Health and Intellectual Property Rights: Thoughts on Ensuring Access to Medicines in 2005 and beyond

I. Introduction

From 1977 to 2002, the number of people with regular access to most of the medicines they need has increased from 2.1 billion to nearly 4 billion [1]. While a significant achievement, the other side of the same coin is however that some 2 billion people do not have such access. In order to expand access to the latter group, it may be useful to draw on the experience of the 'positive side' of this coin. So how was it possible to almost double access to most medicines?

While many efforts and interventions, such as improved drug supply and management in different countries and settings, have contributed to this success, two elements seem to underpin them all: the introduction of the concept of -- and the subsequent focus on -- *essential* drugs, and the provision of *generic* drugs. In essence, the former helped to significantly reduce duplications and the wasting of resources on drugs with limited therapeutic value -- thereby simplifying supply management -- while the latter reduced costs due to the lower prices of generic medicines and the introduction of competition, which meant that limited resources were spent in a more cost-effective way.

Into this context, the Agreement on Trade-Related Aspects of Intellectual Property Rights (or TRIPS Agreement) was introduced. The TRIPS Agreement has to a large extent harmonised the standards for intellectual property protection, including patents. For developing countries, the TRIPS standards are usually higher than their previous standards. Moreover, TRIPS mandates effective enforcement of these standards. This will delay the marketing of generic versions of new drugs and, thus, the competition they entail. As a result, access to medicines is bound to become further compromised.

For most developing countries, the TRIPS Agreement has entered into force in 2000. Least-developed countries may defer the implementation of patents and data protection for pharmaceuticals until 2016 [2]. Meanwhile, for a limited number of developing countries, namely those that did not grant patents for pharmaceutical products on 1st January 1995, TRIPS will enter into force on 1st January 2005. The most important country in the latter group is India. The entry into force of TRIPS in India is significant not only because of India's huge population, but also because Indian companies are major suppliers of generic medicines and of the active pharmaceutical ingredients (APIs) necessary for their production to other developing and developed countries. Thus, India's application of the TRIPS standards is expected to have ramifications far beyond India's borders.

Implications of 2005

When thinking about the implications of '2005' it seems useful to distinguish three categories of drugs:

- old drugs, i.e. those drugs already off patent when TRIPS entered into force,
- new drugs, which had some 'patent life' left when TRIPS entered into force; the most prominent -- though not the only -- example in this group are antiretroviral drugs for HIV/AIDS, and
- future drugs, i.e. those drugs that are yet to be discovered and/or developed.

'Old' drugs are not affected by TRIPS standards, hence for medicines in this category, there is no issue. On the other hand, there are many questions and uncertainties regarding the production and supply of new drugs from 2005 onwards -- and the biggest questions probably relate to research and development of, and subsequent access to, future drugs.

The distinction between new and future drugs is useful, not only because it reflects that the situation will progressively change, but also because possible strategies to try to protect access to medicines in developing countries may differ[1].

Moreover, in each of these cases, two perspectives need to be considered: whether or not the medicine is under patent in the county where it will be used, and what the source of supply will be. The latter is an obvious concern for countries that depend on importation of medicines, while in the case of local production, these two considerations overlap (at least insofar as the drug is really produced locally: see below).

II. The problem

The problem is easiest to describe -- though probably not easiest to address -- for future drugs. Future drugs will be developed in a world were patents are available in virtually every country[2]. Since it is safe to predict that companies will patent their future drugs at the very least in all countries with meaningful production capacity, generic equivalents of future drugs will only become available once all relevant patents have expired -- that is, many years after the launch of the originator product. Meanwhile the lack of competition is bound to result in prices that are unaffordable for all but a wealthy minority in developing countries.

The challenges related to new drugs meanwhile are more difficult to portray -- and more immediate. Each new drug may be protected by multiple patents, some of which may completely block competitors, while others can probably be challenged or circumvented (depending on a competitors' willingness and capability to do so). The remaining patent life will vary for different patents on the same molecule, as well as among different molecules, and (at least to some extent) among different countries. For a variety of

[1] Note however that these are not absolute categories, since once a 'future' drug has been developed, it becomes a 'new' drug.
[2] With the possible exception -- at least initially -- of LDCs and the shrinking list of non-WTO member countries.

reasons, some patents may not have been filed, or not have been granted, in certain countries[3]. As a result, the 'patent landscape' for a given drug may be complex and will be country-specific. Furthermore, while in principle patented inventions are disclosed, in practice patents can be difficult to trace, at least in a number of countries in the region. Moreover it may be cumbersome to obtain the necessary details, such as the claims. Finally, once obtained, the interpretation of patent claims requires specific expertise, which in many developing countries is relatively scarce.

Into this scenario, an additional uncertainty is introduced by the TRIPS Agreement's transitional provisions (the so-called 'mailbox provisions') for India.

India's mailbox

Developing countries that did not grant patent protection for pharmaceutical products when TRIPS entered into force have been given until 1st January 2005 to introduce such protection. However, since 1st January 1995, they had to have a 'mailbox' system in place where applications for pharmaceutical product patents could be filed. From January 2005 onwards, these applications will have to be assessed; if found to be patentable vis-à-vis their filing or priority date, a patent will have to be granted for the remainder of the patent term. Moreover, in case a pharmaceutical product that is the subject of a 'mailbox' application obtains marketing approval prior to the decision on the grant of a patent, exclusive marketing rights of up to five years may have to be granted.

As mentioned, the most important country to which these mailbox provisions apply is India; reportedly, more than 5,000 applications are pending in India's mailbox [3]. In view of the fact that the average number of new chemical entities developed during that period is only 40-50 per year [4], the mailbox potentially contains numerous trivial patents, such as formulation patents.

Unfortunately it is not known which applications are pending in the mailbox, nor how Indian authorities will deal with them. It is to be expected that some patents will be granted. Other applications might be rejected. But which ones would be refused? How long will examination and granting take? And what will happen if a 'mailbox-patent' is granted while generic versions are already on the market? Will generic production stop, or will Indian companies challenge or oppose such patents? Will they request compulsory licenses? Will generic companies have sufficient incentives to act, or will they rather abandon those products? And if requests for compulsory licenses are made, will the Government of India grant them? If so, what will be the criteria? And will those compulsory licenses allow for export? For the moment, the answers to these interlinked questions are not known.

[3] With regard to developing countries, it is more likely that they have not been filed, since developing countries do not have a reputation for rejecting patent applications. However, due to -- among others -- a (perceived) lack of enforcement, in the past patent holders did not always bother to file in the first place.

Indian authorities have, thus far, been silent on the topic, presumably because they, too, feel unable to provide reliable forecasts. After all, different parties and departments play a role here: the patent office will review the applications and decide which patents to grant, individual commercial companies will decide whether or not to oppose or appeal a patent, or to request a compulsory license – and eventually the courts may come in. And whereas it would in principle be possible for the Government of India to develop an overriding policy on this issue, such a policy appears not to be in place as yet. This furthermore implies that ultimately these questions will be answered on a case-by-case basis. Because of these uncertainties, it is difficult to predict what will happen.

So how can access to essential and needed medicines in developing countries be safeguarded? What measures should countries take?

III. New drugs

The most immediate question that developing countries in Asia and beyond will have to face is: how can the continuity of supply of generic versions of new medicines be assured?

Identifying 'gaps'

The fact that the 'patent landscape' is molecule- and country-specific implies that there are bound to be 'gaps'. Thus it is possible, and maybe even likely, that certain drugs are not or no longer under patent in certain countries. For example, there is some reason to believe that in the past, the basic patents were not always filed in all developing countries, and while some secondary or trivial patents may have been filed (and granted) more widely, generic versions do not necessarily infringe those patents. Alternatively, it may be possible to circumvent secondary patents; probably the most well-known example of the latter is the local production, in Thailand, of the antiretroviral drug didanosine in powder form, which fell outside the scope of a patent on didanosine tablets [5].

In the context of ensuring access it is especially relevant to look at 'gaps' in the patent thicket in the countries that are major producers of generics, notably India and China. Taking the example of anti-retroviral drugs, the basic patents on most WHO recommended drugs for first line treatment have priority dates well before 1995 [6]; hence they should not figure in India's mailbox – or if they do, they should not be granted due to lack of novelty[4]. Similarly, trivial or secondary patents pending in India's mailbox, if any, may not be granted, depending on the standards of patentability that will be applied. And as mentioned, even if granted, trivial patents may not be infringed by generics. Alternatively however, supplies may have to be sourced from countries where no patent is in force for the product concerned – which will require some investigation.

[4] However, depending on the standards applied, fixed-dose combinations of anti-retroviral drugs might be patentable.

But while a strategy of carefully manoeuvring through the mazes in the patent thicket may offer some possibilities for continued supply of generic versions of some drugs, and hence for continued access to some drugs in some places, it should be recognized that this is not a structural solution. Moreover, even though new drugs will keep coming off patent over time, ultimately this is a short-term strategy due to the progressive implementation of TRIPS as well as the gradual replacement of old and new drugs by better, future drugs. But where, when and while applicable, these strategies may provide some relief.

Standards and criteria

The complex patent landscape, which significantly limits the possibilities for generic introduction and competition, would be considerably simplified if countries refrained from granting patents for 'new uses' or marginal improvements of known drugs, such as polymorphs, dosage forms and formulations. Applying strict criteria for novelty and inventiveness could substantially reduce the scope for such secondary and trivial patents [7], and thereby contain the sheer volume and complexity of the patent thicket surrounding individual pharmaceuticals.

Unfortunately at the moment few Asian countries appear to be inclined to apply such strict criteria, though there are some signs that China might be emerging as an exception [8-11]. From the perspective of ensuring access to medicines and the availability of generics it would be positive if other countries, especially India, were to follow this example. But predictions and expectations regarding India's criteria for patentability differ markedly [3, 12].

Safeguards

Failing the above, developing countries would have to become more adept at making use of the 'TRIPS safeguards' such as compulsory licensing and parallel importation, notwithstanding political pressure to refrain from doing so [5, 13], since this may be the option of last resort. Having workable legal provisions for using these safeguards may therefore be crucial for ensuring access to medicines in the (near) future. Unfortunately many countries in Asia have, in their domestic legislation, not incorporated to the full the safeguards and flexibilities that exist under TRIPS. Meanwhile, implementation has been even more limited -- though this may be changing slowly[5].

In this context it is regrettable and worrisome that the agreed solution to the so-called 'paragraph 6 problem'[6] appears unduly cumbersome and complex [14, 15], to the extent that more than one year after its adoption, it remains yet to be used.

[5] Malaysia has invoked a "Government Use" license for certain patented antiretroviral drugs in October 2003; more recently, Indonesia has done the same.
[6] This refers to the problem (pointed out in paragraph 6 of the Doha Declaration on the TRIPS Agreement and Public Health) how countries with no or insufficient production capacity can make effective use of a CL. A solution to this problem was agreed by the WTO General Council on 30 August 2003.

Bilateral trade agreements

Several recent bilateral or regional trade and/or investment agreements between the US and a number of different developing countries impose TRIPS-plus conditions [16, 17], for instance limitations on the grounds for issuing a compulsory license[7] and provisions for data exclusivity and patent term extensions. There have also been demands for making the registration of generic medicines subject to the absence or expiry of relevant patents. These various conditions and requirements will limit the use of TRIPS safeguard mechanisms such as compulsory licensing, expand the duration of the patent monopoly or introduce new exclusive rights; as such they will complicate and delay the entry of generics on the market. Thus, if they are serious about safeguarding their people's access to medicines and/or the survival of their generic pharmaceutical industry, developing countries should refrain from entering into agreements imposing such onerous requirements.

Negotiations

Other strategies that can be pursued include of course price negotiations. Moreover, companies can seek voluntary licenses at reasonable royalty rates. However, if recent experiences with antiretroviral drugs in Brazil and South Africa are any indication, these strategies are bound to be most successful when they are backed up by a realistic 'threat' to use TRIPS safeguards or competition laws.

Short term actions

In line with the above, and while recognizing that there is a lot of uncertainty and lack of information as to what exactly will happen and which drugs will be affected, there do seem to be several lines of action that developing countries can take in order to mitigate the anticipated problems of lack of access to generic medicines. Apart from the ad-hoc strategy of identifying and making use of gaps in the patent thicket, these include[8]:

- Apply strict criteria for patentability; 'new use' patents, formulation patents etc. should not be allowed. Strict criteria will furthermore help to prevent the patent thicket from expanding unnecessarily.

- Allow for opposition both pre- and post grant, in order to provide ample opportunity for local and generic companies, as well as other interested parties, to challenge and prevent the issuing of trivial and 'frivolous' patents[9].

[7] For example, in the US-Jordan BTA, concluded in October 2000, the only allowable grounds for a compulsory license are: i) to remedy anti-competitive behavior, ii) for public non-commercial use, iii) in case of emergency or iv) in case of insufficient supply. The last ground does not figure in the more recent US-Singapore BTA.
[8] NB: this is not an exhaustive list.
[9] Pre-grant opposition is important, since it c prevents the issuing of trivial patents without litigation, which is often time consuming and expensive and may be beyond the means of local companies and organizations.

- Make patent information easily accessible, including via an on-line, searchable database. In order to not unduly increase the workload of the patent office, applicants could be asked to provide their application in electronic format. The possibility to set up easily accessible, regional patent databases could also be explored.

- Generic industry associations could monitor the publication and issuing of pharmaceutical patents and pass all relevant information on to their members[10]. They could also perhaps oppose 'unjustified' patents before they are granted, and thereby help to screen out 'bad' patents.

- Set up an alert system that provides information about patent revocations in developed countries. This system, which ideally should be publicly accessible, would help stakeholders to decide whether to challenge a patent. It could also be used as prima facie evidence in patent challenges, while patent offices could gauge their own assessments against these 'applied' foreign standards.

- Ensure that domestic laws provide for TRIPS-safeguards such as parallel import[11] and especially compulsory licensing and Government Use. Countries should also consider adapting their legislation to allow implementation of the '30 August Decision' (see above). These safeguard provisions should be workable and should not create undue delays. Finally, it is important to ensure that non-supply or insufficient supply is retained as a ground for issuing a compulsory license, among other grounds.

- Gain experience in using those safeguard provisions that already exist in national law. The first time is bound to be relatively slow and cumbersome, so countries should not wait for an emergency situation to use these mechanisms. Testing the provisions will also help to find out whether they are workable.

- Avoid TRIPS-plus measures (such as data exclusivity, linkages between patent and registration status, but also making patent infringement a criminal offense), and avoid signing treaties that impose such measures.

While these strategies could (and probably should) be applied by all developing countries, their implementation in India and China is especially crucial since, as major generic producers, the policies of these two countries will have ramifications for the availability of generics throughout the developing world.

Other strategies that countries may consider include:

- Use pooled procurement to create bargaining power.

[10] This idea originates from a discussion with Peter Drahos.
[11] Parallel importation can be undermined relatively easily by originator companies by charging one 'worldwide' price. It can also be undermined by restrictions in the contract of licensees.

- Consider the use of price control mechanisms -- though price controls may lead to artificial shortages[12], which in turn however should be able to trigger the issuing of a compulsory license.

- Consider expanding the coverage of (social) health insurance schemes that include (essential) medicines[13].

- It may be possible to use competition policy and anti-trust laws to facilitate access to medicines: governments should consider this and develop appropriate policies and legislation [18]. In this context it is worthwhile to recall that TRIPS does not impose any limitation on export when a compulsory license is issued to remedy anticompetitive behaviour.

IV. Future drugs

The distinguishing feature between new and future drugs is that the latter have yet to be invented. Thus, whereas the thinking about new drugs can solely focus on access, the discussion on future drugs will have to touch on research and development (R&D) as well.

While the negative implications of the exclusive rights conferred by patents on access to (generic) medicines in developing countries are widely known, it is becoming increasingly clear that the current business model also has its limitations with regard to innovation. Notably, it provides insufficient incentives for R&D for drugs for diseases that are commonly encountered only in developing countries. In fact, even R&D for diseases prevalent in rich countries is becoming distorted, focusing increasingly on me-too products and chronic diseases [19].

Transforming the business model?

It is important to realize that these skewed R&D priorities are a logical result of both the peculiarities of the pharmaceutical market and the industry's economic success. The latter has created high expectations among investors and shareholders, and for individual companies having to live up to those expectations in the face of disappointing R&D output, substantial price increases -- as well as efforts to expand patent protection -- may appear virtually inevitable [20].

[12] The pharmaceutical industry loathes price controls, and may react by refusing to supply, as has for example happened in Pakistan [30]. There also have been suspicions that sudden, unprecedented shortages of certain (generic) drugs in the UK were artificially created in order to force an increase in price [31, 32]. Furthermore, some companies have apparently threatened to delay launching new treatments on the European market because of what they view as Europe's excessive price controls [33].

[13] Note however that the introduction of such schemes in developing countries is bound to be difficult and time-consuming [34]. Moreover, insurance essentially is a *financing mechanism*, and while it could lead to more equitable access within countries, it does not address the affordability of medicines to the health system as a whole.

Yet as a result of the continuously rising prices, fewer and fewer people can afford the newest medicines, even in developed countries[14]. This trend of denying medicines to growing numbers of people worldwide cannot continue forever, since ultimately, without consumers/clients, the industry cannot survive either. It furthermore seems unlikely that the industry -- with all its financial clout -- will disappear. Thus, it would appear that the only change that *can*, and eventually may have to, occur is a change in the industry's modus operandi, or a take-over of some of its functions by other parties.

The prerequisites for an overhaul of the business model should at least include a greater awareness that the current situation is unbalanced and (ethically) untenable, and alternative models/mechanisms. In fact, concerned academics and activists have already floated ideas for alternative incentive systems, such as a proposal for an 'R&D treaty' [21]. Most of those alternative proposals[15] seek to provide incentives for R&D while dissociating R&D choices from anticipated sales of the resulting medicines. At the same time, they endeavor to create a competitive market for the latter.

Yet for any of these proposals to be actually implemented, the collaboration of governments of industrialized countries appears to be a prerequisite. Thus, it is bound to take some time before any of these models is tried or implemented on a sufficiently large scale.

V. The transition

With probably more luck than wisdom, developing countries may be able to muddle through the immediate future (see III). In the distant future, things might change -- that is, things may *have* to change, change may be unavoidable. The big question is: how will we get from one to the other, and at what price?

Steering R&D?

Hopes have been voiced that companies from developing countries may pay more attention to diseases specific to or relatively prevalent in the developing world. Yet this reasoning ignores the fact that these companies have to operate in the same market, with the same market failures, and that they are increasingly subject to the same incentive system, as their developed world counterparts. In fact, the larger Indian companies -- the very ones that increasingly can and do invest in R&D -- are known to target the global rather than the national market [3]. Thus, while it is possible that some developing

[14] Among industrialized countries this is most obvious in the US, where a relatively large portion of the population (notably the elderly) does not have comprehensive health insurance that covers the cost of medicines.
[15] For a discussion of several such proposals, see Dean Baker, Financing Drug Research: what are the issues? Issue Brief. Center for Economic and Policy Research, Washington DC, Sept. 2004. Available at: http://www.who.int/intellectualproperty/news/en/Submission-Baker.pdf [accessed 23/10/04].

country companies may do some work on tropical or neglected diseases, R&D by local companies should not be viewed as a magic solution.

The shortcomings of the current IPR system have given rise to a number of proposals for reform. And while the more radical proposals referred to in the previous section have yet to be tried, a number of moderate initiatives have been launched in recent years. Most of these take the form of public-private partnerships, and are dedicated to finding new cures for a specific disease; examples include the Medicines for Malaria Venture, the Global Alliance for TB Drug Development and the Drugs for Neglected Diseases Initiative. In addition to developing new cures, these initiatives hope to facilitate access to those cures in developing countries. They expect to achieve this for instance via a pull mechanism of guaranteed purchases, via agreements on preferential pricing for developing countries or via arrangements to allocate intellectual property rights for different geographic areas to different partner organizations[16].

And while it is too early for any of these initiatives to have delivered new drugs yet, it will be important to monitor and compare their performance in the future. Especially, it is crucial not just to assess their performance with regard to developing and launching new drugs and vaccines, but also with regard to the actual availability and affordability of the products thus developed in developing countries. In fact, any model found to be successful on both accounts may well provide important clues as to how to proceed.

Domestic production

Meanwhile, domestic production of medicines is an attractive option from the perspective of advancing industrialisation and development of the country, and because of the real or perceived independence it entails. This notion of independence may seem even more appealing in view of the fact that one of the crucial TRIPS safeguards, namely compulsory licensing, appears easiest to implement via local manufacturing. Yet domestic production of medicines will only enhance access if the medicines produced are those that are needed, if they are of good quality and are being sold at an affordable price. The latter will depend largely on economies of scale.

Many developing countries in Asia do have some domestic pharmaceutical production capacity. Those countries that lack local manufacturing capacity have very small markets and/or are least-developed countries (LDCs), where local production would not be economically viable. Since this is unlikely to change in the near future, domestic production in these countries may not be a realistic option, except possibly as a basis for relocation of an established foreign generic company wishing to exploit the absence of patent protection for pharmaceuticals[17], or in case of a joint venture with such a company. Nonetheless, LDCs that already have some manufacturing capacity in the pharmaceutical

[16] For more details, see Roy Widdus: Product development partnerships on 'neglected diseases': How they handle intellectual property and how this may contribute to improving access to pharmaceuticals for HIV/AIDS, TB and Malaria. Paper presented at the ICTSD-UNCTAD Dialogue on Ensuring Policy Options for Affordable Access to Essential Medicines, Bellagio, 12-16 Oct. 2004.
[17] Obviously, this applies only to LDCs that do not yet have pharmaceutical patent protection in place.

sector, such as Bangladesh, are probably in a better position to take advantage of any such opportunities.

At the other end of the spectrum are China and India, with a number of large generic companies[18]. Indian companies especially play an important role in the production and supply of affordable generics to all developing countries -- and increasingly to developed countries too. Yet the imminent introduction of pharmaceutical product patents in India has compelled these companies to adjust their strategies. Thus, major Indian companies are increasingly investing in R&D, while at the same time fostering collaboration with the MNCs [3] and the largest Chinese companies reportedly are set to follow suit [22]. It is anticipated that these Indian companies will pursue a dual strategy, that is, they will at the same time continue their traditional business of generic production of drugs that are not or no longer under patent [3]. Yet it remains to be seen whether they will seek to aggressively invalidate trivial/unjustified patents and pursue compulsory licenses. Moreover, in the long term, as their revenue from collaborative arrangements and R&D increases, there is a risk that these companies would gradually concentrate on the more profitable segments of the generic market. Yet regardless of the latter, it has been estimated that the lag time before generic versions of new drugs appear on the Indian market could increase from the current 4-5 years after their launch in industrialised countries, to about 15 years [3].

Somewhere in between these extremes are all other Asian countries, with some generic manufacturing capacity. Companies based in these countries usually do not venture into R&D, but focus solely on generic production of off-patent drugs. They could also produce generic versions of patented medicines under a compulsory license. Yet their production capabilities are generally limited to formulation, using imported active pharmaceutical ingredients (APIs). In fact, this is potentially an important weakness; the vast majority of APIs for the production of generic essential drugs originate from China and India. With product patents in place in both these countries, sourcing of patented APIs may become a bottleneck for generic production of new drugs.

Active ingredients

It is worthwhile to recall that APIs are included in the '30 August Decision'. Thus, by implementing the system set out in this decision, countries may be able to get around patents that are blocking access to APIs[19].

But while the future availability of APIs for generic drug production may be a matter of concern, it may also create opportunities for some LDCs; for instance, there have been reports that Bangladesh is considering investment in API production [23], though it remains to be seen whether new players will be able to catch up with already well-

[18] In addition, both countries have numerous smaller companies as well.
[19] Though as stated previously, the procedures for implementing this Decision appear to be cumbersome. This will certainly be true from a manufacturer's perspective, since companies cannot implement the Decision themselves, but need the cooperation of their government.

established competitors. Their main, and initially probably their only, advantage would be a possible head-start due to the absence of patent protection.

Nonetheless, conventional (chemical) APIs are not always patented/patentable, since they may not be new. More importantly perhaps, *all* active ingredients will only be offered at interesting prices once production reaches economies of scale[20] -- that is, once the respective medicines come off patent and generic sales take off in the large markets of the developed and/or major developing nations. As a result, the indirect effect of the introduction of product patents in India (and other large developing countries) will probably be at least as significant as the effect of patents on the actual APIs. Reflecting the before mentioned slowdown in generic market entry in India, it should be anticipated that the production of low priced APIs too will accrue a delay of about a decade – that is, they may not become available on the world market until the main patents on the originator drug are about to expire.

Finally, some analysts have reported early signs of collaboration between Indian and Chinese firms, and believe that the combination of their respective strengths in chemistry and manufacturing may eventually lead to extremely competitive prices for APIs and intermediates [24], once they are off-patent.

Biotechnology

However, while tackling the impending problems developing countries should not lose sight of challenges that are likely to occur in the future -- and it is widely believed that biotechnology-based products are the future. Thus, it is important that developing countries do not just focus on conventional (chemical) APIs and drugs, but think beyond.

Developing biotech products requires scientific and technical expertise, while producing them on a commercial scale furthermore requires substantial investment. Some developing countries, with China and India again at the forefront, are making considerable headway in generating such expertise. Meanwhile, investment will largely be determined by market prospects.

It is difficult to predict whether and how the advent of product patent protection in line with TRIPS standards will impact on domestic biotech companies in developing countries, but the hopes and concerns largely mirror the general debate on intellectual property rights, innovation and access. Yet two features do set biotechnology apart from conventional pharmaceutical science.

First, biotechnology is characterized, at least in industrialised countries, by heavy patenting, particularly of processes. In addition, patenting of research tools has reached unprecedented levels in this sector, to the point that researchers in the commercial and academic sector alike complain that it is stymieing research [25, 26].

[20] The production of APIs tends to be (much) more sensitive to volume than the production of medicines.

The second distinguishing feature relates to 'bio-generics' or, rather, to their non-existence on the market. This is not only because apparently "no-one knows exactly how to make a generic version of a biochemicalogical product without violating process-related patents" [27], but also because of the lack of regulatory standards for generic biological products. Yet the process of developing such standards has already started in industrialised countries, and regulators as well as researchers/scientists working in the biotechnology sector in developing countries should start to define 'bio-generics' and to set standards of their own, based on public health as well as access criteria. Failing that, developing countries risk to end up simply endorsing standards set elsewhere, which is not necessarily in their best interest [28].

Medium term actions

Taking clues from the above, a number of additional strategies ought to be considered by developing countries, in order to try to protect their people's access to medicines in the future. These strategies build on and expand the short-term actions listed above, and include[21]:

- Insist on sufficient disclosure of the invention in patent documents. Disclosure of inventions is a basic part of 'the patent bargain', though it is not always respected [29]. Adequate disclosure can help domestic researchers and industry (including in the biotechnology sector); there is no conceivable benefit in foregoing it. Generic or domestic industries or their associations could again play a role here, as 'watchdogs'.

- Ensure that both a research exemption and a 'bolar provision' are incorporated in the national patent law, and that they apply to bio-pharmaceuticals as well as conventional pharmaceuticals[22].

- Start thinking and discussing, at a national or regional level, about possible criteria and regulatory requirements for 'bio-generics'.

- Develop biotech capacity in pharmaceuticals, and involve companies and scientists in the discussion on 'bio-generics'.

- At a global level, a pharmaceutical patent broker could be set up which -- somewhat like the WHO Special Programme for Research and Training in Tropical Diseases -- fosters linkages between holders of patents that are relevant for 'tropical' or neglected diseases and potential producers in developing countries [3]. Alternatively, the WHO program could be expanded.

[21] The division between short and medium term actions/strategies is gradual, not sharp or absolute. Note that this is an initial list; it is not meant to be exhaustive. Moreover, not all strategies listed here may be appropriate for all countries.
[22] In the US, the 'Bolar provision' (essentially an exemption to patent rights that allows generic companies to prepare for registration before the patent expires) does not apply to bio-pharmaceuticals [35].

- National (human) resources could be pooled by setting up a regional patent office that has the capacity to really examine patents critically and to apply strict criteria; this could be a 'virtual' regional office, i.e. a network of national offices, each specializing in certain areas of technology.

Other actions that could be considered include:

- Stimulate (commercial) research and encourage technology transfer[23].

- Promote health-oriented research in national universities and research institutions, as well as participation in collaborative research. A clear and fair framework for intellectual property rights should be established beforehand, for instance drawing on the examples and lessons of recently established public-private partnerships.

- Maybe an international treaty on differential pricing for medicines (for example based on GDP per capita) can be negotiated?

- Is it possible to imagine what the Essential Drugs List would look like, 20 years from now, and if so, can that be used as a basis from which to work backward towards what the focus should be today?

- Would there be a role for a 'non-profit' pharmaceutical manufacturer, either real or virtual?

VI. Building blocks

While the list of recommended and potential actions pertaining to the intellectual property system seems long, a few principles underlie them all. These are:

- Adopt a critical attitude towards standards and criteria for patentability, and toward efforts to further expand the realm of exclusive rights;

- Ensure openness and transparency, to facilitate the dissemination of information about patents and the full disclosure of inventions;

- Take an assertive stance with regard to trivial patents and the use of safeguard mechanisms such as compulsory licensing;

- Promote inclusiveness and collaborate with all concerned government departments and other stakeholders; and

[23] For more details regarding technology transfer (and its limitations) see for example Keith Maskus, Transfer of technology and technological capacity building, Paper presented at the ICTSD/UNCTAD Dialogue on Development and Intellectual Property, Bellagio, 18-21 Sept. 2003.

- Coordinate policies and actions, within and possibly even between countries.

VII. Conclusion

Developing countries are faced with the challenge to preserve and expand access to basic and life saving medicines in an increasingly complex, imposed and 'alien' legal environment. To deal with this, they should enact appropriate intellectual property laws, which enable them to make full use of the flexibilities in TRIPS. They may also have to rely on other, equally unfamiliar but potentially countervailing legal and regulatory mechanisms, such as competition law. But it is at least as crucial that countries learn how to make use of these sophisticated legal tools.

Yet they also can and should take a number of relatively simple steps to avoid cluttering the patent system and to ensure that they do not unduly limit their own freedom to operate. For this to be accomplished, a change in attitude towards and administration of intellectual property appears to be the main prerequisite.

References

1 World Health Organization. Annual Report Essential Drugs and Medicines Policy. WHO, Geneva, 2002.

2 WTO. Declaration on the TRIPS Agreement and Public Health. Doc. WT/MIN(01)/DEC/2. Doha, 14 November 2001.

3 Cheri Grace. The effect of changing intellectual property on pharmaceutical industry prospects in India and China: considerations for access to medicines. Department for International Development, UK, June 2004.

4 World Health Organization. The World Medicines Situation. WHO, Geneva, 2004.

5 Nathan Ford, David Wilson, Onanong Bunjumnong, Tido von Schoen Angerer. The role of civil society in protecting public health over commercial interests: lessons from Thailand. The Lancet, 2004, 363: 560-563.

6 Medecins Sans Frontieres. Drug patents in the spotlight. Geneva, May 2003.

7 Carlos M Correa. Ownership of knowledge – the role of patents in pharmaceutical R&D. Bulletin of the World Health Organization, 2004; 82(10): 784-787.

8 Gardiner Harris. Pfizer reports China has lifted its Viagra patent. New York Times, 8 July 2004.

9 Andy Ho. The hoopla over Viagra patenting in China. Straights Times, July 16, 2004.

10 Richard McGregor. Challenge to GSK patent. Financial Times, 28 July 2004.

11 Diabetes drug patent challenged. Straights Times, 29 July 2004.

12 Anand Grover (for the Affordable Medicine and Treatment Campaign). Letter to the Chairman of the Group of Ministers on the Patent Amendment Bill. 8 September 2004.

13 Ministry of Health, Malaysia. The use of Government's rights to increase access to antiretroviral drugs: Malaysia's experience. Presentation at the TWN/HAI Asian Regional Workshop on WTO/TRIPS Agreement & access to medicines. Kuala Lumpur, 29 Nov. 2004.

14 Carlos Correa. Implementation of the WTO General Council Decision on Paragraph 6 of the Doha Declaration on the TRIPS Agreement and Public Health. WHO, Geneva, 2004.

15 Oxfam. Robbing the poor to pay the rich? How the United States keeps medicines from the world's poorest. Oxfam briefing paper, November 2003.

16 Medecins Sans Frontieres. What to watch out for in Free Trade Agreements with the United States. Briefing Note. Geneva, May 2004.

17 Carlos Correa. Bilateral Investment Agreements: agents of new global standards for the protection of intellectual property rights? GRAIN, August 2004. Available at http://www.grain.org/briefings/?id=186 [accessed 06/09/2004].

18 Jonathan Michael Berger. Advancing public health by other means: using competition policy to mitigate the impact of patent protection. Paper presented at the ICTSD/UNCTAD Regional Dialogue on IPRs, Innovation and Sustainable Development in Eastern and Southern Africa, Cape Town, 29 June - 1 July 2004.

19 David Henry, Joel Lexchin. The pharmaceutical industry as a medicines provider. The Lancet, 2002; 360: 1590-1595.

20 Gardiner Harris. Drug firms, stymied in the lab, become marketing machines. The Wall Street Journal, 6 July 2000.

21 Tim Hubbard, James Love. A new trade framework for global health R&D. Plos Biology, 2004; 2(2): 0147-0150. Available at http://www.plosbiology.org/plosonline/

22 Indian drug R&D has bright future. The Economic Times (India), 20 Oct. 2004.

23 Plant for pharmaceutical raw materials on cards. The Daily Star (Bangladesh), 26 August 2004.

24 George Karris. API Manufacturing: how will changes in India and China affect the outsourcing of APIs? Contract Pharma, September 2002.

25 Nicolas Thompson. Drug abuse: where have all the new meds gone? The New Republic, 7 October 2002.

26 Michael A Heller, Rebecca S Eisenberg. Can patents deter innovation? The anticommons in biomedical research. Science, 1998, 280(5364): 698-671.

27 Gil Y Roth. Biomanufacturing: what's going on in the bio-outsourcing industry? Contract Pharma, June 2003.

28 Karin Timmermans. Harmonization, regulation and trade: interactions in the pharmaceutical field. International Journal of Health Services, 2004, 34(4): 651-661.

29 Masaharu Kubo, Yukinori Itoh. Problem pharmaceutical patents. World Patent Information, 1996; 18(4): 227-233.

30 Khabir Ahmad. "Withdrawal of antipsychotics in Pakistan", in *The Lancet*, 1999; 354(9181): 846.

31 Linda Beecham. "MPs say the market for generic drugs is 'ripe for manipulation'", in the *British Medical Journal*, 2000; 320(7226): 7.

32 T Walley, P Burrill. "Generic prescribing: time to regulate the market?", in the *British Medical Journal*, 2000; 320(7228): 131-32.

33 Geoff Dyer et al., "Pfizer threatens boycott of new drugs in France: bid to force higher prices in Europe", in the *Financial Times*, 10/12/01.

34 World Health Organization. Social Health Insurance in South-East Asia Region. New Delhi, WHO/SEARO (draft version 22/05/03).

35 Enrico T. Polastro, Arthur D. Little. The future of biogenerics: when will we see legal generics of top biopharmaceuticals? Contract Pharma, Oct. 2001.