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Trade, TRIPS, and pharmaceuticals

Richard D Smith, Carlos Correa, Cecilia Oh

The World Trade Organization’s Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) set global minimum standards for the protection of intellectual property, substantially increasing and expanding intellectual-property rights, and generated clear gains for the pharmaceutical industry and the developed world. The question of whether TRIPS generates gains for developing countries, in the form of increased exports, is addressed in this paper through consideration of the importance of pharmaceuticals in health-care trade, outlining the essential requirements, implications, and issues related to TRIPS, and TRIPS-plus, in which increased restrictions are imposed as part of bilateral free-trade agreements. TRIPS has not generated substantial gains for developing countries, but has further increased pharmaceutical trade in developed countries. The unequal trade between developed and developing countries (ie, exporting and importing high-value patented drugs, respectively) raises the issue of access to medicines, which is exacerbated by TRIPS-plus provisions, although many countries have not even enacted provision for TRIPS flexibilities. Therefore this paper focuses on options that are available to the health community for negotiation to their advantage under TRIPS, and within the presence of TRIPS-plus.

Introduction

The effect of stringent intellectual-property protection in the pharmaceutical market is contentious, focused in recent years on the World Trade Organization’s (WTO) Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS). In January, 1995, the TRIPS agreement established global minimum standards for the protection of intellectual property, including a minimum 20 years’ patent protection on pharmaceuticals. Compliance was postponed until 2005 for developing countries and 2016 for least developed countries. The agreement greatly expanded intellectual-property rights, including rules on the protection of test data for the effectiveness and safety of drugs. This change in intellectual-property rights generated clear gains for industry and the developed world, but the crucial question is whether it generated gains for developing countries in the form of increased exports.

This question is addressed in this paper by consideration of the importance of pharmaceuticals in health-care trade, and then the essential elements, implications and issues related to TRIPS, and the new emerging issue of TRIPS-plus (in which increased restrictions are imposed as part of bilateral free-trade agreements) are outlined, concentrating on options open to the health community in negotiating to their advantage under TRIPS, and within the presence of TRIPS-plus. The experience in Malaysia in dealing with these issues is discussed, providing an example from which lessons might be learnt and extrapolated to low-income and middle-income countries.

Global pharmaceutical market

Pharmaceuticals are the most important health-related products that are traded, accounting for 55% of all health-related trade (the share of the next most substantially traded health-related goods—small devices and equipment—is 19%). In 2006, the global pharmaceutical market was valued at US$650 billion, of which the generic market contributed less than 10% ($60 billion), growing at a compound yearly growth rate of 10% between 1999 and 2006, and forecast to grow to $900 billion by 2011, equivalent to a compound yearly growth of 7% over the next 5 years. This reduction is mainly the result of increased competition from generic products and the effects of cost-containment measures across major markets, although there are expectations of strong growth in the ten European markets that joined the European Union in 2004 and continued double-digit market growth in China, which will become the seventh largest sales market by 2010.

The global market is highly polarised, with North America, Europe, and Japan accounting for around 75% of sales. A clear divide exists within the global market between developed countries, producing and exporting high-value patented pharmaceuticals, and developing countries importing these products and involved in the production of low-value generic or alternative medicines. This difference leads to many developing countries having a trade deficit in modern medicines, which often results in an overall health-sector deficit. There is little evidence that this pattern has reversed through adoption of improved intellectual-property rights. For instance, Thailand over the past decade has increased dependency on pharmaceutical imports despite strengthened intellectual-property rights, market exclusivity, and differential pricing. The promise of increased foreign direct investment seems elusive and the comparative advantage of adoption of stronger intellectual-property rights tends to last only as long as the next developing country does not adopt them; once these rights are harmonised globally, no advantage accrues to one country compared with another.

The pharmaceutical market is also characterised by substantial concentration within a few very large
transnational corporations; the ten largest account for nearly 50% of the total market (table 1). This market consists of the major element of foreign investment in health. The top 20 transnational corporations, based in the USA, the UK, Germany, Switzerland, and France, each have an average of more than 100 foreign affiliates in more than 40 countries (including 19 developing countries), with average sales of over $20 billion. However, the sales market is similarly concentrated, with North America, Europe, Japan, and Latin America accounting for more than 85% of sales. Thus, although developed countries hosting these large transnational corporations have considerable gains in revenue (table 2), the overall consumption of medicines means that even in some of these countries (notably the USA) a trade deficit remains.

Industry consolidation, which generates this concentration, continues for several reasons. For instance, companies might acquire generic manufacturers to reduce generic competition (eg, acquisition of Hexel and Eon by Novartis in 2005), or national companies might merge to reduce threats of foreign acquisition (eg, Sankyo and Daiichi in 2005 before the introduction of a new Japanese law in 2006 making foreign investment easier). However, the main reasons remain the need to bolster flagging research and development through merger and acquisition, creation of economies of scale from pooled research and development resources, and positioning for new markets in biotechnologies.

For most developing countries, the domestic industry is small, usually focused on generic production and traditional medicines. These countries consequently have to pay high prices for imported medicines, and are affected by intellectual-property rights, especially TRIPS and TRIPS-plus standards. For most countries, developed and developing, the escalating cost of medicines—even those recognised as essential (panel)—means that aspects of the pharmaceutical industry (especially in the context discussed here), trade, TRIPS, and TRIPS-plus are thus a major global concern at the moment.

There are some exceptions—eg, Brazil, Thailand, and India that have substantial capacity to produce generic medicines. For India, a thriving competitive domestic pharmaceutical industry has kept generic prices at amongst the lowest in the world, helped by not granting patents on medicines until 2005, when it was required to do so by the WTO (table 2). Two-thirds of these drugs are now exported to the developed world, although potentially threatened by enhanced patent protection (likely to drive prices up unless voluntary or compulsory licences to continue production are granted), making the TRIPS and TRIPS-plus process essential. Noteworthy, Ranbaxy—India’s largest pharmaceutical company and ranked among the top ten generic companies worldwide—was sold to the Japanese company Daichi-Sankyo in June, 2008, raising concerns for generic manufacture and access to generic medicines, within India and several other countries in which Ranbaxy has operations.

### Patents, trade, and pharmaceuticals

Information is a public good, meaning that it is impossible to exclude anyone from consuming it once it is produced, providing no market incentive for its production. Intellectual-property rights—and patents more specifically—grant legal excludability to information to remove this disincentive. Patents have been the mainstay of policy to ensure investment in pharmaceutical research and development, acting as guarantor of monopoly rents. However, by their nature, these rents

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**Table 1: Top world pharmaceutical corporations, 2006**

<table>
<thead>
<tr>
<th>Country</th>
<th>Sales (US$ millions)</th>
<th>Market share</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pfizer</td>
<td>45 983</td>
<td>7.6%</td>
</tr>
<tr>
<td>GlaxoSmithKline</td>
<td>36 702</td>
<td>6.1%</td>
</tr>
<tr>
<td>Novartis</td>
<td>31 366</td>
<td>5.2%</td>
</tr>
<tr>
<td>Sanofi-Aventis</td>
<td>30 877</td>
<td>5.1%</td>
</tr>
<tr>
<td>Johnson &amp; Johnson</td>
<td>27 112</td>
<td>4.5%</td>
</tr>
<tr>
<td>AstraZeneca</td>
<td>26 566</td>
<td>4.4%</td>
</tr>
<tr>
<td>Merck</td>
<td>24 854</td>
<td>4.1%</td>
</tr>
<tr>
<td>Roche</td>
<td>23 300</td>
<td>3.9%</td>
</tr>
<tr>
<td>Abbott</td>
<td>17 552</td>
<td>2.9%</td>
</tr>
<tr>
<td>Amgen</td>
<td>16 054</td>
<td>2.7%</td>
</tr>
<tr>
<td>Top 10</td>
<td></td>
<td>46.4%</td>
</tr>
<tr>
<td>Wyeth</td>
<td>14 888</td>
<td>2.5%</td>
</tr>
<tr>
<td>Lilly</td>
<td>14 623</td>
<td>2.4%</td>
</tr>
<tr>
<td>Bayer</td>
<td>12 404</td>
<td>2.1%</td>
</tr>
<tr>
<td>Bristol-Myers Squibb</td>
<td>12 240</td>
<td>2.0%</td>
</tr>
<tr>
<td>Boehringer Ingelheim</td>
<td>11 157</td>
<td>1.9%</td>
</tr>
<tr>
<td>Takeda</td>
<td>9 962</td>
<td>1.7%</td>
</tr>
<tr>
<td>Teva</td>
<td>9 282</td>
<td>1.5%</td>
</tr>
<tr>
<td>Schering-Plough</td>
<td>8 641</td>
<td>1.4%</td>
</tr>
<tr>
<td>Daiichi Sankyo</td>
<td>5 617</td>
<td>0.9%</td>
</tr>
<tr>
<td>Novo Nordisk</td>
<td>5 589</td>
<td>0.9%</td>
</tr>
<tr>
<td>Top 20</td>
<td></td>
<td>63.7%</td>
</tr>
</tbody>
</table>

**Table 2: World trade in pharmaceuticals, 2004**

<table>
<thead>
<tr>
<th>Country</th>
<th>Exports (US$ millions)</th>
<th>Imports (US$ millions)</th>
<th>Balance (US$ millions)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Switzerland</td>
<td>22 778</td>
<td>12 268</td>
<td>10 510</td>
</tr>
<tr>
<td>France</td>
<td>23 251</td>
<td>15 143</td>
<td>8 108</td>
</tr>
<tr>
<td>Germany</td>
<td>23 074</td>
<td>29 030</td>
<td>6 056</td>
</tr>
<tr>
<td>UK</td>
<td>23 349</td>
<td>16 333</td>
<td>7 016</td>
</tr>
<tr>
<td>Sweden</td>
<td>7 715</td>
<td>2 841</td>
<td>4 874</td>
</tr>
<tr>
<td>Netherlands</td>
<td>12 347</td>
<td>11 318</td>
<td>1 030</td>
</tr>
<tr>
<td>Italy</td>
<td>11 480</td>
<td>12 644</td>
<td>-1 164</td>
</tr>
<tr>
<td>Australia</td>
<td>2 156</td>
<td>5 135</td>
<td>-2 979</td>
</tr>
<tr>
<td>Spain</td>
<td>5 133</td>
<td>9 131</td>
<td>-3 997</td>
</tr>
<tr>
<td>Japan</td>
<td>3 170</td>
<td>7 237</td>
<td>-4 067</td>
</tr>
<tr>
<td>Canada</td>
<td>3 430</td>
<td>7 624</td>
<td>-4 194</td>
</tr>
<tr>
<td>USA</td>
<td>22 659</td>
<td>36 097</td>
<td>-13 438</td>
</tr>
</tbody>
</table>

Data from IMS International.

Data from Global Trade Information Services (DTI), UK Customs and Excise.

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Panel: Definitions

• WHO defines essential medicines as “those drugs that satisfy the health care needs of the majority of the population; they should therefore be available at all times in adequate amounts and in appropriate dosage forms, at a price the community can afford”

• Evergreening is a method by which patent protection is maintained for longer periods than would normally be legally permissible. For instance, shortly before a patent expires, a company might file a new patent application that revises or extends the original such that this new patent is in effect when the original patent expires, thus in effect granting an extended period of patent protection

• A parallel import is a product imported from another country without the permission of the intellectual-property owner. This situation occurs because companies might set different prices for their products in different markets, which means that goods can be purchased in one country at a lower price than in another country

• In accordance with 2007 US Trade Representatives’ special 301 report, “the U.S. Government provides extensive technical assistance and training on the implementation of the TRIPS Agreement to a large number of U.S. trading partners... The United States will continue to work with WTO members and expects further progress in the near term to complete the TRIPS implementation process. However, in those instances in which additional progress is not achieved, the United States will consider other means of encouraging implementation, including the possibility of recourse to dispute settlement consultations”

• The Australian patent office has been active, particularly, in providing technical cooperation to the Pacific islands

• One of the objectives of the European Community and the Association of Southeast Asian Nations (ASEAN) Intellectual Property Rights Cooperation Programme is to “achieve further economic co-operation by upgrading the ASEAN intellectual property rights systems, in line with the highest international standards and practices”

• Examples of such bilateral agreements include the USA-China intellectual-property-rights agreement, the USA-Korea intellectual-property-rights and insurance understandings, the USA-Sri Lanka intellectual-property-rights agreement of March 17, 2004, and the USA-Philippines intellectual-property-rights understanding of March 20, 2004. For instance, the USA-Sri Lanka bilateral agreement on intellectual-property rights restricted the grounds for the granting of compulsory licenses. These can only be granted to rectify adjudicated violations of competition laws, to address a declared national emergency or when necessary to enable compliance with air pollutant standards

• International reference pricing refers to the use by governments of other countries’ prices when negotiating with pharmaceutical companies the amount they will pay for pharmaceutical prices. However, reference pricing has been argued to prevent access to essential pharmaceuticals in underdeveloped countries and decrease pharmaceutical innovation in developed countries

The implications for public health of the TRIPS agreement brought about a giant shift in the global market for medicines. With the temporary exception of the poorest countries, it obligates WTO members to recognise pharmaceutical product patents under the threat of trade sanctions.

The plan of action contains several specific actions for relevant stakeholders classified according to eight core elements designed to promote innovation, build capacity, improve access, and mobilise resources: assess and prioritise research and development needs; promote research and development; build and improve innovative capacity; improve transfer of technology between developed and developing (and between developing) countries; encourage and support the application and management of intellectual property in a manner that promotes access to medicines; improve delivery and access to all medicines; secure and promote sustainable financing mechanisms for research and development; and establish mechanisms for monitoring and evaluation for implementation of the plan of action.
The plan is relevant for TRIPS according to the fifth action, which seeks to support the application and management of intellectual property in a manner that maximises health-related innovation, especially to meet the research and development needs of developing countries, protects public health, and promotes access to medicines for all (WHA 61:21, annex). It seeks to achieve this mainly through use of TRIPS flexibilities. The plan recognises that TRIPs flexibilities provide for measures to protect public health, and that new mechanisms to generate research and development focussed on developing country needs, and to promote technology transfer, might be consistent with this provision within TRIPS. One practical recommendation as a result is the call for improved education and training in the application and management of TRIPS from a public-health perspective so that flexibilities might be understood clearly and used.

Although these flexibilities might allow reconciliation of the protection of intellectual-property-rights with public-health needs, the pharmaceutical industry, supported by the US Government and European Commission, continued to seek increased protection, resorting to unilateral or bilateral routes to obtain TRIPS-plus conditions, when protection of intellectual-property-rights standards beyond TRIPS are incorporated in exchange for trade concessions, particularly the promise of free access to markets for agricultural goods. Free-trade agreements, signed by the USA and European Union, especially with an increasing number of developing countries, have constituted one of the main routes for TRIPS-plus standards, which might typically be found in seven main areas.

First, TRIPS obliges members to protect product and process patents in all specialties of technology. Although many developing countries granted process patents for pharmaceuticals in the pre-TRIPS era, such patents did not ban the use of alternative processes to legally produce the same drug. However, under TRIPS there is an obligation to grant product patents, giving the patent holder the possibility of monopolising the drug independently of the process used to obtain the drug. Yet some free-trade agreements go further. For instance, the US free-trade agreements with Australia, Morocco, Bahrain, and Oman require the protection of second indications of a known product (eg, nimodipine, a known cardiovascular drug that has an application for the treatment of cerebral disorders). Thus, off-patent products can come under patent protection for an important therapeutic use.

Second, many patent laws, including those in developed countries, provide procedures to oppose a patent application or to review a granted patent. Constraints to such opposition (such as those included in the US free-trade agreements with Singapore, Morocco, Bahrain, and Oman) remove an important mechanism for developing countries to challenge patents. For example, the opposition filed in India to prevent the grant of a patent filed by Novartis on a polymorphic form of imatinib mesilate (an anticancer drug) might avoid concerns over non-accessibility to the drug if priced on the basis of patent monopoly.

Third, under TRIPS, patents must last for at least 20 years from the filing date, yet US free-trade agreements often require an extension of this patent term, ostensibly to compensate for delays in assessment of a patent or approve a medicine for marketing. Drugs can remain unaffordable to a large part of the population under these extensions.

Fourth, TRIPS-plus standards require a period of exclusivity for test data relating to the effectiveness and safety of drugs. When adopted, this period of exclusivity prevents generic companies from relying on data developed by the originator company to obtain approval for cheaper versions of a medicine, even when patent protection does not exist, and can substantially increase the price of, and reduce access to, medicines.

Fifth, although TRIPS lets countries identify the reasons for granting compulsory licences (eg, to address public-health needs), limitations have been imposed in some cases about the reasons that might be invoked. For instance, the USA–Jordan free-trade agreement only allows compulsory licences to remedy anticompetitive practices in cases of national emergency or other extreme urgency and for non-commercial public use. By contrast, the Italian Competition Authority granted a compulsory licence to produce an active ingredient (imipenem and cilastatin) needed for the production of an antibiotic (carbapenem) used in the treatment of infectious diseases. In another competition case, Merck was required to grant free licences to allow the manufacture and sale in Italy of the active ingredient finasteride and related generic drugs.

Sixth, article 6 of TRIPS allows parallel import of products. This important flexibility is also restricted, for instance, in the US free-trade agreements signed with Morocco and Singapore.

Last, pharmaceutical products can be subject to additional protection in countries where, because of the demands of the USA, the drug regulatory authority is
prevented from approving a medicine for marketing when patents are in force. With the wide proliferation of evergreening patents, this linkage can become an important barrier to generic competition. Even in the USA, the drug approval-patent protection linkage has been misused considerably.23

Implementation of TRIPS-plus
TRIPS provides high standards of protection that ensure recognition of pharmaceutical patents for products and processes, and measures to enforce conferred intellectual-property rights. There is no first-sight justification to further increase such protection (often in excess of that applied in developed countries) in countries with weak scientific and technological infrastructures or where a large part of the population is poor.20 In this respect, a bipartisan agreement was reached in June, 2007, between the Republican and Democratic parties at the US Congress, when suggestions were made to revise TRIPS-plus standards contained in free-trade agreements signed by the government. Although restricted to agreements with Peru and Panama, such revision mitigated the TRIPS-plus requirement in public-health-sensitive areas, notably data exclusivity, linkage, and patent-term extensions, which might set a wider precedence. Nevertheless, the objectives of TRIPS-plus can be implemented in other ways.

First, countries can adopt TRIPS-plus standards without explicit obligations to do so in the belief that they might attract foreign technology and investment, or political or other support from developed countries.21 Adoption of such standards is often encouraged by active lobbying from industry, and through technical assistance provided by the World Intellectual Property Organization and patent offices of some developed countries, such as the USA, Australia, and the European Patent Office (panel). Such advice often does not contain all legislative options that countries have or directly promote protection that is suitable to the country’s condition. For instance, the European Patent Office greatly determines the policies of the Chinese and Vietnamese patent offices, notably with regard to granting patents on second indications.22

Second, there might be the threat of trade sanctions under unilateral mechanisms, such as the special 301 section of the US Trade Act.23 For instance, China is on the 301 priority watch list because it allows for a “narrow scope of patentable subject matter” that “makes patents for...methods of treatment or diagnosis virtually unobtainable”.23 China is not obliged under TRIPS, however, to protect such information. Argentina is on the same list on the basis of the argument that it “still does not provide adequate protection against unfair commercial use for data generated to obtain marketing approval” and there is no “effective coordination system between its health and patent authorities to prevent the issuance of marketing approvals for patent-infringing pharmaceutical products”.24 However, Argentina protects test data under the discipline of unfair competition, as required by TRIPS, and is not obliged to establish the effective coordination system, which is generally known as the linkage between drug registration and patent protection. Many countries have ceded to pressures exerted through the threat of special section 301 application, thereby accepting to introduce TRIPS-plus standards. For instance, Australia introduced data exclusivity as a result of a complaint by the USA.24

Third, a feature of the WTO accession process is that an applicant for membership is expected to satisfy all existing members, so that one member can effectively veto an application. Countries negotiating their accession have been compelled to accept a large list of TRIPS-plus conditions either directly (as part of commitments made) or indirectly as a result of demands posed during the negotiation process. Some of those conditions affect public-health policies, notably the commitments to provide data exclusivity. For instance, Jordan and China agreed to protect test data under exclusive rights for a period of 6 years (beyond what is required in the USA), whereas Saudi Arabia and Cambodia committed to provide 5 years exclusive protection and to establish a linkage between drug registration and patent protection.25

Last, in some cases, the adoption of high protection of intellectual-property rights has been the result of signing bilateral agreements focused on these rights. The USA promoted such agreements in the 1990s, many with former socialist countries and with some developing countries (panel). Unlike free-trade agreements, these bilateral agreements did not offer trade concessions in exchange for the high protection of intellectual-property rights. Some countries were willing to accept them for political reasons or with the hope of creating a more favourable climate for foreign direct investment (there is no conclusive evidence, however, suggesting that enhanced protection of intellectual-property rights leads to an increase in foreign direct investment).24

Intellectual property became, with the adoption of TRIPS, essential in trade agreements. High protection for pharmaceutical patents is increasingly traded against potential access to developed-country markets. The impetus behind changes in intellectual-property rights is hence not health improvement, but the need to pay for trade concessions. The immediate effect of such deals is to prevent access to medicines. This outcome is questionable not just from a public-health perspective and on ethical grounds, but also on economic grounds, as there seems no clear evidence that the costs incurred will be compensated by the often volatile trade advantages obtained in exchange.

Trade and the pharmaceutical market in Malaysia
Malaysia provides a good example of how patent protection can create inequalities in pharmaceutical trade between developed and developing countries; with developed countries exporting high-value patented drugs,
and developing countries prevented from producing them, compelled to import them, with consequent issues for access to affordable medicines.

Although Malaysia’s health system has been a model for other developing countries (eg, ranked 31 of 191 countries in the 2000 World Health Report), increasing health-care expenditure (from 3·6% of gross domestic product in 1993 to 6·33% in 2003) is an increasing challenge, especially with respect to medicines, which is likely to become more acute in the future. Although at the moment a young population, the proportion of those older than 60 years is expected to increase from 5% to 11% by 2020. This rise, along with increasing incidence of cardiovascular diseases, cancer, and diabetes, is likely to increase demand for medicines.

Medicine prices rose by 28% on average each year between 1996 and 2005. WHO-Health Action International survey showed essential medicines to be “very expensive and not universally available”, and priced much higher (2·4-fold to 16 times higher) than the International reference price (panel). The absence of government regulation or control, which leaves industry to set prices, is blamed for much of this price rise.

Some 65–80% of Malaysia’s pharmaceutical needs, especially new generation antibiotic, cholesterol-lowering, anti-diabetic, cardiovascular, and anticancer drugs, are imported, mainly from Germany (8·3%), France (8·0%), and the UK (7·7%). The heavy reliance on imported medicines is similar to most developing countries.

Local industry is small, with sales in 2006 of about $272 million (compared with chemicals [$39 billion] and manufacturing [$139 billion]). 80% accounts for low-value generics, over-the-counter treatments, vitamins or food supplements, and medical devices. The export revenue of the industry was about $137 million in 2006, largely caused by vitamin manufacture.

Innovative domestic pharmaceutical research and development is restricted. Only 87 of 246 pharmaceutical companies registered with the Drug Control Authority manufacture modern medicines; most produce traditional and herbal medicines. The Malaysian Organisation of Pharmaceutical Industry claims capacity to manufacture almost 80% of various categories from the Malaysian essential drugs list, but these are restricted to off-patent generic versions of medicines. Although some off-patent medicines within the high-selling therapeutic classes (antibiotics, and antiviral, antulcer, and cholesterol-lowering drugs) are produced, most manufacturers are small-sized or medium-sized enterprises, producing low-value generic versions of antibiotics and pain-killers. The actual production of patented medicines in Malaysia is largely through contract manufacture by a few local companies.

Some product modification does take place, such as innovations in drug-delivery mechanisms to meet local needs, but the absence of technological capacity, high investment costs, and heavy reliance on imported active ingredients restrict research and development. Additionally, patent protection is also a factor that restricts innovations.

Malaysia, like most developing countries, is thus a technology importer: 94% of patent applications and 97% of patents granted in Malaysia are from outside the country. It is TRIPS-compliant; its 1983 patents act has provided protection for both processes and products since 1988. The act was amended in 2000 to extend patent terms from 15 to 20 years, as required by TRIPS. Although foreign transnational corporations tend to consider the Malaysian patent system to be sufficiently robust, they have not promoted the transfer of technology (in terms of location of research and development, and manufacturing facilities) to Malaysia. Although the patents act incorporates several TRIPS flexibilities, including government use, compulsory licensing, and parallel importation, there is no record of flexibilities having been used in pharmaceutical specialty, other than compulsory licence.

In 2003, a compulsory licence was granted to permit the import of generic antiretroviral drugs from India. The decision was compelled mainly by pressure from health activists and civil-society organisations to put into effect a policy of free antiretroviral drugs, and the failure of negotiations with the patent-holding drug companies to produce the desired price reductions. The adoption of the Doha Declaration might have reinforced the government’s decision; its confirmation of the right of countries to use compulsory licensing alleviated concerns that an emergency situation was a prerequisite to a compulsory licence being granted. The importation of generic antiretroviral drugs in Malaysia reduced the cost of treatment, with both generic and originator products. For example, in 2001 Combivir (lamivudine plus zidovudine) and efavirenz cost $363 per month; in 2004, with the introduction of generic version of Combivir, the monthly cost of generic Combivir and patented efavirenz was $115.

The 2-year compulsory licence has since expired and was not renewed; ostensibly because the government was keen to promote the local production of generic antiretroviral drugs. The debate about the effect of patents on the accessibility and affordability of medicines continues, however, to be at the forefront as a result of Malaysia’s negotiations for a free-trade agreement with the USA. As stated already, US free-trade agreements have been a means by which tighter patent provisions have been introduced in developing countries. Unsurprisingly, negotiations caused consternation in the local industry on the potential tightening of the patent laws, such that one of the large generic manufacturers announced plans to establish a manufacturing facility in India ostensibly to “offset any disadvantage that we might come up against from the upcoming US Free Trade Agreement (USFTA).
Malaysian pharmaceutical companies may no longer be competitive in international markets with the proposed data exclusivity constraint in the USFTA. The negotiations, however, were put on hold, pending the US Presidential elections and changes in the Malaysian government.

Intellectual-property rights will have implications for the pharmaceutical industry in Malaysia. Yet the chapter on the pharmaceutical industry in the Third Industrial Masterplan 2006–20, although identifying the importance of the production of newly off-patent drugs, cancer treatments, and drug-delivery technologies for the growth of the local pharmaceutical industry, makes no mention of intellectual-property rights, which are an essential consideration for the future of the industry.

Conclusion
Intellectual property is a strategic asset for industry and public health. The growth of new global public–private partnerships, such as the malaria vaccine initiative, have shown that the management of an intellectual-property system is essential for development of, and subsequent access to, medicines. Work, including that done by WHO Commission on Intellectual Property and Innovation, also shows that the creative management of intellectual property is required to help product development and dissemination. However, the intellectual-property system is managed poorly, and can perpetuate high prices and reduce access.

Importantly, developing countries are not making full use of flexibilities built in to TRIPS to overcome patent barriers, such as compulsory licences and parallel imports, as in Malaysia. The main reason might be due to the absence of domestic resources and capacity, resulting in dependency on donor financing and in turn constraining the ability to exploit international trade provisions. Similarly, inequalities in power and influence between countries leave many vulnerable to pressure to protect broad trade and economic interests. However, widespread misunderstandings also exist, such as the misconception that countries have to declare all intellectual property elements of TRIPS-plus, are recent, increasing evidence suggests that they subvert TRIPS flexibilities, reducing access to medicines yet further and thus have a detrimental effect on public health. However, few studies have investigated why developing countries enter into such agreements and the extent to which any perceived benefits from agreeing to TRIPS-plus conditions outweigh any public-health costs. Therefore global surveillance and management of cases when TRIPS-plus additional conditionality is contained in any free-trade agreements are urgently needed.

Several other measures can be undertaken or advocated for by the public-health community in this respect. For example, developing countries with substantial markets, such as India, Brazil, and Thailand, could establish precedence by adopting TRIPS flexibilities into national patent laws; south–south partnerships could mitigate resource and capacity constraints; and pharmaceutical companies might recognise that creation and development of these markets is vital to long-term sustainability and growth. The key to these and other measures is the recognition that protection of public health under TRIPS must take precedence over measures subsequently adopted under other trade agreements, as already stressed in many World Health Assembly resolutions since 1996 (eg, WHA49.14, WHA52.19, WHA54.11, WHA55.14, WHA56.27, WHA59.24, WHA60.30, and WHA61.21). This recognition will require strong advocacy from all in the public-health community in both developing and developed countries.

Conflict of interest statement
We declare that we have no conflict of interest.

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