

Appendix E: Understanding Drug Patents

M.J. Peterson with research assistance by Osman Kiratli and Sarah Keister
Version 2, April 2010

Efforts to ensure access to medicines for all who need them regardless of income often focus on the prices individuals, households, or government health services are charged for particular medicines. When the medicine is a standardized one developed several decades ago, the relative ease of making both the active pharmaceutical ingredients that provide the treatment effect, and the inactive ingredients which add chemical stability and other desired characteristics to the medicine, means multiple manufacturers can offer either branded or generic versions of the medicine. Competition among them creates, as expected in standard supply and demand economics, pressures to keep prices low. When the medicine is a new one, particularly if the active pharmaceutical ingredients or their compounding into the final medicine involves complicated production processes, fewer companies are likely to be offering the medicine so competition will be weaker and downward pressure on prices much less. Pressure on prices is least prevalent when the medicine is under patent because the patent gives the originating firm a temporary monopoly on production and sale of the particular medicine.

This means in any situation where access to newly-developed medicines is regarded as essential to the treatment of some disease that is widespread among a population, there will be strong political pressures to deal with the problem of prices by abolishing, restricting, or breaking patents. Patent systems in general raise three basic questions, two obviously ethical and the third more immediately practical. These questions, and their sub-questions, are displayed in Table 1.

The first ethical question concerns the legitimacy of creating private property rights over something. Even in societies where there is considerable consensus that issuing patents covering new medicines is legitimate, demands that "essential medicines" be made available to all who need them regardless of income or ability to pay can lead individuals, groups, and government officials who are generally supportive of the patent system to seek grounds for making an exception. This effort highlights the fact that patents, though often discussed in all-or-nothing terms, can be formulated in a number of ways because they are simply one type of property rights. Property rights themselves are human-created conventions rather than

This case was created by the International Dimensions of Ethics Education in Science and Engineering (IDEESE) Project at the University of Massachusetts Amherst with support from the National Science Foundation under grant number 0734887. Any opinions, findings, conclusions or recommendations expressed in this material are those of the author(s) and do not necessarily reflect the views of the National Science Foundation. More information about the IDEESE and copies of its modules can be found at <http://www.umass.edu/sts/ethics>.

This case should be cited as: M.J. Peterson. 2010. "Access to HIV Treatments in Developing Countries." International Dimensions of Ethics Education in Science and Engineering. Available www.umass.edu/sts/ethics.



© 2010 IDEESE Project

naturally occurring objects. Their content can be altered as societies develop new understandings regarding the legitimate balance between the rights of property holders and the rights of the rest of society.

Table 1

Ethical concerns	Legitimacy of Intellectual Property Rights	Possession who may own what may be owned
		Terms of Possession rights of ownership duties of ownership
	Distributional Effects of Intellectual Property Rights	Static Effects relative income relative wealth reward for effort benefit/burden sharing
		Dynamic Effects implications for economic growth
Practical concern	Efficiency Effects of Intellectual Property Rights	Static Effects on market structure on transaction costs
		Dynamic Effects incentives created by income derived from property rights

This 3-question format and breakdown of Distributional and Efficiency concerns is derived from Timo Goeschl's powerpoint slides for the first lecture in the course on The Economics of Innovation and the Life Sciences he taught in summer session 2008 at the University of Heidelberg. Available at [http://www.eco.uni-heidelberg.de/lehrstuhl/SS2008/Econ of Innov & LS-intro.ppt](http://www.eco.uni-heidelberg.de/lehrstuhl/SS2008/Econ%20of%20Innov%20&%20LS-intro.ppt) (accessed 14 July 2009)

The second obviously ethical question concerns the distributive effects of permitting private property rights, however defined, in a particular thing. Distributive effects come in two forms well conceptualized in standard economic analysis. "Static effects" occur at any particular moment while "dynamic effects" unfold over longer periods. The two may not be identical. Thus, fully understanding distributional effects requires looking at both types of effect; an analysis that typically involves applying sophisticated econometric analytical techniques. Yet, the final decision about whether the observed or anticipated distributional effects are acceptable rests on alignment between those effects and basic social values. When dealing with medicines, the balance drawn between distribution under the current prices and the distribution that would be socially desirable usually depends on the severity and prevalence of the disease being treated and the availability or non-availability of alternate treatments or preventive measures. In virtually all societies, there is strong sentiment that any medicine within the category of "essential medicines" should be available to all who are in need of it. While the category is stable, the contents of the category -- that is, the list of medicines to be regarded as "essential" -- is constantly changing as new diseases emerge and as medical science advances.

A widespread belief that patenting causes huge increases in drug prices shapes much of the debate about distributional effects. A typical version of this view was expressed in Dean Baker's observations regarding ways government can define programs to redistribute income from poor to rich. While focusing primarily on Wall Street firms, he includes the following comment on drug prices:

The government grants pharmaceutical companies patent monopolies that allow them to mark up the price of prescription drugs by several hundred percent or even several thousand percent above what the same drugs would sell for in a competitive market. As a result of patent protection, many drugs sell for hundreds or even thousands of dollars per prescription. By contrast, if all drugs were sold as generics in a competitive market, the overwhelming majority could be bought for \$4 or \$5 per prescription.¹

The widespread perception that patents last a long time, given reality by recent extensions of copyright (a different form of intellectual property right) from 20 to more than 100 years and by clever patent lawyer success in "evergreening" 20 year patents by securing separate patents for follow-on innovations, reinforces the public perception that drug patents impose unnecessary barriers to securing treatment of disease.

The third concern, efficiency, is often treated as a technical question that can be resolved with economic analysis. However, even the most narrowly economic calculations proceed from two ethical presuppositions: that efficiency is a legitimate concern, and that it should be ranked fairly high in the hierarchy of values to be attained. Economists assume others agree with this second judgment; however, other members of society may not rank efficiency as highly. Once discussion moves from the narrow calculations to judgments about what sort of social arrangements are more or less efficient the normative component becomes more obvious. Adam Smith regarded competitive markets as more efficient than other sorts of economic arrangements he regarded competition as a spur to greater effort and inventiveness. In contrast, Karl Marx regarded planned economies as more efficient because they would eliminate exploitation; he viewed competitive markets as a mechanism by which stronger (larger) firms eliminated weaker ones and were thereby enabled to intensify exploitation of the workers. Thus, even when people agree that "efficiency" is desirable, there is room for considerable ethical disagreement about the merits of any particular arrangement. Yet, there may be one area where efficiency inspires less ethical disagreement – judgments about the extent and possibility of reducing transaction costs. Arranging exchanges always involves a certain amount of effort: to find out about what is available, to identify willing providers, and to agree with a provider on terms of the exchange. There is a point beyond which the effort involved becomes too great for anyone and exchanges do not occur. While different people start feeling frustrated by the complexities of particular transactions at different points of complication, the idea of making information about what is available, who can provide it, and what the terms of exchange will be easier to acquire makes eminent sense to nearly everyone.

After summarizing the development of the intellectual property rights developed in drug patents, this note takes up the variety of ways in which those who believe drug patents are creating price barriers that impede access to needed medicines have sought to limit patent rights in this particular area.

¹ Dean Baker, "Ending the myth of 'market fundamentalism,'" *Dissent* Spring 2010, pp. 58-62. Price comparisons used later in the article shift to a ten-fold difference in price when giving figures for total national spending (\$250 billion a year for all drugs in the current US market vs \$25 billion in a hypothetical free market.)

I. Development of Intellectual Property Rights in Patent Systems

The notion that people who invented new devices should be rewarded for their ingenuity with a temporary monopoly on the making and use of their invention was first expressed in the patent law adopted by Venice in 1474. Many inventors had kept their methods of making products to themselves, treating them as what in later centuries were named “trade secrets” kept within the originator’s workshop. Since most workshops were small – employing less than 10 people – and labor mobility limited by guild rules and government measures to keep skilled artisans at home, trade secrets were often effective in reserving the advantages of a new method to its originator. However, any advance embodied in a physical object could not be kept secret so easily: someone else could buy an example of that object, disassemble it, copy its various parts, and then reassemble those parts exactly. The primary limits on this activity were access to tools and assembly skills at least as good as those used by the object’s original maker.

The Venetian system, later emulated by other European rulers, created a new use for a longstanding government practice. European monarchs had used “letters patent” (open letters – unsealed written notifications of decisions transmitted to the monarch’s ministers – as distinct from “letters close” – folded and sealed written communications meant for the private information of the addressee) to grant pensions, property, special rights, or permission to undertake particular activities to the person or persons named in the letter. Because letters patent were the typical way monarchs established or confirmed monopolies on trade or provision of particular services, their use was easily extended to awarding limited-duration monopoly rights to use an advance in applied science. The rights enjoyed by inventors under their letters patent (quickly shortened to “patents”) were defined by three key provisions of patent law. First, an inventor desiring a patent had to “disclose” the invention by describing it in sufficient detail for anyone skilled in the relevant technical practice to understand how it works and how to make it. Venetian authorities imposed this requirement from the start; English courts added it to their country’s preexisting patent law during the reign of Queen Anne in 1702-14. By the end of the eighteenth century disclosure was a standard element of patent law. Second, the monopoly created by the patent was temporary, typically lasting 20 years, and could be cancelled earlier if the patent holder failed to “work the patent” by producing the physical object or objects covered by it or to meet other requirements, such as payment of maintenance fees.² Third, patents were regarded as protection for “technology” – very specific advances in goods or processes for making them.

² In the USA, the maintenance fees for a utility patent vary by size of the enterprise. Large enterprises wishing to retain their patent must pay \$900 after 3 years, \$2300 after 7 years, and \$3800 after 11 years; small enterprises pay \$450, \$1150, and \$1900 on the same schedule. Fees noted at www.uspto.gov (accessed 4 February 2010).

Today, patents take several forms:

product, process, or utility patent	applies to products, processes, machines, or synthetic composition of matter typical term = 20 years
utility model/innovation patent	applies to smaller improvements on existing products, processes, or machines typical term = 7-10 years
plant patent	applies to new varieties of asexually propagated plants typical term = 20 years (25 for trees and vines)
plant variety protection	applies to plants propagated from seeds typical term = 20 years
design patent	applies to ornamentation or other features of the external appearance of products typical term = 14 years

Patents covering new medicines are typically product, process, or utility patents with a 20-year term.

Even a limited-duration monopoly is a monopoly, and patent holders can frustrate others' efforts to further advance applied knowledge if they refuse to sell others licenses to use their invention. The degree to which a particular patent holder's refusal to sell use rights inhibits further advances depends on the nature of the innovation covered by the patent. James Watt's patent for steam engines was what is now called a "pioneer patent" – a patent covering an invention so central to a particular area of applied science that it is difficult to work in that area without using that invention. The inventions covered by most patents are not as fundamental, and others often find a way to "invent around" the patent to produce a device or a medicine having the same use or effect without directly copying the patent-holder's design and method of fabrication. However, a cluster of several different patents covering less fundamental advances than Watt's can become barriers to further development in a particular area of technology if developing new inventions fully requires securing licenses from multiple patent-holders. If even one patent-holder refuses to license, efforts to develop additional improvements can be frustrated during the term of the unwilling holder's patent.³

Patents initially covered only newly developed inanimate objects – tangible products or the machines and processes needed to make them. As both the general chemical industry and the specific application of chemical knowledge to developing new medicines advanced in the second half of the 19th century, their products were generally viewed as "works made by man" and included within the patent system.

The approximately 100 governments participating in negotiations to create the World Trade Organization in 1994 agreed to standardize many of their rules on intellectual property rights through the Trade-Related Intellectual Property Rights (TRIPS) Agreement. Article 27 deals with patents, with Paragraph 3 most relevant to advances in medicines and other medical treatment of diseases:

³ See M.A. Heller and R.S. Eisenberg, "Can Patents Deter Innovation? The Anticommons in Biomedical Research," *Science*, 280: 698-701 (1 May 1998) for an introduction to this problem. Heller coined the evocative "anticommons" to highlight the negative impacts that can arise from such situations.

1. Subject to the provisions of Paragraphs 2 and 3, patents shall be available for any inventions, whether products or processes, in all fields of technology, provided that they are new, involve an inventive step and are capable of industrial application. Subject to Paragraph 4 of Article 65, Paragraph 8 of Article 70 and Paragraph 3 of this Article, patents shall be available and patent rights enjoyable without discrimination as to the place of invention, the field of technology and whether products are imported or locally produced.

2. Members may exclude from patentability inventions, the prevention within their territory of the commercial exploitation of which is necessary to protect *ordre public* or morality, including to protect human, animal or plant life or health or to avoid serious prejudice to the environment, provided that such exclusion is not made merely because the exploitation is prohibited by their law.

3. Members may also exclude from patentability:
 - (a) diagnostic, therapeutic and surgical methods for the treatment of humans or animals

 - (b) plants and animals other than micro-organisms, and essentially biological processes for the production of plants or animals other than non-biological and microbiological processes. However, Members shall provide for the protection of plant varieties either by patents or by an effective *sui generis* system or by any combination thereof. The provisions of this subparagraph shall be reviewed four years after the date of entry into force of the WTO Agreement.⁴

The language is subtle, as befits an agreement worked out after hard negotiation among highly skilled trade lawyers, but the terms most relevant to medicines in Article 27.2 and Article 27.3 can be broken down as follows:

member states must protect intellectual property rights in:	member states may decline to create patent rights covering:
new products or new production processes that are truly new, whose development involve a distinct inventive step beyond the existing "state of the art" in the area(s) of technology used, and can be made into physical products by industrial fabrication processes	diagnostic, therapeutic, and surgical methods for treating human or animal diseases and injuries goods that threaten the local public order or morality goods that endanger human, animal or plant life or health goods that would cause serious environmental damage

⁴ Official text available from the World Trade Organization, at www.wto.org/English/docs_e/legal_e/27-trips_04c_e.htm (accessed 29 April 2010).

The difference between providing “intellectual property rights” and “excluding patentability” (in more ordinary English, “refusing to issue patents for”) has not been central to controversies over new medicines, though it has featured prominently in debates over whether and to what extent patents or other intellectual property rights should be extended to new varieties of plants and animals that are developed with conventional breeding methods or newer genetic modification techniques.

The TRIPS also included provisions addressing the situation of developing countries, which typically did not have national patent laws conforming to TRIPS standards. They were given extra time to adapt their patent laws in Article 65, Paragraph 4:

To the extent that a developing country Member is obliged by this Agreement to extend product patent protection to areas of technology not so protectable in its territory on the general date of application of this Agreement for that Member, as defined in Paragraph 2, it may delay the application of the provisions on product patents of Section 5 of Part II to such areas of technology for an additional period of five years.

This provision meant that while industrial states had to make their national patent law fully consistent with TRIPS by 1 January 1996, developing countries were given until 1 January 2000. Developing countries that did not already provide patent protection on all the technologies covered by TRIPS had an additional five years to amend their patent law. Thus Brazil, which already had laws covering all the technologies, had to conform its national law to TRIPS in 2000 while India, which did not, had until 2005.

Article 70, Paragraph 8 specified some transition measures that had to be taken immediately:

Where a Member does not make available as of the date of entry into force of the WTO Agreement patent protection for pharmaceutical and agricultural chemical products commensurate with its obligations under Article 27, that Member shall:

- (a) notwithstanding the provisions of Part VI, provide as from the date of entry into force of the WTO Agreement a means by which applications for patents for such inventions can be filed;
- (b) apply to these applications, as of the date of application of this Agreement, the criteria for patentability as laid down in this Agreement as if those criteria were being applied on the date of filing in that Member or, where priority is available and claimed, the priority date of the application; and
- (c) provide patent protection in accordance with this Agreement as from the grant of the patent and for the remainder of the patent term, counted from the filing date in accordance with Article 33 of this Agreement, for those of these applications that meet the criteria for protection referred to in subparagraph (b).

The requirements that countries which had been limiting patentability of medicines now adopt and enforce national laws comparable to those prevailing in the advanced industrial states where large pharmaceutical firms are based, made the TRIPS Agreement the object of considerable criticism among advocates of universal access to health care, advocates of universal access to “essential medicines”, and members of the most anti-market segments of the anti-globalization movement. All three regard TRIPS as restricting

access to medicines by making it more difficult for generic drug makers and the more advanced developing countries, such as India, Brazil, China, and South Africa, to make lower-price versions of newly-invented medicines. In all of these countries, locally based generic drug makers were able to rely on the fact the government either did not provide patents for drugs or would not enforce foreign patents to pursue their parallel production. As the more advanced developing countries with large generic drug industries approached their deadline for applying the rules, criticisms of the TRIPS system intensified.

II. Challenging Patents on Medicines

Those seeking to challenge drug patents can pursue any or all of three avenues of change: 1) seek to abolish patents on medicines entirely, 2) seek to limit the price implications of patents, 3) seek to limit the number and coverage of drug patents by challenging the newness or innovativeness of the particular medicine for which the maker is seeking a patent, and 4) limit the effects of patents by resort to provisions for compulsory licensing. The first involves arguing that medicines should be in the public domain immediately. The others start from accepting the idea that innovators can be allowed to possess intellectual property rights for the 20-year term of a patent, but try to limit the impact of those rights on patients or governments having little money to spend on medicines in different ways. The second addresses prices. The third attempts to limit the number of drug patents in effect, thereby increasing the number of medications that can be produced by all interested manufacturers. The fourth uses the public health emergency exception in patent law to speed the distribution of particular medicines to needy patients by use of government powers to issue compulsory licenses authorizing production by makers other than the patent-holder.

Seeking Abolition of Patents on Medicines

A few activists have pursued the first route in the controversy over access to HIV medicines, but have not had much success even when confining their demands to HIV treatments or other “essential medicines.” In the countries where the major drug innovating firms are located, a combination of supportive public opinion and highly active pharmaceutical firm lobbying have kept drug patents in place. However, proposals for replacing or significantly modifying the patent system continue to appear. These began to gain traction even in the USA, where public opinion is generally supporting of patent rights, in the 1990s. AIDS activists in the USA became an important part of the wider coalition criticizing the pharmaceutical industry and digging out information about its actual income and expenditures. Revelations of organized campaigns to encourage physicians to prescribe one company's medications rather than another's, which involve considerable spending on gifts, social occasions, and free samples of the drugs involved⁵ significantly weaken the plausibility of claims that patent protection was necessary to funding research and development. Critics also pointed out that a considerable portion of the research involved was actually carried out at taxpayer expense in the form of research grants to university-based or institute-based scientists. The overlap between publicly-funded scientific research and privately-funded corporate research and development became greater after 1980 with adoption of the Bayh-Dole act permitting

⁵Data on the extent of these practices is provided in Eric G. Campbell, Russell L. Gruen, James Mountford, Lawrence G. Miller, Paul D. Cleary, and David Blumenthal, “A national survey of physician-industry relationships,” *New England Journal of Medicine* 356 (17): 1742. Available at <http://www.nejm.org/doi/pdf/10.1056/NEJMsa064508> (Accessed 17 November 2010).

researchers with government grants to take out patents on any localizable innovation derived from their research.⁶

The scandals and the overlap encouraged proposals for replacing drug patents with some other way of promoting research and innovation. One proposal calls for conducting all drug research with public funds and placing all of the results into a public domain information bank from which any firm with sufficient manufacturing capacity could draw. Another suggests leaving the patterns of drug research as they are, but bringing particularly promising advances into the public domain by having the government adopt a prize system for buying out the patent. However, neither proposal has much support.

Controversies over changing the patent system itself are most relevant in the USA because the government does not maintain any drug price controls (though health insurers often do as noted below). Yet, because the US market is still the world's single largest market for medications, it is central to the economic calculations of all major drug firms wherever they are located. Thus, the debates in the USA about the extent to which the major drug firms actually "need" the extra income derived from monopoly pricing on patented drugs are familiar elsewhere and themes raised by US critics of the pharmaceutical industry are echoed by critics and activists in other countries as well.

Limiting the Price Effects of Patents

Many governments around the world address drug price questions directly, rather than through modification of the patent system. Most countries have national health services that centralize drug purchases through the national government's health ministry. The ministries are generally able to use their volume buying to negotiate favorable prices. Some countries also maintain separate drug price regulation schemes covering sales to private buyers. In the United Kingdom, the Office of Fair Trading, which enforces both consumer protection and competition law, is charged with administering the Pharmaceutical Price Regulation Scheme. The OFT reviews drug company income and costs every five years and determines a reasonable rate of profit for the next five; drug companies then use these determinations to set their prices. The OFT is required to take several considerations into account, including providing taxpayers with value for money and ensuring there are "adequate rewards" for development of new and useful drugs.⁷ While there are no national regulations in the USA, both the government-run Medicare system and major private health insurers exert pressure on prices through the tiered co-payment systems, which establish a low co-payment that the person using the medicine has to pay for generic drugs and sets increasingly higher co-payments for other classes of drugs. However, this system has significant effect on prices only when there are multiple medicines available for the same ailment and at least one of them is in generic production because the relevant patents have expired. Efforts by some patients and private insurers to reduce their drug prices by importing drugs from Canada were frustrated in the 2000s by pharmaceutical lobby's success in persuading the GW Bush administration to prohibit such imports.

⁶Public Law 96-517. A well-formulated critical analysis of this law and later developments is provided by Janet Hope, 2008. *Biobazaar* (Cambridge: Harvard University Press). It should be noted that the law did not create an entirely new situation. Donald S. Fredrickson. 2001. *The Recombinant DNA Controversy: A Memoir* (Washington DC: ASM Press), p. 311, note 32. Notes that by the mid-1970s the US government was allowing universities to take out patents on about 90% of the innovations spun off from government-funded research.

⁷Kristina M. Lybecker & Elisabeth Fowler. 2009. "Compulsory licensing in Canada and Thailand: Comparing regimes to ensure legitimate use of WTO rules." *Journal of Law, Medicine and Ethics* 27(2): 222-239.

The major pharmaceutical firms make most of their sales, and hence earn most of their profits, in the major industrial countries, and until recently were paying much less attention to markets in other parts of the world.⁸ This inattention opened opportunities for developing countries to extend industrial policy into the pharmaceutical sector and consciously foster local drug production by neither issuing nor enforcing drug patents. Brazil and India had the greatest success in developing local drug production in this way, but similar policies were adopted in a number of developing countries. As these countries grew more prosperous in the 1990s, the revenue potential of their markets became more attractive and the major pharmaceutical firms (known collectively as "Big Pharma" to industry critics) energetically supported conclusion of the TRIPS agreement to reduce that drain on their patent-related earnings. By one estimate, generic drug production in India alone was costing the major pharmaceutical firms between \$69 and \$100 million a year in the late 1990s;⁹ a 2005 estimate put the lost income at \$500 million a year.¹⁰ When the patent on AZT lapsed in mid 2005, it was the 13th bestseller in standalone retroviral medications worldwide, with total sales of about \$36 million in 2004. AZT is also a constituent of the combination therapies Combivir and Trizivir, which had global sales totaling \$31 billion and \$400 million respectively in 2004.¹¹ As the more advanced developing countries brought their patent legislation into line with TRIPS standards, HIV activists and others continued to complain about TRIPS but also shifted effort to other methods of limiting the price effects of patents. The global market for medicines remains highly uneven, and the industrial countries still provide the largest part of sales income. This ongoing market reality is still reflected in pharmaceutical companies' pricing: econometric analyses suggest they practice "market-skimming" by setting prices in different countries in relation to local income levels, paralleling major firms' participation in the tiered pricing schemes for HIV medicines that institutionalize having different prices for industrial, developing, and least developed countries and their willingness to make price concessions to governments so they will not issue compulsory licenses.¹²

While amending their laws to provide foreign patent holders with greater protection, governments of the more advanced developing countries remained energetic regulators of drug prices within their territories. The Brazilian government reinforced its price regulations with Law 10,742/2003 by strengthening the system under which the Chamber for the Regulation of the Market of Medicines regulates the private market. Though the government is committed to assuring universal provision of medicines for certain diseases, and typically negotiates aggressively on the prices it will pay, the private market still accounts for

⁸ See Amir Attaran and Lee Gillespie-White. 2001. "Do patents for antiretroviral drugs constrain access to AIDS treatment in Africa?" *JAMA* 286(15): 1890; Robert Weissman, 2007. "Big Pharma and AIDS, Act II: Patents and the price of second-line treatment," *Multinational Monitor*, March/April: 11-13.

⁹US drug companies' estimate quoted in Donald G. MacNeil Jr. 2000 "Selling cheap 'generic' drugs India's copycats irk industry." *New York Times* 1 Dec. 2000, p. A1.

¹⁰ "Days of cheap HIV drugs numbered." 2005. *Nature Reviews Microbiology* 3(5): 370 (May) reported an estimate that Indian generic production was costing major makers of patented drugs about \$500 million in income a year but without providing a source.

¹¹ According to "New patent laws may threaten India's supply of cheap anti-retroviral drugs." 2005. *APBN (Asia Pacific Biotech News)* 9 (1-2): 39.

¹² For examples see Lybecker & Fowler (note 7) and Amy Stewart Nunn, Elize Massard da Fonseca, Francisco I. Bastos and Sofia Gruskin. 2009. "AIDS treatment in Brazil: Impacts and challenges." *Health Affairs* 28 (4): 1102-1133.

most of the drug sales in the country. The government effectively sets prices there as well by requiring the Chamber to approve the price charged for any drug, whether made by a local or by a foreign firm, before it is released on the Brazilian market. The maker may apply for review of the price later; the Chamber reviews prices once a year.¹³

Canadian experience also suggests governments can treat compulsory licenses and direct price regulation as alternatives. Between 1922 and 1970 the Canadian government used compulsory licenses to reduce drug costs by authorizing local production 22 times. In 1970-87, it shifted methods and encouraged the import of active pharmaceutical ingredients to be made into finished products by Canadian firms. When Canadian patent law was revised in 1987 to bring it into line with patent rules prevailing in Europe and the USA, it established a Patented Medicines Price Review Board to regulate prices.¹⁴

Limiting the Number of Patents in Effect

HIV activists and others resorted increasingly to this strategy, as more countries were required to bring their patent law into conformity with the TRIPS Agreement. TRIPS itself never defines the terms "invention" or "inventive step," WTO member states retain some discretion in this matter.

Contests over whether a particular invention deserves a patent are a longstanding feature of national patent systems. All patent systems distinguish clearly between the publicly accessible knowledge open for use by all and the proprietary knowledge gained by individual effort that deserves protection. The issue has traditionally come to the fore when a patent holder complains that others are infringing on the patent – using the innovation covered without a license from and agreed royalty payments to the patent holder. Those accused of infringement can defend themselves in any of several ways by demonstrating that:

- a) the knowledge used to develop the advance was already in the public domain,
- b) though the patent has not expired, it is no longer valid because of the patent-holder's failure to "work" it or pay the required maintenance fees,
- c) the activity did not infringe on the patent because it did not use or depend on the particular technological advance protected by the patent, or
- d) the patent is invalid -- it should not have been issued -- because the innovation it covers embodies insufficient novelty to qualify for a patent.

Settling the first type of argument requires assessing the state of freely available basic and applied knowledge that the accused infringer may legitimately use. Settling arguments about which elements of current applied knowledge are available for anyone to use requires identifying the knowledge and material applications of knowledge in working products or manufacturing processes that are in the public domain because they are products of nature regarded as not patentable, were never patented by their inventor, or are no longer covered by a patent because its term has expired.

¹³ Deborah Portillo & Rana Gosain. 2007. "IP Focus-Americas: Drugs dispute demands action," *Managing Intellectual Property*, October: 28.

¹⁴ Lybecker & Fowler (note 7), 225.

Even in the USA, the country regarded as having some of the strongest patent protections in the world, things produced by nature are not patentable. The USA has gone further than many countries in permitting patenting of bacteria and other life forms produced using genetic engineering, but the courts do distinguish between results of active human involvement in creation of the life form and human perception of ways an existing life form might be used. In *Diamond vs Chakrabarty*, the first case in which the US Supreme Court ruled on the question of whether results of employing genetic modification techniques could be patented, the distinction was explained as follows:¹⁵

This is not to suggest that § 101 has no limits, or that it embraces every discovery. The laws of nature, physical phenomena, and abstract ideas have been held not patentable. *See Parker v. Flook*, 437 U. S. 584 (1978); *Gottschalk v. Benson*, 409 U. S. 63, 409 U. S. 67 (1972); *Funk Brothers Seed Co. v. Kalo Inoculant Co.*, 333 U. S. 127, 333 U. S. 130 (1948); *56 U. S. 112-121 (1854)*; *55 U. S. 175 (1853)*. Thus, a new mineral discovered in the earth or a new plant found in the wild is not patentable subject matter. Likewise, Einstein could not patent his celebrated law that $E=mc^2$; nor could Newton have patented the law of gravity. Such discoveries are "manifestations of . . . nature, free to all men and reserved exclusively to none." *Funk, supra* at 333 U. S. 130.

Judged in this light, respondent's micro-organism plainly qualifies as patentable subject matter. His claim is not to a hitherto unknown natural phenomenon, but to a nonnaturally occurring manufacture or composition of matter -- a product of human ingenuity "having a distinctive name, character [and] use." *Hartranft v. Wiegmann*, 121 U. S. 609, 121 U. S. 615 (1887). The point is underscored dramatically by comparison of the invention here with that in *Funk*. There, the patentee had discovered that there existed in nature certain species of root nodule bacteria which did not exert a mutually inhibitive effect on each other. He used that discovery to produce a mixed culture capable of inoculating the seeds of leguminous plants. Concluding that the patentee had discovered "only some of the handiwork of nature," the Court ruled the product nonpatentable:

"Each of the species of root-nodule bacteria contained in the package infects the same group of leguminous plants which it always infected. No species acquires a different use. The combination of species produces no new bacteria, no change in the six species of bacteria, and no enlargement of the range of their utility. Each species has the same effect it always had. The bacteria perform in their natural way. Their use in combination does not improve in any way their natural functioning. They serve the ends nature originally provided, and act quite independently of any effort of the patentee" (333 U.S. 131).

Here, by contrast, the patentee has produced a new bacterium with markedly different characteristics from any found in nature, and one having the potential for significant utility. His discovery is not nature's handiwork, but his own; accordingly it is patentable subject matter under § 101.

A particular advance in knowledge or technology might also be part of the public domain because the inventor decides to announce and explain it without seeking a patent. This was the case with the Salk polio vaccine. After it had been proven safe and effective, and was in widespread use, Salk was asked who

¹⁵*Diamond V Chakrabarty* 447 U.S. 303 (1980), pp. 309-310.

owned the patent. Salk replied, "Well, the people I would say. There is no patent. Could you patent the sun?" Though it is clear the vaccine would have been eligible for a patent, neither Salk himself, nor his employer, nor the entity that provided the money supporting Salk's research applied for a patent.¹⁶

Salk, a researcher at the University of Pittsburgh with funding from the National Foundation for Infantile Paralysis, functioned in a research context. Then as now most drug development occurs in a commercial context. Some pharmaceutical manufacturers, typically the larger ones, use innovation as a way to gain competitive advantage on the market and hence enhance their income. The commercially-oriented activity of developing new medicines requires laboratory equipment and research competence comparable to those possessed by experimenters in basic science, neither of which come cheap. In addition, concern about potential harm from ineffective drugs or unanticipated side effects of effective drugs have led many governments to require clinical trials on human subjects before new drugs can be put on sale. Clinical trials on humans occur only after considerable preliminary work indicating that the proposed medicine is likely to be both effective against the condition for which it is to be used and safe for human consumption. In the more advanced areas of drug development today, the process of moving from initial perception that a particular molecule or particular chemical formulation will be effective against some disease to the completion of human clinical trials can take 12 to 14 years.¹⁷ The pharmaceutical manufacturer or independent developer working on a potential new medication typically applies for a patent before conducting clinical trials with humans and may end up waiting several years before the new medication is approved for sale.¹⁸

Settling the second type of argument is sometimes more complex than it appears. Failure to "work" a patent should be obvious from lack of production of the good covered or non-use of the production process covered. However, in some jurisdictions, it is possible to hold a patent for a considerable period of time without active engagement in using the process or producing the good covered by it. A patent holder may have good reasons to fail to work a particular patent, and may also be reluctant to license use of the innovation to others. However, in countries where the authorities do not insist on evidence of working the patent, unworked patents can be used to frustrate competitors' efforts to develop better products or manufacturing processes. A company may try to hold its market advantage by taking out patents on related advances that it has no intention of using because their use would reduce sales of the existing product, simply to keep competitors from developing innovations that would displace its products. This has become a significant problem in the USA, where some federal courts are known to be reluctant to rule that a patent has not been worked.¹⁹ In fact, it is sufficiently widespread that patent lawyers in the country have a pejorative term, "patent troll" for companies using this strategy.

¹⁶ Quoted in M. Mitka. 2005. "Happy 50th birthday, Salk vaccine." *JAMA: Journal of the American Medical Association* 293: 1581-83.

¹⁷Noted in the US Food and Drug Administration's information on drug patents. See <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/default.htm> (accessed 29 April 2010).

¹⁸E.g., Michael Rosen. 2003 "The complexities, cost of Midwest biotech drug development," posted on the Wisconsin Technology Network's WTN News page at <http://wistechnology.com/articles/377/> (accessed 20 July 2010).

¹⁹ There is considerable controversy about the impact of patent trolls. See, e.g., Daniel P. McCurdy, "Patent Trolls erode the foundation of the U.S. Patent System" arguing that they are a problem, at <http://www.scienceprogress.org/2009/01/patent-trolls-erode-patent-system/> (accessed 22 April 2010) and Ron Epstein, "Debunking the "patent troll" myth," *Businessweek*, 1 Feb. 2010

Even without patent trolls, the existence of multiple patents covering related innovations held by different individuals or companies can make further advance more difficult. Any innovator needing a license to use more than one patent to develop and market its own invention will be vulnerable to hold up by which ever holder of an existing patent is least interested in issuing a license. This may involve having to offer higher royalty payments, which could make the newly invented good too expensive to market competitively. At the most extreme, the patent holder might refuse licenses to anyone, which would prevent developments based on the innovation covered in that patent. In an area like HIV treatments, where the medicines are combinations of different drugs, the potential for unwilling patent holders to make life difficult for others is significant. This accounts for recent proposals, like the one advanced by UNITAID, to promote creation of patent pools. A patent pool is typically set up among a group of companies holding patents on distinct but related technological advances that are likely to be used together in developing new products. They create a jointly owned firm that becomes the owner of all the related patents and the single source of licensing arrangements. The pool allows member firms to use each other's advances more effectively and, when members are willing, offers third entities one-stop licensing for any or all patents owned by the pool. Patent pools have sometimes been used to cement a cartel, a danger patent and competition (anti-trust) offices have addressed by developing rules for distinguishing between patent pools likely to promote access to new technology from those likely to prevent others' ability to offer comparable products.²⁰

Settling the third type of argument, whether the later innovation required use of the earlier one, is particularly complicated. The terms of argument vary from country to country because of differences in what patents cover. Between 1970 and 2005, drug patents in India covered manufacturing processes rather than the active ingredients of a drug or the particular formulation of active and inactive ingredients. Thus an Indian pharmaceutical company was free to manufacture the same medicine as a patent holder if that pharmaceutical company could develop a different manufacturing process.²¹ By the time HIV emerged as a major disease, several Indian drug manufacturers were sophisticated enough not only to develop and market generic copies of most HIV medications, but also to develop some innovative combinations of medications into single dose pills. In most countries, however, the law is not as hospitable to copycat manufacturers. However, defending a patent against unlicensed use ("infringement") can become very expensive if the lawsuit drags on. Thus, patent holders typically make strategic choices about how much effort they will put into defense against infringers. In some instances, however, patent holders are particularly stubborn and aggressive, blocking rival firms and keeping others out of the market by active defense of patent rights.²² In industries where much of the profit derives from sale of patented or

arguing that they are not, available at http://www.businessweek.com/technology/content/feb2010/tc2010021_330487.htm (accessed 22 April 2010).

²⁰ Jeanne Clark, Joe Piccolo, Brian Stanton, & Karin Tyson, "Patent Pools: A Solution to the Problem of Access in Biotechnology Patents?" United States Patent and Trademark Office 5 December 2000. Available at <http://www.uspto.gov/web/offices/pac/dapp/opla/patentpool.pdf> (accessed 29 April 2010).

²¹ "New patent laws may threaten India's supply of cheap anti-retroviral drugs." 2005. *APBN (Asia Pacific Biotech News)* 9 (1-2): 39.

²² The Wright Company and the Curtiss Company each owned enough patents on important elements of aircraft design to block each other or any third party from making further advances in aircraft manufacture until the US government, concerned about availability of aircraft as the likelihood of involvement in World War I increased, pressured them into forming a patent pool and ending their blocking behavior. Harry T. Dykman, "Patent Licensing within the Manufacturer's Aircraft Association (MAA)," *Journal of the Patent Office Society* 46: 646-659 (1964).

copyrighted goods, companies are likely to be extremely aggressive, as any university student who has received harsh notices from the Record Industry Association of America after downloading music files can attest.²³

The pharmaceutical industry is one such industry: the major ways of making significant profit (even within government price controls) are either large volume production of generic drugs that are inexpensive to manufacture or large volume production of patented drugs during the period when the patent gives its holder a monopoly on sales. The major manufacturers of innovative medicines argue that they need the patent monopoly to recover research and development costs because these are particularly high in their industry. Not only do they face a lengthy process of human clinical trials and regulatory review, but also a significant number of potential drug formulations turn out to be less promising than anticipated, and their development is abandoned at some point in the process. Recent advances in genetics, which permit identifying particular genes or particular mutations in genes that correlate with susceptibility to particular diseases or conditions, have accelerated the search process in some areas of drug development but have not yet had a significant impact on the expense because clinical trials are still necessary.

The fourth type of argument between patent holders and accused infringers, that the patent is invalid because the invention it covers is insufficiently novel to qualify for patent, also differs from country to country because of variations in national definitions of novelty. The basic requirement that an invention be “novel” – sometimes reinforced by additional qualifications as embodying a “non-obvious” improvement or as representing something greater than an “incremental improvement” is an element of the patent law in every country. The basic principle is also affirmed globally in the Paris Convention for the Protection of Industrial Property, the rules of the World Intellectual Property Organization, and the TRIPS Agreement. Yet, none of these global sources define the term novelty, leaving that to the legislatures, patent offices, and other authorities of individual states.

Most national patent laws permit any citizen to challenge a patent or patent application. Thus a competing company, one or more actual or potential buyers of a good, or an activist group concerned about some social implication of issuing a patent can all ask the patent office or the relevant tribunal to reconsider a patent. In recent years, AIDS activists and others seeking to stem the increasing costs of treating HIV-positive persons have become more active in challenging patents covering HIV medications on this basis. Much of the impetus stems from changes in the supply of and need for particular HIV medications. Many of the first-line (first generation) ART medications and combinations developed in the mid 1980s to early 1990s have or are about to become public domain because the 20-year terms of their patents is expiring. However, second-line drugs were developed more recently and their patents remain in effect. Anyone with these drug resistant strains of HIV needs to use the second line treatment, and the number of such patients is growing in rich and poor countries alike.

Success in persuading the patent office to deny a patent application or to revoke an already issued patent because the innovation is insufficiently novel depends very much on the terms of the particular national law. The government of India was persuaded by a combination of activist-mobilized public outcry and lobbying from some of the generic drug makers to adopt relatively demanding standards of what constitutes

²³ W. Triplett “RIAA targets university students,” *Variety*. 28 February 2007. Available at: <http://www.variety.com/article/VR1117960319.html?categoryid=18&cs=1> (accessed 4 Feb 2010).

“novelty” by including a proviso that the advance should be “nonobvious” and more than a minor variation on an existing product or manufacturing process. Section 3 of India’s Patent Act specifies that:

The following are not inventions within the meaning of this Act:

- a. an invention which is frivolous or which claims anything obvious contrary to well established natural laws;
- b. an invention the primary or intended use of which would be contrary to law or morality or injurious to public health;
- c. the mere discovery of a scientific principle or the formulation of an abstract theory;
- d. the mere discovery of any new property of new use for a known substance or of the mere use of a known process, machine or apparatus unless such known process results in a new product or employs at least one new reactant;
- e. a substance obtained by a mere admixture resulting only in the aggregation of the properties of the components thereof or a process for producing such substance;
- f. the mere arrangement or re-arrangement or duplication of known devices each functioning independently of one another in a known way;
- g. a method or process of testing applicable during the process of manufacture for rendering the machine, apparatus or other equipment more efficient or for the improvement or restoration of the existing machine, apparatus or other equipment or for the improvement or control of manufacture;
- h. a method of agriculture or horticulture;
- i. any process for the medicinal, surgical, curative, prophylactic or other treatment of human beings or any process for a similar treatment of animals or plants to render them free of disease or to increase their economic value or that of their products.²⁴

In 2005, clause d was amended to make it even more restrictive:

(d) the mere discovery of a new form of a known substance which does not result in the enhancement of the known efficacy of that substance or the mere discovery of any new property or new use for a known substance or of the mere use of a known process, machine or apparatus unless such known process results in a new product or employs at least one new reactant.

Explanation.—For the purposes of this clause, salts, esters, ethers, polymorphs, metabolites, pure form, particle size, isomers, mixtures of isomers, complexes, combinations and other derivatives of known substance shall be considered to be the same substance, unless they differ significantly in properties with regard to efficacy;”.²⁵

AIDS activists, healthcare activists, and other groups have had considerable success of the strategies in Thailand and India, as noted in the case summary. The process has also worked at last once in the USA, the country considered by most AIDS, healthcare, and anti-globalization activists as the primary force for the extension of intellectual property rights through the TRIPS Agreement. While success in such

²⁴ India. The Patents Act 1970, as amended by the Patents (Amendment) Act of 1995. Available at <http://ipindia.nic.in/ipr/patent/patents.htm> (accessed 29 April 2010).

²⁵ India. The Patents (Amendment) Act of 2005. Available at http://www.patentoffice.nic.in/ipr/patent/patent_2005.pdf (accessed 29 April 2010).

challenges may not lead to revoking the patent protecting the main active ingredient in a particular medication, collectively they curb efforts to secure patents on relatively minor changes, such as whether a particular drug combination is provided as a powder or as a compressed pill. Though seemingly small, such differences can be important to HIV positive persons. Thai activists were particularly keen to get Bristol-Myers Squibb's patent on ddi voided because the pill version was safer to use than powdered version then being produced by Thailand's Government Pharmaceutical Organization.²⁶

Issuing Compulsory Licenses

The government-created nature of patent law is revealed most clearly in the provisions institutionalizing the patent-granting government's right to issue compulsory licenses. With a compulsory license the government authorizes makers other than the patent holder to produce the particular good or use the particular production process covered by the patent. In return, the patent holder is protected by stipulations that the holders of compulsory licenses cannot assign those licenses to anyone else, must confine the extent of their production to that which is necessary for the purpose of the license, and must cease production when the circumstances leading to issuance of the compulsory license are resolved. Holders of compulsory licenses must also provide the patent holder with "reasonable royalties." This is obviously a vague term, which patent holders and others are likely to interpret it differently. Any dispute about what constitutes a "reasonable" royalty will ultimately be settled by the government that issued the compulsory license.

Provisions on compulsory licenses require that the issuing of compulsory licenses meet some public need important enough to justify overriding intellectual property rights. Even governments, which generally respect intellectual property rights, issue compulsory licenses from time to time. Most compulsory licenses are issued in situations where there is clear public need for greater production of a particular good or wider use of a particular manufacturing process proven to be particularly effective. With HIV medications, the most frequently invoked justification is that of a "public health emergency" in which the government has determined that access to a particular medication is so central to protecting or restoring the health of a significant portion of the population that the patent holder's monopoly needs to be displaced. Many national patent laws also allow the government to issue compulsory licenses for production of goods to be supplied directly to the government. Many national patent laws also allow use of compulsory licenses to overcome certain patent holder abuses of rights. In Brazil, the government can issue a compulsory license if the patent holder has failed to work the patent. In some other countries compulsory licenses may be issued when the patent holder's refusal to license others to produce a good or use a process covered by the patent is judged to have amounted to abusive or anti-competitive conduct. Some also use compulsory licenses to break innovation logjams created when a firm holds a "blocking" or "dependent" patent that inhibits further innovation by others. Some governments maintain special patent rules for certain products, such as drugs and food, with broader provisions for compulsory licensing in those areas.²⁷

²⁶ This feature of the controversy is mentioned in Pascale Boulet, Christopher Garrison, & Ellen 't Hoen. "Drug patents under the spotlight: Sharing practical knowledge about pharmaceutical patents." Geneva: Médecins Sans Frontières (May 2003), p. 20. Available from the WHO website at http://www.who.int/3by5/en/patents_2003.pdf (accessed 26 November 2010). Lybecker & Fowler (note 7) discuss the broader patents controversy in Thailand; Weissman (note 8), 16-21 provides an activist's perspective focused mainly on the contentions over patents covering HIV drugs.

²⁷The website of the Consumer Project on Technology at <http://www.cptech.org/ip/health/cl/> provides good information on compulsory licensing in medicine. Note particularly the health-related compulsory licensing examples given in <http://www.cptech.org/ip/health/cl/recent-examples.html> (accessed 4 February 2010).

Patent holders are unenthusiastic about compulsory licensing because it limits their rights, and the major pharmaceutical firms are known for particularly energetic opposition. However, even they concede that real "public health emergencies" exist, and there are times when the availability of a particular medicine becomes so important that patent rights should be set aside temporarily. At the same time, they are extremely concerned about and will use all of their political clout to avoid situations in which "public health emergencies" are invoked to justify the issuance of compulsory licenses motivated more by industrial policy. Such industrial policies might involve the fostering of state-owned pharmaceutical companies, or it might involve helping locally based private companies compete against the major drug firms by offering generic versions of patented drugs.

AIDS activists and other healthcare advocates, take a more generous view of what qualifies as a "public health emergency," an impulse that has been strengthened in recent years by increasing public support for the idea that access to either health care in general or to "essential medications" in particular should be regarded as a human right, that is, as something that societies have an obligation to provide to each individual.

The general notion of compulsory licenses, and their use in situations of overriding public need, was institutionalized even in the TRIPS agreement. However, the initial provisions were fairly restrictive. A government could issue a compulsory license, but the holder of that license could only produce for the domestic market in that country. For trade lawyers, this was a reasonable compromise. The country faced with a sufficient health emergency that it was prompted to issue a license would be able to supply its own population, but its licensees would not be competing with the pharmaceutical firm holding the patent in other countries' markets. Thus the problem of "parallel selling" to a third market would be avoided, and the impact of compulsory licenses on international trade minimized.²⁸ Clearly the compromise was based on assumptions that consumers in other countries desiring the good would be able to buy it from the patent holder. However, this assumption breaks down with HIV medications. Even after Indian generic pharmaceutical firms helped bring the price of ART down from approximately \$10,000 per person per year in 1996 to approximately \$350 per person per year in 2001, governments and individuals in many parts of the world -- including all of sub-Saharan Africa where HIV was spreading most rapidly -- could not afford to pay for the treatments. Even though effective treatment of HIV requires three things -- an initial blood test to determine whether the virus is present, consistent daily taking of medications, and periodic blood tests to determine whether the current medications are still working or the patient needs to be shifted to a different therapy -- the expenses of providing drugs became the primary focus of discussion.

Lack of what economists call "effective demand" -- desire for a good by consumers who can pay for it -- in much of the world meant the TRIPS provision could not work as anticipated by the trade lawyers. In fact, it was quite easy for AIDS activists and anti-globalization movements to present the TRIPS Agreement as a separate barrier to provision of HIV medications to people in poor countries who needed them for survival because compulsory licenses were limited to production for the home market. In response to activist

²⁸ J. Love, *Compulsory Licensing: Models for State Practice in Developing Countries, Access to Medicine and Compliance with the WTO TRIPS Accord*: Prepared for the United Nations Development Programme. January 21, 2001. Available at: <http://www.cptech.org/ip/health/cl/recommendedstatepractice.html> (accessed 4 February 2010) provided an early guide to using the exception.

campaigns and government concerns, the WTO Ministerial Conference, held in Doha, Qatar, in November 2001 agreed that compulsory licenses issued to deal with public health emergencies could also extend to production sufficient to supply needs in developing countries that lack any domestic production capacity. While this change had no immediate effect because the main sources of generic supply, the large Indian generic manufacturers, were not yet covered by TRIPS Agreement rules, it became important in January 2005 when India's transition period ended. Under India's new patent law, Indian generic producers would not be able to make any HIV medication patented after 1995 unless they held a license from the patent holder or a compulsory license from the Indian government.²⁹

AIDS and health care activists have been very successful in garnering public support for compulsory licenses. Theirs is a clear and compelling case: HIV can be managed, but not cured, and it can only be managed by consistent following of combination ART therapy. Consistent following of therapy requires continuing access to the medications; it has been demonstrated repeatedly that interrupting ART not only allow the HIV virus to rebound in the patient's body but also facilitate the virus' mutation against the medications the patient had been taking. HIV treatments thus fit well within the emerging notion that there are certain "essential medicines" no one should be denied because of inability to pay. This is true even in the USA, where public support for government provision of healthcare is significantly lower than in other countries. In a mid-June 2007 Harris poll contacting a nationwide sample of approximately 2250 adults, 61% of the respondents agreed that poor countries should be allowed to "break drug patents" (issue compulsory licenses), 20% of respondents disagreed and 19% were not sure.³⁰

Yet, issuing compulsory licenses need to be done with care. The licenses must go to firms that are capable of producing bioequivalent generic versions of the HIV medicines. Bioequivalent drugs have the same physical effects in the human body even if there are slight variations in the compositions of active and inactive ingredients used to produce them. Bioequivalence is regarded as particularly important in HIV treatments because any weakening of drug's effects from variations in the formulation allows the HIV virus to develop drug resistance more rapidly.³¹ Attaining bioequivalence is particularly difficult with combination HIV treatments.³² This problem came to the fore in 2004 when the World Health Organization formally delisted several generic versions of HIV medications because their bioequivalence had not been fully

²⁹ Noted in "New patent laws may threaten India's supply of cheap anti-retroviral drugs." 2005. *APBN (Asia Pacific Biotech News)* 9 (1-2): 39.

³⁰ "Compulsory licensing: Embracing the common good," *Pharmaceutical Executive*, August 2004, p. 24. More specifically, 29% agreed strongly, 32% agreed somewhat, 12% disagreed somewhat, and 8% disagreed strongly. In a related question 8% agreed strongly, 25% agreed somewhat, 26% disagreed somewhat and 14% disagreed strongly with the related statement that "when poor countries break drug patents for HIV/AIDS drugs, they hinder the development of new drugs."

³¹ A consumer-oriented discussion of bioequivalence requirements in the USA is provided by the Food and Drug Administration at <http://www.fda.gov/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/UnderstandingGenericDrugs/ucm167991.htm> (accessed 20 July 2010).

³² Roger Bate & Lorraine Mooney. 2006. "WHO's comprehensive HIV treatment failure: Will we learn the real lessons from 3 by 5?" *AEI (American Enterprise Institute) Working Paper #133*, p. 17. Note that it took Bristol-Meyers Squibb and Gilead Pharmaceuticals' developers 3 years to make the combination treatment Atripla bioequivalent to its component medications even though the firms had developed all three of the component medications themselves.

established.³³ While established generic firms like India's Cipla, Matrix, and Ranbaxy or South Africa's Aspen are capable of producing fully bioequivalent versions, that skill eludes some of the smaller producers that have received compulsory licenses elsewhere.³⁴ Both the US Food and Drug Administration and the EU European Medicines Agency distinguish between "generics" and "true generics," and require bioequivalence before listing a drug as a "true generic." Some other regulatory agencies are less stringent. Though the WHO acknowledged the need for bioequivalence, until 2004 its list of pre-approved treatments eligible for UN funding included any drug regarded as effective in treating HIV and being produced legally in any member state. In contrast, the Accelerated Access Initiative, UNITAID, the Clinton Foundation, and the US government's PEPFAR all insisted on proven bioequivalence before including a generic version of HIV medications they supplied to poor countries.

The strong public support for access to HIV medicines seems to suggest that major pharmaceutical companies are risking considerable public hostility to defend a portion of their income that their own conduct in setting tiered prices suggests they are willing to let go. However, the pharmaceutical firms are keenly aware that governments can use compulsory licenses for purposes other than ensuring their population's access to critical medicines. As the TRIPS Agreement limited the ability of developing countries to foster a generic drug industry at home through weak patent legislation, some realized that compulsory licensing would be another way to open up opportunities to domestic producers who either could not afford to secure licenses from patent holders or with whom patent holders might be reluctant to deal because of concerns about their ability to produce quality medicines. This potential for abuse of compulsory licensing was made most visible in Thailand, where both the military government that came into power in late 2006 and the civilian government that replaced it in early 2007 issued compulsory licenses not only for HIV medications but also for medications to treat cancer and heart disease. While cancer and heart disease are also serious conditions, frequently leading to death, the public health rationale for issuing compulsory licenses on the particular medicines involved was not particularly strong. There were other drugs available and the number of cancer patients in Thailand at the time was relatively small, much smaller than the population afflicted with HIV. AIDS and health activists present the pharmaceutical firms as interested only in profits, and certainly that is a major consideration. However, many of their presentations fail to note that the Thai compulsory licenses also appear to be elements of an industrial policy intended to foster growth of a domestic pharmaceutical industry. Advocates of using compulsory licenses to advance industrial policy can legitimately make the argument that greater global competition among drug makers will benefit consumers. Claiming that compulsory licenses are necessary to meeting a public health emergency or ensuring access to essential medicines should be reserved for those occasions when health is actually the primary concern.

<end>

³³ See "WHO withdraws" 2004 and Bate & Mooney (note 25). Some of the de-listed generics were not bioequivalent; others were removed because the testing for bioequivalence had been inadequate.

³⁴ Lybecker & Fowler (note 7), 232 identify the Government Pharmaceutical Organization in Thailand as one such firm.