

# **RESEARCH, INNOVATION, PROFIT AND EQUITABLE ACCESS TO ANTIRETROVIRALS IN THE UNDER-SERVED MARKETS: MERGING INTO A MULTI-PRONGED, INCENTIVE-BOUND VOLUNTARY LICENSE STRATEGY**

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## **Summary**

This contribution explores fitness of a multi-pronged, incentive-bound WHO-mediated voluntary license strategy for attuning together research, innovation, profit and equitable access to antiretrovirals in the under-served markets.

Model potentials were investigated through examining: 1) the predictable effect on current regulatory practices (TRIPS rules and TRIPS-plus measures), 2) the expected benefits, either in terms of equity or safeguard of the generic and brand name manufacturers's interests, 3) the interplay dynamics with drug trading policies of deeply concerned countries (China, India, European Union, United States, Brazil, South Africa and Thailand), 4) the suitability for helping generic plants for antiretrovirals, including home plants in Sub-Saharan Africa, undertake research & development partnerships encompassing innovation, technological catch-up, exploitation of TRIPS flexibilities, as well as raised marketing power and domestic employment increase.

This study suggests that explored strategy, though far from being the ideal solution, looks reliable to help expand, as long as it entwines with WHO's brokerage, equitable and sustainable access to appropriate antiretrovirals by resource-limited populations, while boosting know-how, technology transfer, innovation, research & development, as well as national industry plants development and penetration of the wealthy and under-served markets by generic drug enterprises.

## **FOR-PROFIT POLICIES STILL DISREGARD RIGHT TO HEALTH**

Voices are increasingly skeptical on the fulfilment of pledges to secure universal access to antiretroviral (ARV) treatments by 2010 [1,2]. Actually, unaffordable drug prices still obstruct access in the income-constrained countries, while challenges are complicated by obstacles bound up with enforcement of TRIPS (Trade-Related Aspects of Intellectual Property Rights) inside World Trade Organisation (WTO) [3,4] (Table 1). Definitely, patent rules, along with exacerbated data exclusivity (Table 2), do hamper the development of any new generic ARV formulation containing drugs with exclusive status [5]. Meanwhile, patent protection, by eliminating competition, does skyrocket drug prices. Based on newer antiretrovirals (ARVs) are crucial once first line formulations fail [6-10], this is a clearly worrisome situation despite that TRIPS rules do encompass flexibilities (also including voluntary licenses-VLs and compulsory licenses-CLs) to help poor populations equitably access low-priced ARVs (Table 1).

Again, unceasing pressing by European Union (EU), Japan and the United States (US) on the World Intellectual Property Organization (WIPO) towards global harmonisation of patent laws could herald less autonomy in national decision-making about patents and too expensive medicines on the resource-limited countries horizon [11].

Even worse, evidence is available that Europe is too much enmeshed in intellectual property (IP) protection to quickly approve WTO's 6 December 2005 amendment which would make permanent a waiver inside WTO's 30 August 2003 Decision to help countries insufficient in ARV drug manufacturing (Table 1). Indeed, recently delayed ratification of the amendment by EU Parliament did couple with appeal by some members that Europe stops seeking WTO-plus IP drug protection in bilateral and regional trade transactions with resource-limited countries [12]. Besides, there is concern that European Commission and member states won't be able to meet EU Parliament requests 1) to commit funding for both drug-related technology transfer and drug development for neglected diseases in the developing world, 2) to play a more active role inside World Health Organization's (WHO) Intergovernmental Working Group (IGWG) on public health, innovation and IP, 3) to provide political support to governments seeking ways for making essential drugs available in their public health programmes [12].

Nonetheless, some optimism could arise from resolution on "Public Health, Innovation and Intellectual Property" adopted on 23 May 2007 at the sixtieth WHO's World Health Assembly [13]. Among other points, the resolution requested WHO Director-General to help develop proposals on ".....a range of incentive mechanisms including also addressing the linkage between the cost of research and development and the prices of medicines,....." and to provide "upon request, in collaboration with other competent international organizations, technical and policy support to countries that intend to make use of the flexibilities contained in the agreement on Trade-Related Aspects of Intellectual Property Rights and other international agreements in order to promote access to pharmaceutical products.....".

Regrettably, pharmaceutical industry, represented by the International Federation of Pharmaceutical Manufacturers and Associations (IFPMA) disagreed with the resolution, so playing in attuned wavelength to a US disassociation statement as well [14].

Anyway, the adopted resolution would suggest a key role for WHO as broker and promoter in North-South and South-South negotiations wherein TRIPS flexibilities and incentives to scale up equitable access to life-saving drugs are to be tackled.

Intriguingly, fulfilment of these favourable perspectives will depend substantially on drug trading directions of China, India, Brazil, South Africa and Thailand, as well as on measures to effectively offset US drug policy choices.

### **India and China's ways forward with TRIPS management**

China applied TRIPS in 2002, while India did so on 1<sup>st</sup> January 2005. Overall, industrial plants of both countries supply most of home needs while exporting high volumes of drugs to the under-served markets. Chinese and Indian firms are increasingly being involved with multinational (not only health sector) industries in manufacturing and research & development (R&D) partnerships including nanotechnology, robotics, as well as bioinformatics and genomics [15]. Really, China and India are enmeshed in deeply entwined interests with research-based corporations to support their risky forays into the world major markets. Meantime, the number of patent applications from China and India filed at the US patent Office has rapidly been rising [15]. China and, to a lesser extent, India are, moreover, the major suppliers of active pharmaceutical ingredients (APIs) for ARVs to the developed and developing world [16]. Definitely, this assigns both countries a power in influencing ARV drug price evolution. Indeed, as APIs do represent the largest components of direct manufacturing costs (55-99%) [17], significant decreases in ARVs prices will depend on a concomitant decrease in APIs price.

### ***India: final strategy pending***

Indian patent law is posing uncertainties to keeping on affordable ARVs [18]. Actually, 1995-2005 “mailbox” medicines (Table 1) and newer drugs whose generic versions have not yet made by Indian firms can only be sold as branded originals unless undertaking CLs or straightforward agreements with the patent holders. Conversely, Indian companies currently producing generic versions of medicines for which patent applications were submitted prior to 1<sup>st</sup> January 2005 are allowed to keep on if they have made a “significant” investment and pay a royalty to the patent owner [18]. Definitely, this backcloth alerts that, without incentives, the prices of “generics” produced under such a royalty will only increase making these drugs unaccessible by the poor. It also alerts that CLs will hardly be issued by Indian government because of threats to keeping on with partnerships with research-based enterprises and risks of retaliation by wealthy country governments. In policy terms, Indian government seems to be reluctant to hurt interests of US-based pharmaceutical companies also because India depends on US as far as mutual interests in tricky strategy balance with China and Pakistan are concerned.

### ***China: how to channel escalation?***

China could become the ARV factory for poor world because of its cheapest APIs and industrial scale-up coupled with steady penetration of the under-served markets [19-21]. Chinese producers are already making first-line ARV formulations, as well as raw materials for first and second-line ARVs [19]. Regrettably, while no Chinese ARV drugs have been WHO pre-qualified so far, China is under pressure nowadays for its weak pursuance of TRIPS [22, 19]. Nonetheless, Chinese government should possibly be attracted by TRIPS-bound VLs just for the following needs:

- technological catch-up while aiming to compete with multinational drug corporations.
- trustworthy relations with research-based companies.
- enhanced domestic ARVs production including fixed-dose combinations (FDCs) and paediatric formulations, both of which are not produced in China yet.
- sustainable self-sufficiency in pharmaceutical manufacturing, so breaking away from price fluctuations by foreign enterprises.

Overall, VL model would improve performances of China’s “Four Frees, One Care” policy in that it would expectedly help expand domestic access to free ARVs.

### **Implications from US drug policy choices**

For-equity strategies should be able to offset US policy currently torn among 1) defence of “brand name” (“free trade agreements” with coercive TRIPS-plus clauses are mushrooming) [23], 2) “shy” acknowledgment of generic ARVs, with no reliableness for routine use in PEPFAR (US President’s Emergency Plan for AIDS Relief), 3) incidental opening to generic ARVs from US strategic agreements on the international chessboard: actually, March 2<sup>nd</sup>, 2006 US-India signed “civil nuclear power” agreement [24] resulted in PEPFAR exploitation of Indian ARVs [25-27].

US is steadily witnessing its will to defend IP, regrettably with too few openings so far. Actually, just after agreement on reforms was reached at WIPO Meeting on Development (Geneva, Switzerland, 11-15 June 2007), US stated that, whilst WIPO’s proposals were reinforcing WIPO’s commitment to the needs of developing countries, it was clear WIPO’s mandate to promote IP protection worldwide [28]. Moreover, as far as WHO’s IGWG plan on pharmaceutical innovation is concerned, US already stated that it would not support any new funding mechanism and that topics present in the innovation plan, such as TRIPS flexibilities and bilateral trade agreements, would be more appropriate to the scope and mandate of WTO and WIPO [29]. Subsequently, when resolution on pharmaceutical innovation was adopted by WHO members at the before-mentioned sixtieth World Health Assembly, US disassociated itself [14]. Expectedly, also current debate in US on a move to make free trade agreement language closer in line with WTO-endorsed Doha Declaration (table 1) will likely go unsuccessful or just result in no more than cosmetic make-up [30].

### **Brazil, South Africa and Thailand’s directions**

-Forecasts suggest that costs for ARV therapy in Brazil will continue to climb unless the country violates patents or negotiates better deals with drug multinationals [31]. In 1996, Brazil enforced TRIPS agreement: accordingly, Brazil could produce ARVs patented before, but not improved or new drugs come to market subsequently. Really, Brazil has technical capacity to produce all new ARVs, but CLs have very rarely been issued so far (including for Merck’s efavirenz on May 2007) because of fear of damaging international, mainly with US, trade relations. Today, Brazil spends 80% of \$445 million annual budget on imported ARVs. If government instead made ARVs at state-owned Farmanguinhos industry, the country would save money [31]. Again, also the costs of currently home made ARVs would be reduced if Brazil started to produce APIs instead of purchasing from India and China.

-South Africa seems currently to gain ground as far as national plans to boost HIV prevention and treatment are concerned [32]. Presently, most of ARVs at public clinics are being paid by government, but international organizations and donors pay for costs at many private facilities, and medical insurance covers other individuals. Meanwhile, South-African Aspen company is keeping on with manufacturing most generic ARVs while signing innovatory VL-based deals with drug multinationals [33, 34].

-Thai government issued a CL against Abbott's heath-labile lopinavir/r in January 2007, two months after the government issued a CL for Merck's efavirenz. The country will import the corresponding generics from India until production by state-owned Government Pharmaceutical Organization comes on line [35]. Follow-up is needed to verify hardly foreseeable sustainability of Thai CL policy. Really, negotiations between the government and drug companies are still continuing. Meantime, US Trade Representative's Office placed Thailand on its Priority Watch List on 30 April 2007 [36]. In May, Thai Minister of Public Health intriguingly announced that Brazil and Thailand would sign a cooperation agreement on health development [37].

## **RATIONALE FOR SETTING-UP INCENTIVE-BOUND VL STRATEGIES**

Experience confirms that compulsory licensing (CL) has brought treatment with newer ARVs within reach in the developing world but has resulted in strong pressure and sometimes retaliation from industries and governments in wealthy countries. Therefore, less risky solutions to maximize sustainable access to ARV drugs in those settings should be looked for as well. Really, what matters for governments and the pharmaceutical industry in resource-limited countries is to finance ways agreed upon by all counterparts to make these medicines (including newer ones) stably affordable and accessible to the worst-off.

Current dynamics among the concerned parties would possibly help predict trends and set up appropriately working strategies.

On a world perspective, increasingly multiplying South-South partnerships [38-40] and enhancing R&D leadership of multinational research-based corporations [41,42] are concurrently emerging as leading phenomena in ARV drug production and marketing sector. Together, these dynamics entail a number of consequences which may be worth in-depth analysis:

- New South-South partnerships addressing the building and output of malarial, TB and ARV drug plants (also as wide Southern Africa regional companies to become cost-effective and stronger in resisting pressures by drug multinationals and wealthy country governments) were recently signed in Africa, or are currently under way, between country governments (i.e., Mozambique-Zimbabwe, Mozambique-Brazil) or generic drug companies (i.e., Ugandan Quality Chemicals-Indian Cipla Pharmaceuticals Ltd.) [38-40]. They fall into the African Union self-sufficiency plans [43] and add to already working examples of country-owned drug plants in other African countries [10]. Really, these partnerships do strength generic drug companies competitiveness against the multinationals. In-depth, forecasts from South-South partnerships would mean erosion of both profits and overseas markets for brand-name enterprises, while, for the stronger counterpart in transactions (leading generic industry or developing country government) the advantages would include market expansion encompassing royalties, revenues from APIs selling, as well as entering further the receiving country through wide-sector trade opportunities. Again, for the other counterpart these partnerships would represent self-sufficiency in pharmaceutical manufacturing, escape from dependence on countries guilty of "colonial past", sustained drug supply to home market, domestic employment increase, as well as discounts for APIs purchase.
- On the other side, research-based drug multinationals still keep on with unrivalled R&D leadership and strong policy support by US and Europe. As a consequence, only research-based corporations would be up to new drugs discovery in a medium-long time span. This does imply that patent rights exploitation, control of prices, attraction power and ongoing prestige on the world market will be kept on by them indefinitely. Actually, this links up with exceeding R&D investments made recently in China (Shanghai) and Singapore (Biopolis) by big pharma companies (i.e., Novartis, Merck, AstraZeneca, Roche, Abbott, Pfizer, Glaxo, Aventis, Schering, Wyeth) [41,42]. Really, mutual trade interests there do secure brand-name corporations substantial incentives such as high salaries for research staffs, low cost of local manpower, partial refunding for research expenditures, as well as fiscal exemptions and law favourable environment.

On the whole, awareness of all scenarios above, coupled with TRIPS and TRIPS-plus hindering obligations, should definitely spur generic drug manufacturers into boosting innovation, aiming at new drugs discovery too. This end result would add prestige and let them more easily gain the western markets while enhancing competition with brand-name counterparts. Again, this would let them enjoy the advantages from patent protection adoption while pushing ahead more profitable North-South partnerships [44].

On these perspectives, why should generic manufacturers insist on risky and, after all, poorly profitable CLs rather than fuelling multi-pronged VL deals with brand-name industry as far as exploitation of entwined know-how, training and technology transfer for new ARVs production are concerned? Absolutely, achievement of high-level performances through these opportunities would help generic companies save time while looking for innovation standards.

Conversely, threats to their profits by South-South partnerships and CL issuing are really expected to push multinational brand-name corporations towards more equitably harmonised VL transactions with generic competitors. In such a perspective, the growing potential of Indian and Chinese plants (enhanced by November 2006 China-India signed trade partnership) would predictably catalyze quite more profitable VL agreements for developing country firms as a whole. Ultimately, these agreements would secure all counterparts sustained advantages, while maintaining leadership of brand-name corporations and delaying wealthy markets forays by generic firms. Definitely, working examples of already signed VL agreements are available:

- Bristol-Myers Squibb (BMS) agreement with Aspen Pharmacare and Emcure Ltd. to manufacture and sell the protease inhibitor (PI) atazanavir in Sub-Saharan Africa and India, respectively (February 2006): a royalty-free license to operate under relevant patents was encompassed, along with transfer to Aspen and Emcure of BMS technical know-how related to the manufacturing, testing, packaging, storage and handling of the API and the finished dosage form of atazanavir. BMS provision of technical training both at its manufacturing facilities and at Aspen's and Emcure's facilities in South Africa and India was included too, along with support to the two companies for regulatory filings [33].
- Johnson & Johnson subsidiary Tibotec Pharmaceuticals agreement with Aspen Pharmacare to package and cheaply distribute the new PI darunavir in Sub-Saharan Africa (April 2007) [34].
- Roche agreements with Addis Pharmaceutical Factory (Ethiopia) and Varichem Pharmaceuticals (Zimbabwe) for ARV production training (May 2007): the two African companies will be provided with no-cost technical training and guidance to manufacture generic ARVs based on the processes used to develop Roche's second-line ARV saquinavir. Roche staff will work onsite at the manufacturing facilities in Ethiopia and Zimbabwe and from the company's headquarters in Switzerland. Generic saquinavir marketing will be not allowed outside Sub-Saharan Africa and least developed countries. Thirty-two manufacturers in 15 eligible countries – including Ghana, Kenya, Nigeria and Zimbabwe – have expressed interest in participating in the initiative [45].

Definitely, thoughts expressed so far underscore the reasons for setting up country-owned plants for generic ARVs in Sub-Saharan Africa as well [9, 43]. Home plants, indeed, would add strength for negotiating profitable VLs encompassing equitably expanded ARV drug access. Really, industrial potential will likely be up to drawing branded drug producers into more flexible agreements securing mutual advantages. Under such a perspective, China's cheapest APIs could serve as a key source for the taking off of sub-Saharan plants. This sounds consistent with exceeding China's interests in Africa as by bilateral agreements already signed, or currently under way, with many African countries and encompassing trade, energy supply, investments, as well as infrastructure and health cooperation [20].

Overall, dynamics highlighted here may explain the generic and brand-name industry's confluence of interest towards harmonised VL negotiations for manufacturing and marketing of affordable ARVs. Absolutely, these agreements should include combination incentives and WHO's brokerage to secure both as fairly as possible low-priced drugs and most expanded access to ARVs by poor people as well. Really, this model would promote and enhance:

- sustainable and equitable access to life-saving treatments
- domestic employment and national/international market increases
- R&D and international standard innovation plans.

### **INCENTIVE-BOUND WHO-MEDIATED VLs: A MULTI-PRONGED MODEL FOR APPROPRIATE AND EQUITABLE LONG-TERM SOLUTIONS**

VLs look as an attuning strategy to overall scenarios here, notwithstanding royalties on generic firms are included: VLs, indeed, only imply direct agreements between firms; they do not require changes in national legislation, while encompassing non-exclusivity, openings towards technology transfer, access to owner's data, as well as consent for export (Table 1).

Understandably, VLs are far from being the ideal solution. Actually, the best mechanism for ensuring that prices of ARVs become as affordable as possible would be to manage for unrestrained competition by CLs. Replacing with a managed competition under VLs would represent no more than a second best. Unfortunately, pressures currently placed on the developing world by wealthy country governments look as poor premise for CLs being extensively adopted.

Really, a number of constraints do limit VL model potentials. Indeed, if a patent holder decides to grant a VL it will use the control that IPs bring to determine what the licensee is allowed to do. Additionally, the licensee would likely be forbidden to compete with the brand-name company in their market but would be compelled to supplying a developing country market.

Nonetheless, VLs meet the interest of generic companies to achieve technological catch-up to measure with research-based enterprises into the wealthy and under-served markets. Actually, VL-bound opportunities, rather than CL-bound copying, would better help attain this goal.

VL model, again, as not hindering low-cost API provision by China and India to not APIs producing generic firms, would help them keep on with domestic ARVs manufacturing. This would be crucial as APIs for certain ARVs are still under patent in many countries: with no alternatives in place, this backcloth would restrict the market to very few suppliers and lead to high prices for these APIs and finished drugs [17]. Additionally, VL model would counter IP restrictions enacted under TRIPS-plus agreements that might further limit the sources of APIs [17]. Furthermore, VL policy would help countries with no manufacturing capability still import generic ARVs without undertaking hard CL-bound changes in national law (Table 1). Again, predictability of HIV resistance mutations in the developing world does allow VLs to be assigned a spin-off linking in with urgency for newer ARVs [9].

Actually, as remarked before, VL agreements are expected to work at their best under WHO's brokerage and combination incentives equipment. These incentives are awaited by governments and international players also including the Global Fund to Fight AIDS, TB and Malaria, the World Bank, WHO, as well as UNAIDS and Clinton Foundation. Again, these incentives must encompass funding to give generic manufacturers prompt reasons for keeping prices low. Funding could even arise through securing African governments support to meet Abuja Declaration commitment to set aside 15% of national Gross Domestic Product for health spending [46]. Full debt cancellation to poor countries would actually help [47,48].

Nonetheless, UNITAID-International Drug Purchase Facility can definitely be assigned (also thanks to complementarity with all institutions mentioned above) a special role to help combination incentive strategy succeed [49]. Country governments, indeed, could be allocated UNITAID revenues to finance fiscal relief to their generic companies. These revenues, again, could allow (as in Clinton Foundation-UNITAID-Cipla and Matrix recently signed agreement) multi-year large-volume purchasing programmes with WHO-prequalified generic drug companies to be negotiated by international players [50,51].

In detail, combination incentive strategy should comprise:

***-Generic ARVs exclusive bulk purchasing by international donors, based on acceptance of WHO prequalification***

This would result in slashing of prices. Transparency enjoyed through WHO check would make the model quite trustworthy.

***-Fiscal relief to generic firms by country governments***

Sources of tax allowance: enhanced disbursement by donors, domestic expenditure priority reallocations, debt relief savings from debt cancellation. WHO and UNAIDS, following acknowledgement of country pledges to channel debt relief savings towards tax allowances, should promote approval of debt cancellation while checking for pledge pursuance.

***-WHO brokerage in VL negotiations with research-based corporations***

This would maximize equitable access to drugs.

## **CLOSING REMARKS**

Incentive-bound VLs look reliable to bring, through WHO's brokerage [52], several opportunities to generic enterprises, while cutting prices and promoting equitable access to ARVs. VL model explored here would allow generic manufacturers to overcome patent protection while being not barred by exacerbated data exclusivity which does hurdle, instead, CL use (Table 2). Additionally, it would bear countries against the risk that 6 December 2005 CL-bound public health waiver might not be formally built into TRIPS agreement: as of 10 August 2007, only 8 WTO member states had ratified the waiver, out of 151 asked to do so (see Table 1) [53, 54].

Overall, suggested model appears as a fitting formula nowadays, with some advantages over CLs [8, 9]. Nonetheless, CL threat inside VL-based transactions looks fruitful as it would bring patent owners to more reasonable positions and give generic firms stronger negotiation power.

**Table 1****TRIPS REGULATORY TERMS AND DATES FOR PATENT STATUS OF DRUGS**

|  |  |
|--|--|
| <b>Patent</b>  | A twenty- year warranty securing inventor exclusive rights on the overall drug production and marketing aspects. When countries signed up to World Trade Organisation (WTO) they accepted to protect the patent rights of corporations selling drugs within their boundaries.  |
| <b>TRIPS (Trade-Related Aspects of Intellectual Property Rights)</b> | WTO Agreement (1994) to the safeguard of Intellectual Property Rights (IPRs) around the world. It protects companies by stopping anyone from copying their products for twenty years at least.   |
| <b>Drugs invented before 1995</b>                                    | No need for patent protection by a WTO member State if drugs were not patented before 1995, i.e. before TRIPS came into force.   |
| <b>1995-2005 “mailbox” drugs</b>                                     | It refers to 1995- 2005 invented drugs (including second-line ARVs) for which WTO members which did not recognise drug patents before 1995 were offered diversified time limits to become TRIPS-compliant. Transitional countries have to hold patent applications on these drugs in a so-called mailbox and secure patent applicants exclusive marketing rights (EMRs) for five years once drug was in the mailbox and registration was made by the national drug regulatory authority.   |
| <b>Post-2005 drugs</b>   | All WTO members, with exception of least-developed countries (LDCs), are requested TRIPS compliance.   |
| <b>Dates for LDCs</b>  | LDCs had to become TRIPS-compliant by 2006 but, if national legislation was consistently amended, they are exempted from accepting patent protections and TRIPS enforcement until 2016. Aside from this flexibility, even LDCs have to issue compulsory licenses (see below) for importing copies of drugs already patented in pre-TRIPS domestic law.   |
| <b>Doha Declaration November 14, 2001</b>                            | It stated that each WTO member has the right to use TRIPS-encompassed flexibilities (which include compulsory and voluntary licenses) to secure universal access to drugs in the face of a public health need.   |
| <b>Compulsory Licensing (CL)</b>                                     | It is when a poor country government allows to manufacture domestically or to import copies of patented drugs at prices much cheaper than those imposed by the patent holder and without his consent. Both importing and exporting countries need to have enabling legislation in place (a corresponding CL for export has to be issued by the exporting country). Prior negotiation with the patent owner for voluntary license first is required <u>unless for situations including extreme health crisis and not-for-profit government use</u> . Payment of a royalty to the patent owner is encompassed by CL rules. |
| <b>Voluntary Licensing (VL)</b>                                      | Agreement negotiated with the patent’s owner for manufacturing and marketing. Notwithstanding royalty rates imposition on generic firms, these licenses only imply straightforward agreements between companies; they do not require changes in national legislation, while including non-exclusivity, openings towards technology transfer, access to owner’s data for branded drugs as well as permission for export.  |
| <b>Decision August 30, 2003</b>                                      | It allows non-manufacturing countries to issue a CL to import a generic version of a particular medicine based on a CL for export issued by the exporting country government. Declaration by the non-manufacturing country of insufficiency in manufacturing the specific drug is required. WTO amendment approved on 6 December 2005 made the Decision permanent, <u>based on two thirds of WTO members have ratified it by December 2007</u> [53].   |
| <b>Parallel importation</b>  | Importing of fairly priced patented drugs for which the rights of the patent owner have been exhausted by the first sale.  |
| <b>Bolar exception</b>   | Permission to a generic firm for copying and registering a patented medicine before patent expiry. It could exceptionally be applied only if the normal rights of patent holder are pledged.   |
| <b>Data exclusivity</b>  | Data protection against unfair commercial use only (but five and eight year protection have been respectively requested by US and Europe).   |

## Table 2

### **Exacerbated data exclusivity**

*Term refers to a practice which temporarily bars registration files of an originator from being used to register the generic copy of a brand-name medicine. As long as fixed time period ( five years in the US and eight years in the Europe), Drug Regulatory Authorities are prevented from registering such generic equivalents unless generic producer has carried out independently the required safety and efficacy tests, or bilateral agreements encompassing Voluntary Licensing (VL) use (Table 1) have been undertaken.*

*Data exclusivity impact does actually consist in barring Compulsory Licensing (CL) use (Table 1) until the expiry of data exclusivity itself and, mainly, in securing research-based companies a monopoly period in countries agreeing to data exclusivity even when a medicine is not patented in the specified country.*

*Definitely, this practice goes far beyond WTO's request for data protection against unfair commercial use only (Table 1).*

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