

Need of Data Exclusivity: Impact on Access to Medicine

Gargi Chakrabarti†

National Law University, Nagour Road, Mandore, Jodhpur 342304, India

Received 2 November 2013, revised 22 August 2014

Pharmaceutical companies put reasonable time and money to generate safety and efficacy test data during clinical trials while applying for the marketing approval for any new chemical entity. They need protection for that data to prevent it from being used by generic producer companies for the same compounds. Data exclusivity provisions are different in different countries and each country's pharmaceutical industry usually influences the formulation of those provisions. Data exclusivity adds an extra layer of protection for the drugs irrespective of the patent protection status, thus controlling access to medicine. This paper analyses how pharmaceutical companies are trying to retain the market exclusivity by enforcing data exclusivity and how it is affecting health issues in developing and least developed countries. It also highlights the impact of data exclusivity on accessibility and affordability of life saving drugs. This paper discusses the stand of developing and least developed countries including India; evaluates why these countries are not interested in implementation of data exclusivity in their national legal regime and also proposes how to achieve balance between the economic interest of the originator companies and public interest towards access to medicine.

Keywords: Data exclusivity, access to medicine, pharmaceutical patent, intellectual property protection

Data exclusivity is the provision of protection of test data produced by pharmaceutical companies during the clinical trials (during development of new chemical entities or NCEs) for certain specified period of time, so that no third party can use that data or no other company can ask for market approval based on that data before that period. Pharmaceutical companies put reasonable time and money to generate safety and efficacy test data during clinical trials while applying for the marketing approval for any new chemical entity. They need protection for that data to prevent generic producer companies from using them for the same compounds. Data exclusivity (DE) provisions are different in different countries and the country's pharmaceutical industry usually influences the formulation of those provisions. Since DE adds an extra layer of protection for the drugs irrespective of their patent protection status, it affects access to medicine.

Understanding of DE: Drug Development

Development of a NCE and marketing that product as a safe and efficacious drug is a long journey for a pharmaceutical company, which involves huge amount of time, large human resource and enormous financial expenses. This is best understood by

comprehending the stages of drug development process, as shown in Fig. 1.

Clinical trial is by far the costliest and most time consuming affair. Moreover the data generated by clinical trial is unique for that NCE and is required to be produced before the national drug regulatory authority for the marketing approval. As originator companies spend lot of money to produce that data, they want special protection for the same. Nonetheless, it seems that this kind of protection of clinical data creates an extra layer of protection besides intellectual property protection for the original product.

Many developing or least developed countries do not contain the DE provision in their domestic legal regime yet while developed countries' national legal regime provide DE protection. Before assessing the implication of DE on access to medicine, a discussion of the positions of various countries on DE in the pre- and post-TRIPS era is in order.

DE Provision in USA, Europe and Other Countries

Data exclusivity provisions were available in developed countries like USA and Europe even before the TRIPS Agreement. This section will highlight those provisions.

USA: DE Provisions Pre-TRIPS

The US adopted a data protection regime for pesticides in its Federal Insecticides, Fungicides &

†Email: gargi.nluj@gmail.com

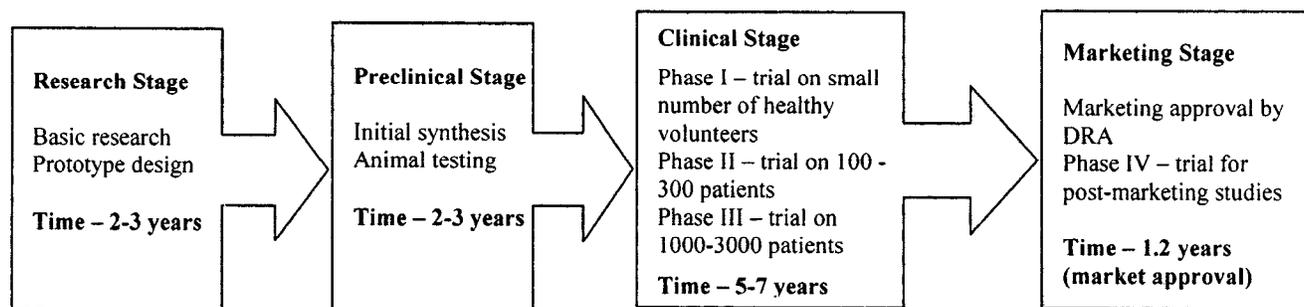


Fig. 1—Stages of drug development (adapted from ref. 1)

Rodenticides Act, 1947 (FIFRA); the Section 3(c)(1)(D)(i) of which provided an ‘exclusive use provision’. According to that section, the first applicant got a 10 year period of exclusivity for data on new active ingredient. Also according to Section 3(c)(1)(D)(ii), the data could be used by any other company by paying compensation to the first applicant.² The US has provided regulatory exclusivity provisions for medicines since 1984 including five years of exclusivity for the NCE and three years for the data supplied in support of its authorization.³

USA: DE Provisions Post-TRIPS

The Price Competition and Patent Term Restoration Act of 1984 (more commonly known as the Hatch-Waxman Act)⁴ and Section 355 of the Federal Food, Drug, and Cosmetic Act (FFDCA) of 1997 provide for DE for medicines in USA.⁵ Though Hatch-Waxman Act came into effect in pre-TRIPS era, its impact is ongoing and hence discussed here in the post-TRIPS period. The US model provides a five-year period of DE to new drugs and three years to new indications of existing drugs.

Different Exclusivity Offered in US

- (i) NCE (data) exclusivity of five years: The FDA will not accept ANDA (Abbreviated New Drug Application) or 505(b)(2) applications for generic drugs during this period, can benefit 505(b)(1) and 505(b)(2) applications.
- (ii) Three-year exclusivity for first generic entrant: While FDA accepts applications for generic drugs during this time, they are not approved.
- (iii) 180-day exclusivity: For 180 days after market launch by first-to-file ANDA generic, the FDA does not approve a subsequently filed ANDA for the same product. This does not delay approval of 505(b)(2) applications for a comparable drug product or the launch of authorized generics.

- (iv) Orphan drug exclusivity of seven years: This is generally limited to ‘rare diseases or conditions’ but can benefit an approved applications filed under Section 505 of the FFDCA or a licence issued under Section 262 of the Public Health Service Act.
- (v) Paediatric exclusivity of six months: This period attaches to the end of existing exclusivity and patent protections and can benefit drug products that are subject to Section 505 of the FFDCA only.

Healthcare Bill⁶

On 23 March 2010, President Obama signed the much-debated healthcare reform bill, known as the Patient Protection and Affordable Care Act (Healthcare Bill). The Biologics Price Competition and Innovation Act of 2009 (Biologics Act) is included as a subtitle of the Healthcare Bill, and creates a framework for FDA approval of follow-on biologics. The most disputed issue in the passage of the Biologics Act involved the length of statutory exclusivity period for biologics. These exclusivities can be divided into two main categories:

- (i) Exclusivity for reference product: No follow-on biologic application may be submitted until four years from the date on which the reference product was first licensed by the FDA. No follow-on biologic application may be approved until twelve years from the date on which the reference product was first licensed by the FDA. An additional six months of exclusivity may be obtained for approved paediatric or rare disease indications.
- (ii) Exclusivity for first interchangeable biological product: If a follow-on biologic is approved by the FDA and is deemed to be interchangeable, then the applicant receives the lesser of one year of exclusivity after the date of first commercial

marketing or eighteen months of exclusivity after FDA approval *vis-à-vis* any other approved, interchangeable follow-on biological products.

Europe: DE Provisions

In EU the Member States have provided protection for data supplied in support of marketing authorization for medicines since 1987. Article 8 of Directive 65/65 (ref. 7) amended by Directive 87/21/EEC⁸ established a minimum six years of data exclusivity for the originator's test data and 10 years exclusivity for high technology products, biotechnology products and NCE. During the exclusivity period, the regulatory authority cannot rely on an originator's data to approve other applications without originator's consent. The authorizing agency, namely, the European Medicines Evaluation Agency (EMA), could grant 10 years protection for medicines delivered by a 'new delivery system involving significant innovation' or for medicinal products containing a new substance or for an entirely new indication of a known substance.⁹

The Directive initiated a non-retroactive, 8+2+1+early-working formula that now grants absolute data exclusivity, as elaborated in Fig. 2.

Some points about the DE provisions in the EU that need to be highlighted are:

- (i) The 10 year period was created at a time when there were no patents for biotech products. This data exclusivity period therefore provided a form of market protection for these products in the absence of patents, which was particularly important to those Member States with developing biotech industries. But patents are now granted for biotech products. The '10 year countries' include: Belgium, Germany, France, Italy, Luxembourg, The Netherlands, Sweden and the UK.¹⁰

- (ii) Half of the EU countries actually operate a six year period of DE instead of 10 year period. The '6 year countries' are: Austria, Denmark, Finland, Greece, Iceland, Ireland, Norway, Portugal and Spain. The 12 newest Member States seeking EU accession are expected to opt for a six year period.¹⁰
- (iii) It is evident from the text of the preamble of Council Directive 87/21 EEC dated 22 December 1986 that the main aim of DE was not to hinder the registration of generic medicines but to enable the registration of 'abridged applications' in order to avoid repetitive testing on humans and animals without superseding cause, and at same time putting real innovation at an advantage.¹¹

Finally, even after this period, commercially sensitive data is still not disclosed to third parties i.e., generic companies or the public at large. Generic companies, on their part do not use the data of the originator but generate their own data (i.e. expert reports referring to official publications, pharmaceutical data and bio-equivalence studies).

Provision for Paediatric and Orphan Drugs

Paediatric extensions (EC Regulation 1901/2006) facilitate the development of medicinal products for use in paediatric population through a system of obligations, records and incentives. A six month extension to the Supplementary Protection Certificate (SPC) is given if (a) the product is authorised in all Member States and (b) the result of studies is included in product information.¹²

Orphan drugs governed by Article 3 (1) of the EC Regulation 141/2000 3(1) are those drugs which are intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition

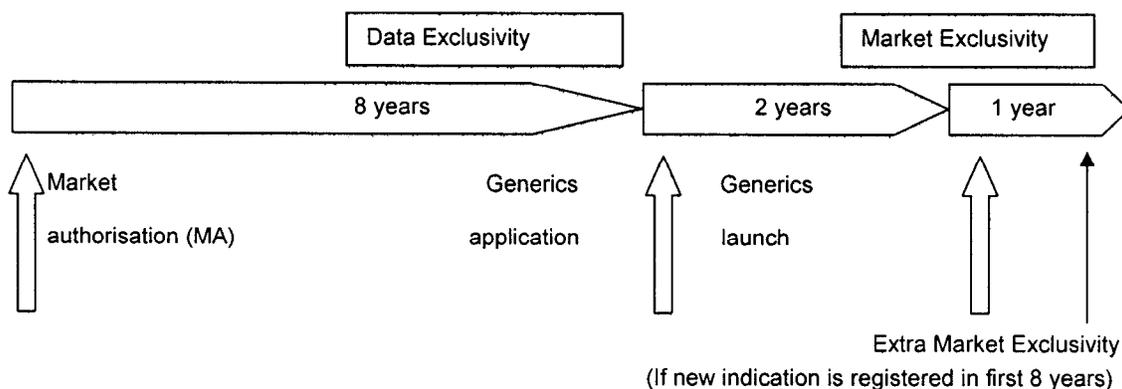


Fig. 2—European data exclusivity model (adapted from ref. 10)

affecting not more than five in 10,000 and with no satisfactory treatment currently. The SPC extension does not apply to orphan medicines.¹³

Data Exclusivity Provisions in Asian Countries

Availability of DE protection varies widely among the Asian countries. Only a few of the countries voluntarily provide the data exclusivity provisions, e.g. Japan and Singapore; some of others have been forced to implement DE as a result of free trade agreements (FTA) with developed countries (with higher bargain power), like Thailand, Korea and Malaysia. The remaining like India, Pakistan, Philippines, Taiwan, etc., do not provide for DE.¹⁴

Japan

Japan provides DE for six years. As per Japanese legal provisions, the applications for approval of new drugs should accompany the data including clinical trial results.¹⁵ In case where an application is made for a drug which appears to be identical to a previously approved drug in terms of the ingredient and content, directions and dosages, indications and effects, during the re-examination period of the said new drug; the application must include such data that will be equivalent or superior to those of the said new drug. Law defines the re-examination period as a 'surveillance period' during which an approved product is subject to 'good post-marketing surveillance practice' monitoring. The aim is to ascertain that no further approval is granted to the same product without a full data set until the safety and efficacy of the pioneer product has been demonstrated clinically.

China

In compliance with Article 39.3 of the TRIPS Agreement, China provides effective protection of six years against unfair commercial use of undisclosed test or other data submitted to authorities in China, which is required to be submitted in support of applications for marketing approval of pharmaceutical when new chemical entities are concerned.¹⁶ The only exception is a situation where the disclosure of such data was necessary to protect the public, or where steps were taken to ensure that the data are protected against unfair commercial use. Within this six year period from the date of obtaining marketing approval, an application for manufacture or marketing approval by another using the above data without the express consent of the original applicant shall not be approved by drug administration authorities.¹⁷

Thailand

Thailand now provides five years DE for new chemical entities as per the demand of USA, after having signed the US-Thailand FTA.¹⁸

Korea

The Korean Pharmaceutical Affairs Act is being amended after the United States-Korea FTA came into effect on 15 March 2012 (ref. 19). The revised Act and its implementing regulations include provisions for DE for patented pharmaceuticals. The new provisions provide for a five year data exclusivity period that is similar to that provided in the United States. Generic companies are prohibited from submitting generic drug applications in Korea for at least five years from the original company's approval date for a new chemical entity.¹⁹

Singapore

Singapore offers a five-year DE period in its national law. No company can submit an application to the drug regulatory authorities for marketing approval and ask the regulatory authorities to use the data submitted by the originator company. In such cases, the second company needs to have the consent from the originator company for use of their data by regulatory authority for marketing approval for a period of at least five years from the date of approval of the original pharmaceutical product.²⁰

Vietnam

Vietnam provides for a five-year DE period, unless the generic applicant has obtained the original manufacturer's permission to use its data.²⁰ If the applicant requests that the data be kept secret, the Vietnamese regulatory authority has to keep the data confidential unless the disclosure is necessary to protect the public.

India

In India DE is not yet available in the national legal provisions. Historically there was immense pressure on India to include data exclusivity from EU as India was negotiating a bilateral FTA with EU. But India stood strictly in favour of not implementing DE provisions. The Indian stand is further explained later on in details. Not only India, specific DE provisions are also not available in Pakistan, Indonesia, Philippines, Taiwan, Hong Kong, Sri Lanka, Bangladesh, Myanmar, etc.²⁰

Data Exclusivity Provisions in TRIPS Agreement

The TRIPS Agreement, which was negotiated as part of the Uruguay Round of trade negotiations under the General Agreement on Tariffs and Trade (GATT),

the predecessor organization to the World Trade Organization (WTO), is the first international intellectual property agreement to include obligations for the protection of trade secrets, especially the proprietary data submitted by innovators to Governments. Provision of DE is not exclusively expressed in TRIPS Agreement, but the interpretation of Article 39 (ref. 21) is done in favour of DE.

In totality, it is important to note that Article 39 represents the section on 'protection of undisclosed information' which relates generally to trade secrets. Article 39.2 is a general clause to respect trade secrets and is an obligation for all WTO members. Article 39.3 constitutes the obligations in the particular case where such trade secret data are submitted to governments or government agencies as a qualification for acquiring market approval.

Article 39.3 states that "Members, when requiring, as a condition of approving the marketing of pharmaceutical or of agricultural chemical products which utilize new chemical entities, the submission of undisclosed test or other data, the origination of which involves a considerable effort, shall protect such data against unfair commercial use. In addition, Members shall protect such data against disclosure, except where necessary to protect the public or unless steps are taken to ensure that the data are protected against unfair commercial use."

Different components of the protection and its understanding are immensely important for the discussion of this article which is done in the following section. Highlights of Article 39.3 are as follows:

- (1) Data submitted for marketing approval – The protection is applicable only if the data is submitted to the national drug regulatory authority (DRA) for market approval. In case of submission of data voluntarily or as an accessory requirement for the approval, the protection is not applicable.
- (2) Scientific data – Subject matter of protected data would be the details of results of scientific health and safety test of drugs and agrochemicals; it also includes the 'other' data which may be the data related to manufacturing process, packaging and conservation of the products.
- (3) Undisclosed data – Article 39.3 protection to the test data will not be applicable for any data which is in public domain, the data must be 'undisclosed' scientific data. If substantial part of the data is published, protection under Article 39.3 will not be available. Even the 'undisclosed' nature of data is subject to scrutiny by the DRA.
- (4) New chemical entities – Data must refer to a 'new chemical entity'. The Agreement does not provide the term 'new' for the purpose of this Article; a Member Country may or may not impose the patent standard of novelty for the purpose of 'newness' for data exclusivity. For all practical purposes DRA will accept a chemical as 'new' if no prior application has been submitted in relation to the same chemical. Moreover, Article 39.3 needs to clarify the territoriality of the newness, whether absolute (universal) or relative (local).
- (5) Considerable effort – Article 39.3 provides the protection for the test data only when a 'considerable effort' is involved in obtaining the data. The term 'considerable effort' also needs clarification, in the sense that it is ambiguous on what is the parameter on which the type of effort involved would be judged - technical or economic. According to Trans Atlantic Consumer Dialogue (TACD) "data exclusivity provisions are designed to protect the investment, rather than innovation". So, it is interpreted that the 'considerable effort' appears to indicate economic effort.
- (6) Unfair commercial use – The test data protection provided by Article 39.3 would be essentially against the 'unfair commercial use' of the data. Thus, an unpatented medicinal product can get market exclusivity for certain period of time, while in case of patented drugs, the marketing of generic medicine will be prevented for the period of data exclusivity.
- (7) Duration – The duration of protection is not mentioned expressly in the text of Article 39.3, so the term of protection is left to the discretion of Member Countries and varies from five years in US, Japan Australia etc., to 10 years in certain EU member countries.

Therefore there is enough flexibility in the provisions of TRIPS Agreement for a country to determine appropriate means of protecting test data. In terms of paragraph 4 of the Doha Declaration, the provisions are to be "interpreted and implemented in a manner supportive of the WTO Members' right to protect public health and, in particular, to promote

access to medicines for all". Hence, there are two categories of countries according to the national provision of DE, one group that provides DE in the national legal regime and the second that does not.

Indian Stand

The Department of Chemicals and Petrochemicals was called for "suggesting measures that should be adopted in the context of data protection provisions as outlined in Article 39.3 of TRIPS" and recommendations regarding legislative changes thereof if required. An inter-ministerial committee was formed to help the Department with this task and a committee report was submitted on 31 May 2007 by Secretary Mrs Satwant Reddy and Joint Secretary Mr G S Sandhu.²² The committee clearly recommended that the obligation under TRIPS Article 39 can be met merely by non-disclosure of the data submitted for marketing approval to the regulatory authority and also mentioned that such non-disclosure did not necessarily preclude the reliance on that data by the regulatory authority for approval of the same product by any subsequent applicant.²² Most of the developed countries have adopted provisions of DE not as a mandate under TRIPS Agreement, but as a legislative policy and/or as a requirement under FTAs.

The recent increase in FTAs signed between different countries has had a direct impact on DE forcing countries with lesser bargaining power to include DE provisions.

Role of FTA in Asian National Data Exclusivity Protection

Free trade agreements play a very important role in the provision of DE in the national regimes of different Asian countries. It is an observed trend that FTAs often enforce certain criteria that are in excess of the TRIPS requirements, i.e. 'TRIPS plus' conditions.²³ Countries with greater bargaining power try to negotiate with countries with lower bargaining power into accepting their own terms and conditions which may not be suitable for the accepting country's socio-economic structure. Notably these provisions are relevant for price rise of medicine, e.g. expanded scope of patentable subject matter, patent term extension, inclusion of data exclusivity provisions in national legal regime and introduction of patent linkage.²⁴ The US in particular is said to be pursuing such agreements and has concluded several FTAs since 1985 (ref. 25). Thailand had to enforce data exclusivity for a period of five years (in the case of pharmaceutical

products) or ten years (for agricultural chemical products) from the initial regulatory approval of the original product. The drug regulatory authority is prevented from granting market approval to generic drugs on the basis of bio-equivalence or on the fact that the original product has got marketing approval in a foreign country.²⁶ The United State Trade Representative (USTR) proposed that Thailand includes a provision obligating the Thai drug regulatory authority to inform the patent holder as to any attempt to register a generic drug. The authority is barred from approving registration for a generic medicine unless it is certain that the manufacturing, importing and selling of the generic will not infringe the patent rights of other companies.²⁶

Vietnam signed US-Vietnam Bilateral Trade Agreement in 2001 which requires Vietnam to provide data exclusivity.²⁰ Vietnamese law requires a manufacturer to prove that the use of the generic drug it seeks to register will not infringe patent rights of other companies. This in effect prevents generic medicines from entering the market as it is almost impossible for the generic company to prove the patent status of the drug.²⁷ In Malaysia, the National Pharmaceutical Control Bureau (NPCB) under the jurisdiction of the Ministry of Health is responsible to ensure safety and quality of a drug before it is allowed to be marketed in the country.²⁰ The NPCB in its assessment used to rely on the results of the clinical trials submitted by the originator company, seeking marketing approval. The NPCB would also grant the marketing approval to the generic drug and there was no need for the generic company to submit new safety and efficacy data based on its own clinical trials. But, because of the FTA with US, Malaysia had to include a five year data exclusivity provision in its legal regime.²⁸ Similarly the US-Singapore FTA put forward similar clauses and Singapore had to amend its national legal regime to include more stringent criteria. For instance, if a company required the marketing approval of a pharmaceutical or agricultural chemical product prior to permitting the marketing of such product, such party shall have to obtain the consent from the originator company to get a marketing approval from DRA on the basis of the data submitted by the originator company for a period of at least five years from the date of approval of the original pharmaceutical or chemical product.²⁹

The India-EU FTA negotiations have been long drawn with EU trying to include certain TRIPS-plus

provisions that India would be forced to implement in the national legal regime.³⁰ Inclusion of DE is one of them. Data exclusivity as demanded by the EU in the FTA negotiations would require generic manufacturers to conduct their own clinical trials to get marketing approval or wait till a specified exclusivity period is over (6 to 11 years) before a generic product is approved.³⁰ This measure creates exclusivity over medicines separate from patents and applies even to medicines that are off-patent.³¹ EU has also included strong provisions on pharmaceutical patents in FTAs with several other countries like Columbia, Peru, regional grouping of South-East Asia, specifically in case of Columbia and Peru the suggested period of data exclusivity was 11 years, which would have devastating effects on global access to medicine, though these are FTAs are still under consideration.³² Presently, negotiation is on for an EU-Thailand FTA and EU is pressurizing Thailand to accept similar stringent terms regarding DE and also to conclude the trade deal before beginning of 2015; but civil society groups in Thailand and Europe have demonstrated their concern for its negative impact on the Thai national health coverage system.³³ Among the non-Asian countries, developing or least developed countries like Morocco, Jordan, Peru have also had to include DE provisions in their national legal regime as a result of FTAs with USA, although they were not really prepared for it.

Impact of Data Exclusivity on Access to Medicine

Almost 90 per cent of the total value of world pharmaceutical production is accounted for by high income countries.³⁴ The figure shows that the high-income developed countries dominate in world pharmaceutical production. The share of those countries in the value of world pharmaceutical output increased gradually from 89.1% in 1985 to 92.9% in 1999 (ref. 35). In contrast, the figures of drug production in middle and low-income countries dropped from 7% and 3.9% in 1985 to 4.5% and 2.6% in 1999 respectively.³⁶ Among the high-income countries, the majority of world pharmaceutical production is accounted for by 5 major countries. The United States has been the biggest producer, accounting for almost one-third of total production (31%), followed by Japan (16%), France (8%), Germany (6%) and the United Kingdom (6%).³⁶ On the other hand, India's pharmaceutical market is the third largest in the world covering 8% of global production and supplies India's market with about

70% of its pharmaceutical products.³⁷ The market is quite well developed but highly fragmented. Not even the biggest producers account for more than 7% of the market share.³⁷ The market is constituted of 270 large R&D based pharmaceutical companies, 5,600 smaller licensed generics manufacturers and 3,000 companies involved in pharmaceutical production.³⁸ This is reflected in the low price of generics enabling drop in their prices in the range of 40–60% of the original drug price.³⁸ Thus, India is counted among the major drug exporters to developing countries. According to a PWC report, from a global perspective, India is responsible for 20% of global generic production. India produces 80% of drugs for HIV/AIDS as well as drugs for cancer and heart disease. The study reveals that 70% of patients who received medicines from India belong to 87 developing countries.³⁸ Only in Africa, there are more than 2.5 million AIDS patients who rely on generic drug production from India for their treatment. Medicins Sans Frontier (MSF) today relies overwhelmingly on affordable generic HIV/AIDS medicines produced in India to treat nearly 180,000 people in 20 countries, as well as use medicines from India to treat other diseases such as tuberculosis and malaria. MSF buys more than 80% of their HIV/AIDS drugs, and 25% of the drugs for malaria, tuberculosis, and antibiotics from India.³⁹ Moreover, approximately 50% of the essential medicines that United Nations Children's Emergency Fund (UNICEF) distributes in developing countries comes from India, while 75-80% of medicines distributed by International Dispensary Association are made in India.³⁹ India has played a pivotal role in supplying affordable generic versions of drugs throughout developing and least developed countries. A strict DE provision can hinder the supply of affordable generic medicines, although generics are not the ultimate answer to access to medicine because generic drugs are based on the originator one.

Data exclusivity provides protection of clinical test data and results submitted to regulatory authorities in order to confirm the safety and efficacy of pharmaceutical products. Therefore, if generic producers wished to produce generic drugs, they would not only have to provide bioequivalence tests and bioavailability tests but also conduct clinical tests. Most likely, this would result in increasing production costs, hence higher generic drug prices.³⁸ Data exclusivity, in principle, is applicable irrespective of the patent status of the drug, and hence will be

applicable to unpatented medicines, as well as medicines whose patent terms have expired. So, essentially it acts as an extra layer of protection for the originator companies. The negative side of the proposed DE would also make it virtually impossible to use compulsory licences for drug production in the case of urgent situations with public health, as opposed to patents.

Data exclusivity has a large impact on the price of the medicine. Following are a few examples of it.

- (1) As a part of the United States-Jordan FTA, Jordan implemented DE. A study conducted by Oxfam in 2007 found that of 103 medicines registered and launched since 2001 that had no patent protection in Jordan, at least 79% had no competition from a generic equivalent as a consequence of DE.⁴⁰ The study also found that prices of these DE protected medicines were up to 800% higher than in neighbouring Egypt.
- (2) A 2010 study by the Centre for Policy Analysis on Trade and Health determined that once Guatemala enacted DE, prices of some medicine rose as much as 846% - even though just a handful of them were under patent protection.⁴¹
- (3) Data exclusivity raises the price of medicines even when no patent exists. For example, in the US, the price of colchicine, a treatment used mainly for gout, rose more than 5,000% after DE law was enacted.⁴² Colchicine has been in use for thousands of years and costs almost nothing to produce, and cannot be patented. Therefore, generic formulations of the tablet have been widely available since the 19th century. However, a new monopoly on colchicine was created in 2009 when the US Food and Drugs Administration accepted clinical data from a one-week trial of the drug and granted data exclusivity to URL Pharma. URL Pharma subsequently sued to force other manufacturers off the market, and raised prices from US\$ 0.09 to 4.85 per pill.⁴²

Economic Rationale behind Data Exclusivity

In order to demonstrate a drug's efficacy and safety for its intended therapeutic use, it is necessary for the originator of the drug to conduct extensive testing on animals and humans in pre-clinical and clinical trials as well as toxicology, manufacturing feasibility and other scientific studies. The results of these tests and studies, which are proprietary, are contained in a registration dossier that is submitted to governmental

authorities to obtain marketing approval for the drug. The generation of this confidential registration data involves a substantial amount of time and expense for the originator. For example, research-based pharmaceutical companies in the United States invested US\$ 21.8 billion in R&D in 1998, a 10% increase over 1997 (ref. 43). With 40% of this R&D expenditures going to pre-clinical functions and 30% towards completing the Phase I, II, and III clinical trials required by the FDA, 70% of all R&D expenditure in the United States are targeted towards gaining regulatory approval. A new drug costs, on an average, US\$ 500 million and requires as long as 15 years to develop taking into account pre-clinical and clinical trial phases. Only three out of ten drugs introduced in the United States from 1980 - 1984 had returns higher than their average after-tax R&D costs. Comprehensive drug testing in the clinical trial stage alone can cost US\$ 150 million or more for a single medication and only 10% - 20% of drugs ever clear the full set of pre-clinical and clinical trials.⁴³

In stark contrast, a manufacturer of a generic alternative, if it is not required to generate its own test data to gain marketing approval, needs to invest only US\$ 1 million to launch a competitor drug, as long as it can demonstrate bioequivalency. When the latter applicant receives the benefit of the data generated by the originator without any investment on its part, the originator is placed at a significant commercial disadvantage. Such a situation undermines the investment potential existing even in countries with strong and effective patent protection, since the results of the originator's tests are immediately available to competitors at no cost. In addition, the burden is placed entirely on the originator to pursue any patent rights; under the data protection scenario, a product is only considered for marketing approval once the period of data protection has passed. Given the imbalance between the cost to the originator in gaining marketing approval for its drug and the copier's cost of coming on to the market, the research-based industry would have a reduced incentive, without such protection, to engage in the important R&D activities that will ultimately benefit patients through the availability of new and innovative drug therapies. The incentive for developing new drug therapies that is provided by a period of data exclusivity is especially critical when the new drug therapy is not patentable. The registrations of data are provided to the authorities in

confidence and are not meant to be referred to by third parties. If these data were immediately available to third parties, there would be no incentive for a company to generate these data in the first instance, unless the investment in terms of both time and costs were protected by other means. In many instances, a patent will cover the pharmaceutical product at issue. However, more and more compounds which are not patent protected (for whatever reason) are being developed and thus data exclusivity in some instances is the only available intellectual property right. It is important that governments protect the confidentiality of these data against its unauthorized use or disclosure in order to protect the proprietary interests of scientists and others and to maintain the economic incentives for further pharmaceutical research and development. However, because of a concern for avoiding repetitive tests and trials on animals and humans, governments have sought to limit the originator's proprietary data rights. Therefore, the USA and the EU have acknowledged the right of data protection for a certain fixed period of time. After the period has expired, reference to the data is permitted by generic companies. This compromise is viewed as protecting the investment of the originator, while at the same time preventing unnecessary repetitive tests and trials. Arguably, if a country had no data protection law at all, then the data submitted as part of a registration should never be permitted to be referred to by a generic company.

The period of data exclusivity is not fixed by the TRIPS Agreement. Earlier drafts of the TRIPS Agreement provided a minimum five year period of protection. However, this specific minimum time frame was removed from the final version and was expected to be sufficient to protect the originator's investment.

Thus, the generation of the data necessary for the original marketing approval requires a substantial investment of time, expertise, resources and money. The originators of the drug must be given an opportunity – and the incentive – to recoup the enormous costs involved in generating such data before a competitor is permitted to rely on those data for the approval of the generic alternative.

For example, had generic copies of Taxol, (paclitaxel), Bristol-Myers Squibb's (BMS) anti-cancer drug, which did not have any patents on its active ingredient, been approved immediately, BMS would not have had any incentive to incur the extensive costs (estimated at well in excess of

US\$ 500 million) to develop, test and bring Taxol to market.⁴³ The fact that both patent protection and DE provide incentives reflects the dual nature of the drug development process.

Exhaustion of Patent Term during Marketing Approval

Pharmaceutical inventions usually require human clinical testing in order to obtain regulatory approval to market the new product. Often a patent application is filed before the invention undergoes human testing, but sometimes a human clinical trial may be started, or even completed before the application is filed. While US patent law provides that a 'public use' of the invention within the US can constitute prior art, a clinical trial often does not qualify as prior art, either because it was not 'public' (e.g., it was conducted under confidentiality) or it qualifies as 'experimental use'. The European patent law takes a stricter view of prior art than the USA in many ways, applying an absolute novelty standard with no grace period.

One strong contention in favour of DE is that, the usual patent term of 20 years is exhausted during the clinical trials and marketing approval of the patented drug. If the whole process takes on an average 10-15 years the patent holder company has very little of the effective patent term left to commercially benefit and recoup the huge investment in the research, development and clinical trials. Then the obvious question will arise - whether clinical trials can be initiated before patent application or patent grant; which is not the usual and regular practice in the industry. The reason behind this is the fact that initiation of clinical trial is related with the loss of novelty issue which may end up with the rejection of patent application based on the above mentioned ground.

Debate against Data Exclusivity: Concern for Access to Medicine

Although the economic rationale behind DE and the support of developed countries is evident, this is only one side of the coin. The world consists of not only developed countries; rather it is made up of large number of developing and least developed countries. The other side of the coin shows a grim picture where millions live below the poverty line without proper house, food, safe drinking water, basic education and medical facilities. For them, buying costly medicines is a luxury. Unfortunately, they are a subset of human population suffering more from the life threatening

infections as well as cancer; the cause of which is largely associated with the poor socio-economic condition of the society. Vast populations of Asia, Africa, Latin America are included in this subset. Irrespective of awareness among the community of their legal and constitutional rights, it is no less a fact that they are eligible for proper access to life saving medicine. Neither personal capacity nor the ability of the government permits them to buy costly original patented drugs; hence they are largely dependent on the cheaper generic versions. But the market of generic drugs is significantly affected by the DE provisions. The effects are twofold; market entry of generic versions are delayed because of DE provisions, and clinical trials if executed by the generic companies will increase the cost of generics manifold thus putting generics beyond the reach of people/government of developing or least developed countries.

Conclusion

The main points of discussion here are the prevention of unfair commercial use of the originator's test data and proper access of life saving medicine in spite of all protection measures. The point to be considered is that R&D by originator companies is the foundation of the invention of medicines for mankind. Originator companies invent the original molecules, the safety and efficacy of which are validated by clinical trials. Only if an original molecule exists can a generic medicine producer make a similar product and only then will the question of reliance on the originator's test data arise. Therefore no R&D by originator companies will mean no original drug molecule and hence no generic medicine. Scientific R&D activities are imperative along with clinical validation of safety and efficacy of medicines. At the same time, proper incentive to originator companies in the form of protection through DE provisions cannot be denied. But, imposition of DE implementation on each and every country irrespective of their socio-economic capacity and pharmaceutical manufacturing capability is creating a state of imbalance, with the result that accessibility to medicines is at stake.

To achieve a balance between the economic interest of the originator companies and public interest towards access to medicine, there is a need to get alternative approaches, like preferential pricing, tax benefits, special benefits from the originator companies for patients of least developed countries,

etc. Generic companies should be encouraged to enter into research based medicinal product formulation, so that the underprivileged population of the world will not be dependent on generic medicine only. These changes usually take lot of time, but given the grave situation of poorer subset of population, who are struggling hard to survive with HIV/AIDS, tuberculosis, malaria or other life threatening infections and/or cancer, the changes have to happen quickly in a specified time frame. The alternative way of treatment for many diseases are available in traditional medicinal knowledge, proper and effective use of that alternative medicine may be possible along with the mainstream medicine in the same hospital setup; more effectivity can be achieved by planning proper R&D activities for the improvement and validation of alternative medicine. The TRIPS Agreement provides flexibility for Member Countries to implement the provisions according to national need in terms of protection of public health. Proper utilization of that flexibility has to be made; the pressure to implement TRIPS-plus measures through FTAs in the national legal regime should be reduced, only then can the world go towards a better tomorrow where most or all of the patients will get the access to medicine and fall prey to inadequate consideration of public health requirements.

Acknowledgement

The author thanks Prof (Dr) T Ramakrishna, Prof (Dr) V C Vivekanandan for their invaluable guidance through the last few years of this research.

References

- 1 Simon N G, Drug Discovery and Development, http://www.lehigh.edu/~inbios21/PDF/Fall2011/Simon_09162011.pdf (accessed 12 August 2014).
- 2 Federal Insecticides, Fungicides & Rodenticides Act, 1947, <http://www.epa.gov/agriculture/lfra.html> (accessed 20 October 2013).
- 3 Hatch-Waxman Act, 1984, <http://www.gpo.gov/fdsys/pkg/USCODE-2010-title21/html/USCODE-2010-title21-chap9-subchapV-partA-sec355.htm> (accessed 20 October 2013); see also Clift C, Data protection and data exclusivity in pharmaceuticals and agrochemicals, *IP Handbook of Best Practices*, Chapter 4.9, p. 433, <http://www.iphandbook.org/handbook/chPDFs/ch04/ipHandbook-Ch%2004%2009%20Clift%20Data%20Protection%20and%20Exclusivity.pdf> (accessed 20 October 2013).
- 4 Clift C, Data protection and data exclusivity in pharmaceuticals and agrochemicals, *IP Handbook of Best Practices*, Chapter 4.9, p. 433, <http://www.iphandbook.org/handbook/chPDFs/ch04/ipHandbook-Ch%2004%2009%20Clift%20Data%20Protection%20and%20Exclusivity.pdf> (accessed 20 October 2013).

- 5 The Federal Food, Drug and Cosmetic Act is based on the United States Government Printing Office Federal Digital System (FDsys) version of the United States Code, 2006 Edition, Supplement 3 current through January 2010 <http://www.fda.gov/regulatoryinformation/legislation/federalfooddrugandcosmeticactfdca/> (accessed 20 October 2013).
- 6 Patient Protection and Affordable Care Act, 2009, <http://www.gpo.gov/fdsys/pkg/BILLS-111hr3590enr/pdf/BILLS-111hr3590enr.pdf> (accessed 11 October 2013).
- 7 Council Directive 65/65/EEC of 26 January 1965 on the approximation of provisions laid down by Law, Regulation or Administrative Action relating to proprietary medicinal products, <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CELEX:31965L0065:EN:HTML> (accessed 20 October 2013).
- 8 Council Directive 87/21/EEC of 22 December 1986 amending Directive 65/65/EEC on the approximation of provisions laid down by law, regulation or administrative action relating to proprietary medicinal products <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CELEX:31987L0021:EN:HTML> (accessed 20 October 2013).
- 9 IFPMA Report on Data Exclusivity: Encouraging development of new medicines, International Federation of Pharmaceutical Manufacturers & Associations, July 2011, http://www.ifpma.org/fileadmin/content/Publication/IFPMA_2011_Data_Exclusivity_En_Web.pdf (accessed 20 October 2013).
- 10 Fries Z, Data exclusivity, market production and paediatric rewards, European Medicines Agency, April 2013, http://www.ema.europa.eu/docs/en_GB/document_library/Presentation/2013/05/WC500143122.pdf (accessed 13 August 2014).
- 11 Supplementary protection certificates (SPCs), Workshop I, 42nd AIPPI Congress, Paris, October 2010, https://www.aippi.org/download/paris10/pres/Part_ABourgouin_Pharma1_part%20one_041010.pdf (accessed 20 October 2013).
- 12 Regulation (EC) no 1901/2006 of the European Council, December 2006 on Medicinal Products for Paediatric Use, <http://eurlex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2006:378:0001:0019:en:PDF> (accessed 20 October 2013).
- 13 Regulation (EC) No 141/2000 of the European Parliament and of The Council of 16 December 1999 on Orphan Medicinal Products, <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2000:018:0001:0005:en:PDF> (accessed 10 July 2014).
- 14 A Guideline on Summary of Product Characteristics by European Commission, Enterprise and Industry Directorate-General, September 2009, http://ec.europa.eu/health/files/eudralex/vol2/c/smpc_guideline_rev2_en.pdf (accessed 11 October 2013).
- 15 Article 18.3, Japanese Drug Regulation.
- 16 Article 31.1, Regulation of Drug Administration Law of China, 2002.
- 17 Article 31.2, Regulation of Drug Administration Law of China, 2002.
- 18 Akalephan C, Extension of market exclusivity and its impact on the accessibility to essential medicines, and drug expense in Thailand: Analysis of the effect of TRIPS-plus proposal, *Health Policy*, 91 (2009) 174-182.
- 19 Park K N *et al.*, South Korea's patent – approval linkage system, IP in the life sciences industries 2014, www.iam-magazine.com (accessed 23 May 2014).
- 20 Miller C, Patent term extensions and regulatory exclusivities for pharmaceuticals in Asia and South America, 2012, Morrison & Foerster Quarterly News, <http://media.mofo.com/files/Uploads/Images/120627-Intellectual-Property-Quarterly-Newsletter-Summer-2012.pdf> (accessed 2 February 2013).
- 21 Part II — Standards concerning the availability, scope and use of intellectual property rights, Section 7 of TRIPS Agreement, http://www.wto.org/english/docs_e/legal_e/27-trips_04d_e.htm (accessed 21 October 2013).
- 22 Reddy S & Sandhu G S, Report on Steps to be taken by Government of India in the context of Data Protection Provisions of Article 39.3 of TRIPS Agreement, <http://chemicals.nic.in/DPBooklet.pdf> (accessed 10 August 2014).
- 23 The domino effect of US FTAs: Public health groups, members of Congress claim CAFTA will choke access to medicines, *Intellectual Property Watch*, 4 April 2004, <http://www.ip-watch.org/weblog/index.php?p=8&res=1024&print=0> (accessed 13 December 2013).
- 24 Abbott F M, The WTO medicines decisions: World pharmaceutical trade and the protection of public health, *American Journal of International Law*, 99 (2005) 350.
- 25 McMahon R, The rise in bilateral free trade agreements, Council on Foreign Relations, 13 June 2006, <http://www.cfr.org/publications/10890/> (accessed 13 December 2013).
- 26 Correa C M, Protection of data submitted for the registration of pharmaceuticals: implementing the standards of the TRIPS Agreement, South Centre, Geneva, 2002.
- 27 Kuanpoth J & Duong L H, Legal and trade issues related to access to affordable anti-retroviral drugs for people living with HIV/AIDS in Vietnam, Ford Foundation, Hanoi, 2004.
- 28 Article 16.8, US-Singapore FTA.
- 29 Galantucci R, Data protection in US-Malaysia Free Trade Agreement: New barriers to market access to generic drug manufacturers, *Fordham Intellectual Property, Media and Entertainment Law Journal*, 17 (4) (2007) 1085-1123.
- 30 Article 16.8, US-Singapore FTA; see also Galantucci R, Data protection in US-Malaysia Free Trade Agreement: New barriers to market access to generic drug manufacturers, *Fordham Intellectual Property, Media and Entertainment Law Journal*, 17 (4) (2007) 1096.
- 31 Wouters J, Some critical issues in EU-India free trade agreement negotiations, Working Paper No 102, February 2013, https://ghum.kuleuven.be/ggs/publications/working_papers/new_series/wp101-110/wp102-wouters-goddeeris-natens.pdf (accessed 2 February 2013).
- 32 The EU-India free trade agreement and access to medicines, <http://www.twinside.org.sg/title2/resurgence/2012/259/cover04.htm> (accessed 19 October 2013).
- 33 Cronin D, Strong EU Trade provisions on IP seen as threat to poor nations' medicines access, 18 February 2009, <http://www.ip-watch.org/2009/02/18/strong-eu-trade-provisions-on-ip-seen-as-threat-to-poor-nations%E2%80%99-medicines-access/> (accessed 10 October 2013).
- 34 Mellema T, The EU-Thailand FTA: What fate for access to medicine?, 12 December 2013, <http://www.ip-watch.org/2013/12/12/the-eu-thailand-fta-what-fate-for-access-to-medicines/> (accessed 10 October 2013).
- 35 This is based on the World Bank classification of countries according to the level of income as follow: (i) High-income: GNP per capita of US\$ 9,361 or more, (ii) Middle-income: GNP per capita of US\$ 761- US\$ 9,360, and (iii) Low-income GNP per capita of US\$ 76 or less in 1999.
- 36 Basheer S, The potency of a middle path, *Livemint*, 9 July 2008, <http://www.livemint.com/2008/07/09215015/The-potency-of-a-middle-path.html> (accessed 19 November 2013).

- 37 The World Medicines Situation, World Health Organisation, WHO/EDM/PAR/2004.5, 2004.
- 38 The Indian pharmaceutical industry: Collaboration for growth, KPMG Report, 2006, <https://www.in.kpmg.com/pdf/Indian%20Pharma%20Outlook.pdf> (accessed 20 December 2013).
- 39 The Indian pharmaceutical market, an ESI International Study, 2010, http://www.esi-intl.com.br/sitecore/content/india/resources/vertical%20reports/~/_media/411664EFB4244D70B26902573DF0026F.ashx (accessed 20 December 2013).
- 40 Kennell K, Antiretroviral drugs to suppress the replication of HIV, <http://www.guardian.co.uk/society/sarah-boseley-global-health/2012/feb/10/hiv-infection-pharmaceuticals-industry> (accessed 20 December 2013).
- 41 All costs, no benefits: How TRIPS-plus intellectual property rules in the US-Jordan FTA affect access to medicines, Oxfam Briefing Paper, March 2007, <http://www.oxfam.org/sites/www.oxfam.org/files/all%20costs,%20no%20benefits.pdf> (accessed 20 November 2013).
- 42 How the trans-Pacific partnership agreement threatens access to medicines, Report, Doctors Without Borders, Campaign for Access to Essential Medicines, TPP Issue Brief, September 2011, http://www.msfacecess.org/sites/default/files/MSF_assets/Access/Docs/Access_Briefing_TPP_ENG_2011.pdf (accessed 20 November 2013).
- 43 Submission to the United States House of Representatives Committee on ways and means regarding the April 3, 2014 Hearing on President Obama's trade policy agenda, Report, Doctors Without Borders, April 2014, http://waysand-means.house.gov/uploadedfiles/doctors_without_borders_040314tr.pdf (accessed 5 May 2014).
- 44 How the trans-Pacific partnership agreement threatens access to medicines, Report, Doctors Without Borders, Campaign for Access to Essential Medicines, TPP Issue Brief, September 2011, http://www.msfacecess.org/sites/default/files/MSF_assets/Access/Docs/Access_Briefing_TPP_ENG_2011.pdf (accessed 20 November 2013).