.<sup>104</sup> If global pharmaceutical appropriation is already supra-optimal, then zero (or a negative value) is the correct price.<sup>105</sup>

<sup>98</sup> These issues of over-inclusion and under-inclusion are discussed at greater length in Outterson, *Pharmaceutical Arbitrage*, *supra* note 5, at § I.D.4.iii.

<sup>99</sup> Dana Gelb Safran et al., *Prescription Drug Coverage And Seniors: Findings From a 2003 National Survey*, HEALTH AFFAIRS, Apr. 19, 2005, at W5-160.

<sup>100</sup> Outterson, *Pharmaceutical Arbitrage*, *supra* note 5, at 206-216.

<sup>101</sup> Within the U.S. market, internal diversion is illegal in many cases. *See, e.g.*, Heather Won Tesoriero & Gary Fields, *FBI, FDA Investigates Big Drug Wholesaler*, WALL ST. J., Sept. 19, 2003, at B1 (reporting alleged diversion from discounted hospital markets to higher-priced secondary markets).

<sup>102</sup> For an expanded discussion on this reference approval idea, *see* Outterson, *Pharmaceutical Arbitrage*, *supra* note 5, at 236-38.

<sup>103</sup> An expanded version of the buy-out price analysis, together with discussion of the literature and alternative models, may be found in Outterson, *Fair Followers*, *supra* note 28, at § 5.3.

<sup>104</sup> *See* Jean .O. Lanjouw & William Jack, *Trading Up: How Much Should Poor Countries Pay to Support Pharmaceutical Innovation?*, 4 CTR. FOR GLOBAL DEVELOPMENT 1-8 (2004), available at <http://www.cgdev.org/content/publications/detail/2842/>.

<sup>105</sup> Outterson, *Pharmaceutical Arbitrage*, *supra* note 5, at 220-22.

Policymakers should have transparent access to reliable data on global pharmaceutical innovation in order to answer that question.

If the goal of the buy-out price is to mimic what would have happened under best-case competitive market conditions, then the price should be based on expected profits rather than sales or costs. Ganslandt, Maskus & Wong used cost data to calculate their buy-out price, which rewards effort rather than success.<sup>106</sup> Gross sales are certainly an element of pharmaceutical appropriation, but the relevant market metrics are the net present value (NPV) of the cash flow or the NPV of the profit stream. The purpose of the buy-out price should be to restore the expected profits, and more particularly, the lost R&D cost recovery.

Expected future profits will of course be difficult to estimate and subject to gaming. The following formula relies to the greatest extent possible on externally generated data, to avoid data manipulation and methodological squabbles, with retrospective experience adjustments:

$$\text{BOP} = \text{NPV}_{t(d)} (U * M) p$$

BOP is the buy-out price; NPV is the net present value over the patent period  $t$  at discount rate  $d$ ;  $U$  is the number of generic units sold in the target markets by all sellers during  $t$ ;  $M$  is the marginal cost of production per unit, estimated as the lowest sustained actual price per unit during  $t$ ;  $p$  is a profit adjustor, reflecting the percentage of revenues allocated to R&D cost recovery (14-17% are the estimates from drug companies).

Estimated payments could be made at buy-out, subject to periodic and retrospective adjustment as actual data developed on  $U$  and  $M$ , and perhaps for changes in  $d$ . The formula minimizes the need to know actual costs, profits, or average sales prices. The only data required are actual number of generic unit sales and the lowest sustained price by any generic seller in the target markets. Both are relatively easy to collect and difficult for the patent holder (or anyone else) to manipulate.

This formula aligns incentives against rent-seeking and allocative inefficiency in helpful ways. The license encourages any pharmaceutical company to manufacture and sell the drug generically in all target markets. Competition will drive the unit price down towards the actual marginal cost of production. In a competitive market with multiple entrants, no single company controls either  $U$  or  $M$ , but they each have strong market incentives to maximize  $U$  and to minimize  $M$ , which translates into the greatest access for a market-determined low price.

## V. CONCLUSION

For a remarkably modest price, the battles over TRIPS and essential medicines could be largely resolved. Pharmaceutical rent appropriation could be avoided in low- and middle-income countries, while fully protecting innovation incentives. As the chronic diseases of the rich and poor worlds converge, a noble opportunity arises for doing well while doing good.

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<sup>106</sup> Mattias Ganslandt et al., *Developing and Distributing Essential Medicines to Poor Countries: The DEFEND Proposal*, 24 *WORLD ECON.* 779-795 (2001).