ORPHAN DISEASE AND PHARMACEUTICAL PATENT: APPROACHING ACCESS TO MEDICINE FOR PUBLIC HEALTH

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ABSTRACT

This paper will identify the prevailing health problem caused by orphan diseases throughout developing countries and the crisis of orphan drugs for curing it as the patent is seen as great obstacle for drug distribution and public access. The thesis will also specify the international agreements concerning right to public health and its implementation associated with TRIPS Agreement under World Trade Organization regulatory framework. A comparative study of the legislative frameworks of both developed and developing countries will reveal to what extent United States of America, Canada, the European Union, Brazil, Russia, India, China and South Africa conformed with patent protection exceptions arising from international patent law to protect public health by ensuring available and easy access to life safeguarding medicine.

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ABBREVIATIONS

AAI - Accelerated Access Initiative
AIDS – Acquired Immune Deficiency Syndrome
AMC – Advanced Market Commitment
BRICS - Brazil, Russia, India, China and South Africa
EC – European Commission
EMEA – European Medicine Evaluation Board
EU – European Union
FDA – Food and Drugs Act
FTA – Free Trade Agreement
GATT – General Agreement On Tariffs and Trade- 1947
GSP – Generalized System of Preference
ICCPR – International Covenant on Civil and Political Rights
ICESCR – International Covenant on Economic, Social and Cultural Rights
IP – Intellectual Property
LDC – Least Developed Country
MMV – Medicines for Malaria Venture
MRDT – Medical Research and Development Treaty
MSE – Medicines Sans Frontieres
NGO – Non Governmental Organization
NIH – National Institute of Health
NDRA – National Drug Regulatory Authority
NORD – National Organization of Rare Disorder
ODA – Orphan Drug Act
ODL – Orphan Drug Legislation
PPP – Public- Private Partnership
PTO – Patent and Trade Office
R & D – Research and Development
ROI – Return on Investment
TRIPS - Trade Related Intellectual Property Rights
UNICEF – United Nations
UDHR – Universal Declaration of Human Rights
WIPO – World Intellectual Property Organization
WTO – World Trade Organization.

INTRODUCTION

One of major health problem in both developed and developing countries is the spread of orphan disease and dearth of orphan drug. It is problem in a sense that orphan disease and drug is ignored and still a hidden matter where a few people are aware of it. The pharmaceutical industries have not adopted orphan disease in their strategic course and provide little financial incentive to make and market new orphan drug to prevent and cure it. Another striking feature is that orphan disease is rare as it is far more prevalent in developing countries than in the developed world. Mostly in least develop countries in Asia, Africa and Latin America these disease is prevailing vast and the governments are incapable to cure it through providing proper medicines and the research and development of those

disease depend on the hands of most developed pharmaceutical industries of the developed world. The world-known pharmaceutical industries never pay attention to invent new orphan drugs as the market of selling it is in the LDCs which will give less profit and outcome as against their invention. The thesis entitled as "Orphan Disease And Pharmaceutical Patent: Approaching Access To Medicine For Public Health" is the vast description of this critical problem that a lot of poor people are facing. Part one of the thesis explains the meaning of orphan disease and orphan drug with a standard description of present orphan drug strategy taken by the most pharmaceutical giants also with some incentives taken by different government of the world. Part two includes the correlation between pharmaceutical patent and orphan drugs that make the problems more complicated. Also it interprets the orphan disease and orphan drug policy inconformity with patent provision in the states of U.S.A., Canada, European Union, Brazil, Russia, India, China and South Africa. Medicine is so costly in developing country to cure the orphan disease and that is stated in this part. The patent laws specified in TRIPS are thoroughly discussed mentioning the national level application in developing countries. Part three relates to the matter of human rights laws of both national and international level that permits the assurance of public health in vast to all. The present human right laws relating to health and medicine is ineffective because of lack of enforcing procedure and government's poor policy. Here the thesis clarifies all relevant human right provisions that are still useless for effective mechanism and organizations. At last the thesis is ended with its findings as well as gives recommendations for future plan.

ORPHAN DISEASE AND PHARMACEUTICAL PATENT: APPROACHING ACCESS TO MEDICINE FOR PUBLIC HEALTH

PART ONE:
ORPHAN DISEASE AND ORPHAN DRUG:

No satisfactory definition of 'orphan disease' is found yet. The words orphan disease is used to describe diseases that are neglected by doctors and affect only small number of individuals.[1] In the USA it is defined as one that affects fewer than 200000 individuals, but in Japan the number is 50000 and in Australia 2000.[2] These numbers clearly relate to the population sizes of these countries but it varies from about 1 to 8 in 10000. The

1 J K Aronson, "Rare Diseases and Orphan Drugs", British Journal of Clinical Pharmacology, March-2006; 61 (3); 243-245, doi: 10. 1111/j. 1365-2125. 2006. 0261. X. PMCID: PMC 1885017. Copyright © 2006 Blackwell Publishing Ltd. See Van Weely S, Leufkens HGM, "Orphan Diseases. Background paper. In: priority medicines for Europe and the world. A public health approach to innovation", http://mednet3.who.int/prioritymeds/report/index.htm=c (last visited on 4th January, 2009).

2 A. Lavandeira, "Orphan Drugs: Legal aspects, current situation", Haemophilia, 2002; 8 (3): 194-8.

European Community definition is less than 5 in 10000. The WHO has suggested a frequency of less than 6.5-10 in 10000. Some genetic disorders and diseases are regarded as being rare originated from 'orphan virus'[1] having no link to a recognized disease. As a group they have nothing in common apart from their rarity, but the lists vary strikingly in length; for example, that published by the US National Organization for Rare Disorders contains about 1200 items,[2] while NIH's Office of Rare Diseases publishes a list of over 6000, ranging from Aagenaes syndrome to Zuska's disease.[3] Orphan disease is also known as neglected and rare disease and the drug used to treat it is called as orphan drug[4] and they are likely to be unprofitable either because the patient population is too small or because the disease is prevalent only in developing nations.[5] Even drugs targeting Chagas disease, which threatens a quarter of the population of Latin America, or African trypanosomiasis, which affects nearly 300000 individuals per year, are considered orphan because of their low profitability.[6] Statistic shows that the number of patients affected by a rare disease could be about 30 million in Europe and 25 million in North America.[7] Six to eight percent of the total population in Europe has a rare disease.[8] But in 20th century, few drugs were developed to treat rare disorders and diseases because the small patient populations made it difficult for pharmaceutical companies to recoup their research and development costs[9] and despite the urgent health need for these medicines, they came to be known as 'orphan' because companies were not

1 JL. Melnick, "Application of tissue culture methods to epidemiological studies of poliomyelitis", American Journal of Public Health. 1954; 44 (5): 571-80.

2 National Organization for Rare Disorders. 26th January 2006. http://www.rarediseases.org/search/rdblist.html (last visited on 5th May, 2009).

3 Office of Rare Diseases. National Institutes of Health. Rare diseases terms. 26th January 2006. http://rarediseases.info.nih.gov/asp/diseases/diseases.asp?this=Z#toplist (last visited on 4th April, 2009).

4 For example see RJ. Hift and PN. Meissner, "An analysis of 112 acute porphyric attacks in Cape Town, South Africa: Evidence that acute intermittent porphyria and variegate porphyria differ in susceptibility and severity", Medicine (Baltimore), 2005; 84 (1): 48-60.

5 DM Davis, "Orphan drugs", Lancet. 1983; 1: 290-291.

6 A Schieppati, G Remuzzi and S Garattini, "Modulating the profit motive to meet needs of the less-developed world", Lancet. 2001; 358: 1638-1641.

7 US Food and Drug Administration. Orphan Drug Act, Pub L. No. 97-414, 96 Stat. 2049. 1982. http://www.fda.gov/orphan/oda.htm (last visited on 02-06-2009). See European Commission Regulation (EC) No 141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products. http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/homev1.htm (last visited on 7th February, 2009). See OrphanXchange, "About orphan drugs", http: 'www.orphanxchange.org/OXC/cgi-bin/oxc_about_drug.php (last visited on 3rd July, 2009). See Wastfelt M, Fadeel B, Henter J-I, "A journey of hope: Lessons learned from studies on rare diseases and orphan drugs", J Intern Med 2006; 1-10. See 21 U.S.C. §360ee (2004).

8 EURORDIS-What is a rare disease? http://www.eurordis.org/article.php3?id_article=252 . (last visited on 10th May, 2009).

9 See 21 U.S.C. § 360aa (2004).

interested in 'adopting' them[1] and the developing nations of Asia, Africa and Latin America are too poor to pay drug prices that render the new drug profitable for the patent-holding manufacturer.[2]

80% rare diseases are originated genetically in the form of either monogenic or polygenic, having life-threatening or chronically debilitating conditions.[3] The other rare diseases are characterized as infectious, auto-immune or poisoning, allergic proliferated by chemicals and radiations having been severe, chronic, degenerative and highly painful. Absence of reliable epidemiological data[4] and quantitative source[5] in regional, national and international level makes it more difficult to assess the true nature, origin, cause of spreading, the diagnosis, the sufferings and cure of rare diseases. Only Netherlands has made success of specifying rare diseases data where the number of patients with several rare cancers is known due to the nationwide Dutch network and registry system[6] and revealing also 1500 haemophilia patients, between 100 and 150 Gaucher patients and 4 with aspartylglucosaminuria.[7] Rapidly the numbers of rare diseases are increasing in the both developed and developing countries for which hardly any therapy exists.[8]

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1 Carol Rados, "Orphan Products: Hope for People With Rare Diseases", FDA Consumer Mag., Nov. –Dec. 2003, at 12, at http://www.fda.gov/fdac/features/2003/603_orphan.html (last visited on 11th February, 2009).

2 CA Gericke, A Riesberg and R Busse, "Ethical issues in funding(last visited on) orphan drug research and development", J Med Ethics 2004.

3 Rados, supra note 12, at 11.

4 Registratie van zeldzame ziekten. Report of the Working group on Epidemiology and patient registration, a working group of the Dutch Steering Committee on Orphan drugs, August 2004.

5 WHO- Genes and human disease. http://www.who.int/genomics/public/geneticdiseases/en/index.html (last visited on 10th December, 2008). See Dionisi-Vici C, Rizzo C, Burlina AB, Caruso U, Sabetta G, Uziel G, Abeni D., "Inborn errors of metabolism in the Italian pediatric population: a national retrospective survey", J Pediatr. 2002 March; 140 (3): 321-327. See also WHO- regional office for Europe, "Children's health and environment: Cancer", http://www.euro.who.int/childrenhealthenv/Risks/CancerTop (last visited on 6th December, 2008).

6 PALGA, The nationwide network and registry of histo- and cytopathology in the Netherlands. http://www.palga.nl/ (last visited on 2nd January, 2009).

7 Dutch Association of Haemophilia patients (NVHP)/Nederlandse Vereniging van Hemofilie-Patienten. http://www.nvhp.nl (last visited on 20th December, 2008). See Dutch Gaucher Society/Gaucher Vereniging Nederland. http://wwwgaucher.nl/(last visited on 10th December, 2008). See also Apartylglucosaminuria. http://www.weesgeneesmiddelen.nl/?menu=0&id=152 (last visited on 22nd December, 2008).

8 Lorenz B, Preising M., "Usher syndrome", Orphanet Encyclopedia, March 2004; 8 pages; http://www.orpha.et/data/patho/GB/uk-Usher.pdf (last visited on 2nd February, 2009). See Faivre L, Cormiere-Daire V., "Progeria", Orphanet Encyclopedia, May 2003; 3 pages; http://www.orpha.et/data/patho/GB/uk-progeria.pdf (last visited on 30th March, 2009). See also Van der Graaff, M., "Amyotrophic lateral sclerosis", Orphanet Encyclopedia, January 2003; 4 pages; http://www.orpha.et/data/patho/GB/uk-ALS.pdf

WHEN DOES A DISEASE BECOME ORPHAN OR RARE?

The following factors are responsible for the advent of rare disease in any place of the world; such as-

Ignorance of experts: At present 1300 rare diseases are medically well identified and described; others have inappropriate descriptions because of doctor's lack experience and proper training. General practitioners and medical doctors do not know and can't be expected to know the symptoms of the many rare disorders.[1] Lack of knowledge associated with orphan diseases creates a wide range of problems which include:

- delay in making the correct diagnosis resulting in patients often receiving inappropriate treatment, unnecessary tests and investigations, and delays in commencing appropriate treatment;
- lack of information for patients and healthcare professionals about the disease itself and where to obtain further help/information;
- lack of scientific knowledge creating difficulties in developing therapeutic tools and defining the best therapeutic strategy for an individual patient;
- inequities in availability of treatment and care- Innovative treatments are often unevenly available due to a lack of experience of treating physicians and an absence of treatment consensus recommendations;
- lack of appropriate quality healthcare- Frequently optimal treatment of rare diseases requires the coordinated efforts of several professionals, e.g. doctors, physiotherapist, nutritionist, psychologist, etc;
- social consequences- Living with a rare disease has implications in all areas of life (school, work or leisure), and particularly family life.

Insufficient information: Lack of sufficient information and its dissemination among developed and developing countries regarding the origin, source, symptom, characteristics of rare diseases are the main hindrance for developing new treatment, research, clinical methods of finding the cure.

Improper Diagnosis: Even for now many of orphan diseases have no proper diagnosis tools due to a lack of research by the concerned authorities. Consequently doctors and scientists are unable to discover the cause and natural history of the disease and the condition of patients suffering from are deteriorating gradually in the whole world today. Most treatment and diagnosis of rare diseases is presently clinical based rather than fostering genetic and biological research due to ignorance of the physician, absence of centers of expertise and unavailability of modern techniques. Absence of advanced medical theory and effective medicine for prevention of orphan diseases leads to late diagnosis and ultimately it brings negative outcome for

(last visited on 11th December, 2008).

1 Nispen RMA van, Rijken PM, Heijmans MJWM., 'Leven met een zeldzame chronische aandoening: Ervaringen van patiënten in de zorg en het dagelijks leven. Nivel', 2003, ISBN 90-69056-14-3, at 148.

all, where as it is urgent to cure soon before it infects others. For example, the incidence of PKU (phenylketonuria) in Europe is about 1 in 12000. Prevention of the burden of disease of this disease has been seen as being that important that PKU has been included in screening programs of several countries to be sure that early diagnosis can lead to early intervention.[1]

Default registration: Lack of modern registration system regarding the history and report of orphan diseases is seemed as main obstacle of proper diagnosis and treatment. This is true not only for the developing countries but also for the same in developed countries as the pharmaceutical companies, governmental institutions, NGOs, private organizations concerning to this matter are paying less attention on it. The studies that are available mainly concern diseases for which a treatment is available or is being developed.[2]

Absence of pharmaceutical research: It is absolutely true that the research, procedure, method and process for inventing and developing new medical product for treatment and cure of rare diseases is difficult, crucial, expensive and time consuming because orphan diseases infect only small amount of people of a specific area of any region where that particular environment, weather, atmosphere, the nature and quality of soil, water, food, animals and specially the hereditary genetic factor played the most important role. The developed pharmaceutical companies of the world pays a little amount of attention to these rare disease as it seems to them unprofitable for marketing the drugs only for that particular area. Orphan drugs are always costly the developing countries are not able to afford treatment with orphan drugs for under-use.[3] A survey in EU Member states has shown that the availability and pricing is clearly different in these countries. So orphan diseases are neglected due to lack of orphan drugs. As a result "more than 90% of all death and suffering from infectious diseases

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1 Orphanet database: http://www.orpha.net, (last visited on 2nd February, 2009). See also Phenylketonuria: Screening and Management. NIH Consens Statement 2000 October 16-18; 17(3):1-28.

2 Maaswinkel-Mooij P, Hollak C, van Eysden-Plaisier M, Prins M, Aerts H, Poll R., "The natural course of Gaucher disease in The Netherlands; implications for monitoring of disease manifestations", J Inherit Metab Dis 2000 Feb;23(1):77-82. See Van den Hout HM, Hop W, van Diggelen OP, Smeitink JA, Smit GP, Poll-The BT, Bakker HD, Loonen MC, de Klerk JB, Reuser AJ, van der Ploeg AT, "The natural course of infantile Pompe's disease: 20 original cases compared with 133 cases from the literature", Pediatrics 2003 Aug;112(2):332-340. See Questionnaires. http://www.worldpompe.org/question.html (last visited on 3rd March, 2009). See Pitt DB, Danks DM.J., "The natural history of untreated phenylketonuria over 20 years", Paediatr Child Health 1991 Jun; 27(3):189-190. See Haverkamp LJ, Appel V, Appel SH., 'Natural history of amyotrophic lateral sclerosis in a database population. Validation of a scoring system and a model for survival prediction', Brain 1995 Jun; 118 (Pt 3):707-719.

3 European Orphan Drug Survey, prices and availability. http://www.eurordis.org/article.php3?id_article=487 (last visited on 5th February, 2009). See EMEA - Report on the first 3-year mandate of the Committee for Orphan Medicinal Products (COMP) (April 2000-April 2003).

occurs in the developing world; some of the reasons are that life-saving essential medicines are either too expensive or are not available because they are not seen as financially viable, or because there is virtually no new research and development for priority tropical diseases."[1]

Diagnosis priority: The quality of life of patients with rare diseases are worse in comparison to other more prevalent diseases[2] due to late diagnosis, lack of understanding and inadequate care which helps to spread the germs in other classes of people easily.

ORPHAN DRUG STRATEGY

Public awareness about the difficulties of patients with rare diseases was first raised by the report of the National Commission on Orphan Disease of the US Government in 1989[3] and assessment of the prevalence of rare diseases was attempted first by the European Organization for Rare Diseases (Eurordis), and Orphanet, with the support of the European Commission.[4] Rare disease are now included as priorities in public-health plans, and research-funding programs in Europe and the USA are increasingly promoting basic and clinical research on these disorders.[5] USA passed Orphan Drug Act in 1983[6] and the EU adopted Orphan Drug Regulation No 147/2000 for research, development and market approval of designated orphan medicinal products.[7] To collaborate internationally to address these problems and their treatments the International Conference on Rare Diseases and Orphan Drugs was first held in 2005 in Stockholm, Sweden, covering a range of issues with support from the Office of Rare Diseases at

1 Speech of James Orbinski, the president of Médecins Sans Frontières (MSF) on receiving the 1999 Nobel Prize for Peace on behalf of the Drugs for Neglected Diseases initiative (DNDi). Source, Declan Butler, "Raiding the medicine cabinet".

2 Informatie voor mensen met een zeldzame aandoening: een onderzoek naar de beschikbare informatie, knelpunten en oplossingen. VSOP 2002.

3 United States Department of Health and Human Services, Public Health Service, Office of the Assistant Secretary for Health. Report of the National Commission on Orphan Diseases. Rockville, MD: Office of the Assistant Secretary for Health, 1989.

4 Orphanet. Rare diseases in numbers: preliminary report from an on going bibliographic study initiated by Eurordis in partnership with Orphanet. http://www.orpha.net/actor/Orphanews/2005/doc/Rare_Diseases_in_Numbers.pdf, (last visited on 10th March, 2009).

5 Schieppati A, Henter J-I, Daina E, Aperia A, "Why rare diseases are an important medical and social issue", Lancet 2008; 371: 2039-41. See Haffner ME, Torrent-Farnell J, Maher PD., "Does orphan drug legislation really answer patients' need?", Lancet 2008; 371: 2041-44. See Fischer A, Cavazzana-Calvo M, "Gene therapy for inherited diseases", Lancet 2008; 371: 2044-47. See Ayme S, Kole A, Groft S, "Empowerment of patients: lessons from the rare diseases community", Lancet 2008; 371: 2048-51. See Buckley BM, "Clinical trials of orphan medicines", Lancet 2008; 371: 2051-55.

6 Orphan Drugs Act, 21 U.S.C. § 360aa et seq (2004).

7 Regulation (EC) No 141/2000 of the European Parliament and of the council of 16 December 1999 on orphan medicinal products. http://pharmacos.eudra.org/F2/orphanmp/doc/141_2000/141_2000_en.pdf (last visited on 20th June, 2009).

the National Institutes of Health, USA, and the European Commission.[1] It is true that the development of medicines over the past several decades may be considered in some aspects as a "public-private partnership": in return for patents, patent extensions, exclusivity of licensing, research and development grants, "orphan" drug legislation, and direct subsidies provided by health care systems (public and private), the pharmaceutical industry develops new drugs in an environment that runs from regulated (Europe) to essentially free market (United States).[2] But it is confined to only developed states and medicine improvements have not been distributed equally without setting set up to tackle the diseases of the poor world. The numbers speak for themselves: of the approximately 1,400 new drugs approved between 1975 and 1999 only 1% was specifically indicated for tropical diseases and only two for tuberculosis.[3] Little is being done for malaria, and virtually nothing for the really neglected diseases such as sleeping sickness, Chagas's disease, and leishmaniasis. The market-based approach of medicines development has not worked for these diseases and will not work for these diseases: they have simply not been on the research agenda of private companies who are not in the business of develop in medicines for people who cannot pay as orphan drugs in poor countries are either ineffective or too expensive.[4] However poor countries often lack or have an inadequate infrastructure capable of delivering medicine services: hence, the creation of a public health infrastructure and a focus on prevention is a critical stage in health service development in the poor world.[5] The provision of health services and care, including the public health infrastructure and the delivery of medicines must be a government responsibility: the rich world must assume the financial and moral responsibility for improving the health of the poor world. Because the notion has evolved that patients suffering from rare conditions should be entitled to the same quality of treatment as other patients with more frequently occurring disorders (Regulation EC 141/2000; preamble 7, article 3.1b).[6] The major pharmaceutical companies are increasing their efforts to defend existing markets through legal challenges to generic manufacturers, through major advertising campaigns direct to the public as more highly

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1 Wastfelt M, Fadeel B, Henter J-I. A journey of hope: lessons learned from studies on rare diseases and orphan drugs. J Intern Med 2006; 260: 1–10.

2 David J. Triggle, "Medicines in the 21st Century Or Pills, Politics, Potions, and Profits: Where Is Public Policy?", Strategic Commentary, Drug Development Research 59:269–291 (2003), Published online in Wiley Inter Science (www.interscience. wiley.com) DOI: 10.1002/ddr.10282

3 Yamey G., "The world's most neglected diseases", 2002, Br Med J 325:176–177.

4 Jacobs S., "An oral drug for leishmaniasis", 2002, N Engl J Med 347:1737–1738. See Sundar S, Jha TK, Thakur CP, Engel J, Sindermann H, Fischer C, Junge K, Bryceson A,. Berman J., "Oral miltefisone for Indian visceral leishmaniasis", 2002, N Engl J Med 347:1739–1746.

5 Specter M., "India's plague", 2001, New Yorker Dec 17:74–85.

6 Regulation (EC) No 141/2000 of the European Parliament and of the council of 16 December 1999 on orphan medicinal products. http://pharmacos.eudra.org/F2/orphanmp/doc/141_2000/141_2000_en.pdf (last visited on 5th March, 2009).

profitable "blockbuster" drugs lose patent protection and replacements are more difficult to find,[1] through aggressive challenges worldwide to any efforts by country or local governments to lower the costs of drugs or to regulate their sales,[2] by increasingly aggressive efforts to ban U.S. consumers from accessing the cheaper and identical drugs in Canada and Mexico,[3] by raising drug prices at rates significantly exceeding that of general inflation,[4] and by "disease mongering"-the extending of disease boundaries- to generate more pharmaceutical sales.[5] There is some evidence, however, that these tactics often displayed very aggressively and publicly, are becoming less effective and leading to significant negative public and political reaction.[6] However, of all biopharmaceuticals approved in the USA by FDA

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1 Abraham J., "The pharmaceutical industry as a political player", 2002, Lancet 360:498–1502. See Goodman L., "Celebrity pill pushers", 2002, Salon July 11. www.salon.com/mwt/feature/2002/07/11/celebrity_drugs/print.html (last visited on 16th March, 2009). See NICHM Foundation. National Institute for Health Care Management Research and Educational Foundation. 2000. Prescription Drugs and Mass Media Advertising, September. www.nihcmorg (last visited on 1st May, 2009). See Petersen M. 2002. Madison Avenue plays growing role in drug research. NY Times Nov 22. www.nytimes.com/2002/11/22/business/22DRUG.html?pageewanted=print&position (last visited on 4th May, 2009). See Rosenthal MB, Berndt ER, Donohue JM, Frank RG, Epstein AM., "Promotion of prescription drugs to consumers", 2002, N Engl J Med 346:498–505.

2 Bowe C., "Industry looks to the Maine chance", 2003, Financial Times (April 16). See Class S., "Pharma overview", 2002, Chem Eng News Dec: 39–47. http://pubs.acs.org/CEN (last visited on 10th May, 2009). See Datamonitor, "Big pharma: tightening the marketer's purse strings", 2002, www.datamonitor.com. See also M. Peterson, "Less return in Marketing of Medicines, a study says", NY Times Dec. 12 www.newyorktimes.com (last visited on 7th May, 2009). See Horrobin DF., "Innovation in the pharmaceutical industry", 2002, J R Soc Med 93:341–345. See Lancet, 2001. Patent protection versus public health. 358:1563. See Mitka M., "Survey suggesting that prescription drug ads help public is met with skepticism", 2003, JAMA 289:827–828. See NICHM Foundation, National Institute for Health Care Management Research and Educational Foundation. 2002. Changing patterns of pharmaceutical innovation. May www.nihcm.org (last visited on 21st May, 2009).

3Horowitz DJ., "Warning letter to Harry Lee Jones", March 21, 2003, www.fda.gov/foi/warning_letters/g3888d.htm (last visited on 3rd May, 2009). See Sanders B (U.S. Congressman), "Americans must have access to cheaper Canadian drugs", Buffalo News March 16, 2003, http:// bernie.house.gov/documents/opeds/20030318085012.asp?print. See Zehr L., "Mail order suppliers under gun", Globe and Mail Feb 8, 2003, www.workopolis.com/servlet/Content/qprinter/20030208/RGLAX (last visited on 12th July, 2009). See Burton TM, Lueck S., "FDA sends letter on Canada drugs", Wall Street J (March 15), 2003.

4 Hensley S., "Concern is growing over spike in prices of prescription drugs", Wall Street J April 16, 2003.

5 Moynihan R, Heath I, Henry D., "Selling sickness: the pharmaceutical industry and disease mongering", BMJ, 2002, 324: 886–890.

6 Rouhi AM., "Beyond Hatch-Waxman: Legislative action seeks to close loopholes in U.S. law that delay entry of generics into the market", C & E. News Sept 23:53–65, 2002. See The Economist, "Protection racket. Brand-name drug makers are going to

between 1995-2000, 46% were orphan medicines;[1] in contrast Japan has established large pharmaceutical companies to develop orphan drugs;[2] in Australia 42 products were designed as orphan drugs and 17 of them got a market authorization in the period between January 1998 and August 2001;[3] and from spring 2000 to spring 2004 in the EU Orphan Drug Regulation over 300 applications were submitted and resulted in about 200 positive opinions of the Committee on Orphan Medicinal Products of the European Medicine Evaluation Board (COMP/EMEA)[4] and in 2003, 33% of the more than 150 orphan designations were purely biotech products.[5] The pharmaceutical manufacturers in the BRICS countries (Brazil, Russia, India, China, or South Africa) known as the 'Southern Quad'[6] may be able to devote more energy to the development of drugs for neglected diseases.[7] These companies may also be more eager to develop traditional medicines or drugs that are compatible with the use of such alternative medicines.[8] The following chart[9] will show the comparison of orphan drugs program

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great lengths to spin out their patents", May 17, 2001 and "Pushing pills. Marketing drugs to doctors is turning into a tricky business", Feb. 13, 2003.

1 Reichert JM., "New biopharmaceuticals in the USA: Trends in development and marketing approvals", 1995-1999.Trends in Biotechnology 2000; 18(9):364-369.

2 Shiragami M, Nakai K., "Development of orphan drugs in Japan: characteristics of Orphan drugs developed in Japan", Drug Inf.J. 2000;34:839-846.

3 Australia: Orphan Drug Program. Therapeutic Goods Administration (Australia) 1998. http://www.tga.health.gov.au/docs/html/orphan.htm (version 2001, last visited on 24th May, 2009).

4Register of Orphan Drugs in the EU, http://www.pharmacos.eudra.org/F2/register/index.htm, (last visited on 23rd May, 2009).

5 Orphan Drugs. EBE Newsletter June 2003.http://www.eheefpia.org/../docs/pdf/newsletter/Newsletter_030616.pdf (last visited on i 1th January, 2009).

6 Frederick M. Abbott, "Toward a New Era of Objective Assessment in the Field of TRIPS and Variable Geometry for the Preservation of Multilateralism", 8 J. Int'l Econ. L. 77, 88 (2005).

7 Peter K. Yu, "The International Enclosure Movement", 82 Ind. L.J. 827, 848 (2007), at 841-43.

8 Peter K. Yu, *id* at 900 (noting the importance of exploring alternative proposals that "can be compatible with existing treatments in less developed countries, such as the use of traditional medicine"); Obijiofor Aginam, From the Core to the Peripheries: Multilateral Governance of Malaria in a Multi-Cultural World, 3 Chi. J. Int'l L. 87, 93 (2002) ("Ethnomedical knowledge of plants by indigenous people across societies and cultures has 'long served as [a] crucial source of medicines either directly as [a source of] therapeutic agents, as [a] starting point[] for the elaboration of more complex semi-synthetic compounds or as synthetic compounds.'"); Nitya Nanda & Ritu Lodha, Making Essential Medicines Affordable to the Poor, 20 Wis. Int'l L.J. 586 (2002). ("In developing countries, up to 80 percent of the population relies on traditional medicine to meet its health-care needs. Such medicine is not only affordable, but it is also widely available and trusted.").

9 Source: International Journal of Health and Planning Management, 2008, DOI: 10.1002, www.interscience.wiley.com (last visited on 6th May, 2009).

continuing by the most developed countries in the world:

Contents	USA	EU	Japan	Australia
Scope	Drugs	Drugs	Drugs &Medical services	Drugs
Designation criteria Disease prevalence	Less than 200000 (75 per 100000)	Less than 50 per 100000	Less than 50000 (40 per 100000)	Less than 2000 (11 per 100000)
Nature of disease	Rare only	Life threatening, chronically debilitating, no alternative treatment	Rare & serious; no other treatment; high efficacy and safety	Rare only
Financial return on product	Yes	Yes(over 7 years)	No	yes
Incentives		Yes	On request	On request
Protocol assistance	Yes			
Fast-track procedure	Yes	Not known	High	Priority
Tax credit	Up to	State specified	priority	No
Registration	50%	Reduced fees	6%	Yes
exemption	Yes	State specified	No	No
Research grants	Clinical		Clinical &	
		10 years	non-clinical	no
Market exclusivity	7 years		10 years	
No. of orphan drugs approved/designated in 2003	238/1200	7/126	94/172	33/63

But all these worldwide incentives prove the less certainty for curing orphan diseases at present.

PART TWO:
PHARMACEUTICAL PATENT AND ORPHAN DISEASE

The large fraction of the world population that lives on less than a dollar a day, the prospects of new medicines and vaccines are totally theoretical under the aegis of strong intellectual property protection dominantly exerted by the rich world. Therefore "the efforts to simply extend the existing standards of patent and copyright protection through different Conventions to the poor world will increase their cycle of poverty and ill health. This extension is significantly one-sided for the poor world since it lacks much of the basic scientific and educational infrastructure that generates patents and copyrights and it cannot afford to pay the costs demanded by the rich world".[1] "TRIPS has increased the global protection afforded to suppliers of high science and technology, but has done little to improve the real global competitive arena that remains very one-sided.

1 David J. Triggle, supra at 32, at 281.

Intellectual property protection in fact imposes costs on most developing countries".[1] Extensive and uniform patent protection regime for pharmaceutical products described in TRIPS[2] marked the beginning of the global property epoch.[3] Before TRIPS, developing countries did not allow patents for pharmaceutical products,[4] only pharmaceutical processes could be patented[5] and some excluded medicines from the ambit of patent laws[6] which allowed local production of generic versions of the patented medicines,[7] and kept the prices of formulation at a much lower level then that in the developed world.[8] Reason is that granting a right to patent is akin to a grant of a monopoly[9] because it allows the patent holder to manipulate the market price of the product.

The DOHA interpretation of TRIPS permits compulsory licensing of drugs for local manufacture during 'national crises' which reduces some pressures on part of developing countries. The patent-based pharmaceutical R&D and distribution systems in most developed countries function well because of elaborate and expensive subsidy and social insurance mechanisms provided by their governments. Poorer countries generally lack these

1 CorpWatch India. 2002., "Intellectual property rights impose costs on most developing countries", Sept 12. www.corpwatch.india.org (last visited on 8th June, 2009). See MacKenzie M., "Protection racket", New Scientist July 21, 2001: 18-20. See Rosenberg T., "Patent laws are malleable. Patents are reducible. Drug companies are evincible. The world's AIDS crisis is solvable", NY Times (Magazine) Jan. 28, 2001.

2 Agreement on Trade Related Aspects of Intellectual Property Rights, Apr. 15, 1994, Marrakesh Agreement Establishing the World Trade Organization, Annex 1C, Legal Instruments- Results of the Uruguay Round vol. 31, 33 I.L.M. 81 (1994) [hereinafter TRIPS Agreement].

3 Peter Drahos, Intellectual Property and Human Rights, Intell. Prop. Q. No.3 349, 356 (1999) [hereinafter Drahos].

4 A product patent is different from a patent over a process. Patenting a process implies that only the process through which a product is made can be patented. The final product is not included under the right. A patent holder can restrict the other party from using the process, but he can make no claims on the product. Thus, another manufacturer can market the same product as long as she uses a different process.

5 E.g., Argentina, India; See Theresa Beeby Lewis, Patent Protection for the Pharmaceutical Industry: A Survey of the Patent Laws of Various Countries, 30 Int'l Law 835 (1996)

6 E.g., Brazil, Thailand, Korea.

7 The success of many Indian pharmaceutical companies, for example Cipla, is attributed to a weak patent regime.

8 For example, AZT (a drug for treatment of HIV) treatment was produced at a supply cost of $ 48 a month in India as compared with $ 239 in the United States; Lariam, a treatment for malaria, at a cost of $ 4 as compared with $ 37 in the U.S., according to a UN document published in 2000. See Audrey R. Chapman, Approaching Intellectual Property as a Human Right: Obligations Related to Article 15(1)(c), discussion paper submitted to the Committee on Economic, Social, and Cultural Rights, 24th Sess., at 22, U.N. Doc. E/C.12/2000/12 (2000).

9 Robert Howse & Michael J. Trebilcock, The Regulation of International Trade at 309 (2nd ed. 1999).

resources. They cannot afford multi-billion dollar National Insurance Health-style grant programs to focus attention on local health conditions. They do not subsidize the cost of the vast array of patented medicines to the point where they are affordable.[1] Their citizens are much poorer and cannot afford most patented medicines. Global pharmaceutical markets simply do not work as well for the world's non-wealthy people, perhaps 85% of humanity.[2] Special provisions for enhanced access to medicines and TRIPS flexibilities are called for in these situations, especially if access can be provided without undermining optimal incentives for innovation in high-income markets.[3] Whether a disease is rare or common, however, the discovery, development, and clinical testing of a drug that can treat it represent a long, arduous, and expensive process. Drug companies are therefore loath to invest in a product for a disease that affects relatively few people unless they can be assured of a return on their investment.[4]

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1 Brazil has fully subsidized the price of AIDS medications as part of its aggressive treatment and prevention program. The high price had prevented Brazil from making similar commitments across other treatment categories. WHO CIPIH Report of the Commission on Intellectual Property Rights, Innovation and Public Health 22 (2006), at 97-100 fig. 4.3; Kevin Outterson, "Pharmaceutical Arbitrage: Balancing Access and Innovation in International Prescription Drug Markets", 5 Yale J. Health Policy, L. & Ethics 193-286 (2005), available at www.ssrn.com/abstract=567742, at 193-286; Outterson & Kesselheim, Market-Based Licensing for HPV Vaccines in Developing Countries, 27 Health Aff. 133, (2008); GAO Trade Policy Report, U.S. Gen. Accounting Office, GAO Report 07-1198, U.S. Trade Policy Guidance on WTO Declaration on Access to Medicines May Need Clarification 15, 19, 23 (Sept. 2007), at 24; World Health Organization, Report of the Commission on Intellectual Property Rights, Innovation and Public Health 22 (2006) , at 111-12. Patricia M. Danzon, "At What Price?", 449 Nature 176 (2007). Brazil's threatened compulsory licenses may have saved US$1 billion in AIDS treatment costs between 2001 and 2005. Amy S. Nunn, et al., Evolution of Antiretroviral Drug Costs in Brazil in the Context of Free and Universal Access to AIDS Treatment, 4 PLoS Med. 1804, 1809 (2007).

2 Paul Hunt, "Human Rights Guidelines for Pharmaceutical Companies in Relation to Access to Medicines", 19 Sept. 2007, at 1 (Draft for Consultation), available at: www.essex.ac.uk/human_rights_centre/rth/docs/PH%20draft%C20guidelines%C2019%C20sept%2007.doc, (last visited on 4th May, 2009) at 1; See also Oxfam, Oxfam Briefing Paper 109: Investing For Life: Meeting Poor People's Needs for Access to Medicines Through Responsible Business Practices, Nov. 2007, at 2, available at www.oxfam.org/en/files/bp109_investing_for_life_0711.pdf/download(last visited on 17th May, 2009), at 1; WHO CIPIH Report, supra note 62, at 23.

3 Kevin Outterson, "Should Access To Medicines And Trips Flexibilities Be Limited To Specific Diseases?", 34 Am. J.L. & Med. 279American Journal of Law and Medicine2008Article, Copyright © 2008 by American Society of Law, Medicine & Ethics Boston University School of Law; This article was presented in a symposium held at Boston University in February 2008. In May 2008, the 61st World Health Assembly met in Geneva and adopted a Global Health Strategy on Public Health, Innovation and Intellectual Property, following the final meeting of the Inter-Govermental Working Group (IGWG 2) on May 3, 2008 and this paper was circulated in draft form at IGWG 2.

4 Marlene E. Hanffner, "Adopting Orphan Drugs- Two Dozen Years of Treating Rare Diseases", N Engl J Med 354; 5 www.nejm.org February 2, 2006, p. 445.

PATENT VERSUS ACCESS TO MEDICINE: DEVELOPING STATES PERSPECTIVE

Patent is main problem in case of access to orphan medicines and thus the question raises whether the patent protection of TRIPS Agreement[1] allows countries sufficient flexibility[2] to deal with domestic health crisis.[3] Where thousands of people are dying every day, the question of access to affordable medicines can no longer be treated as IP or trade related issue. Rather, it requires the assertion of a human rights perspective to facilitate access to public goods, particularly when dealing with rights to the knowledge required producing medicines that combat life-threatening diseases.[4] Access to essential drugs thus becomes a critical part of the fundamental human rights to health.[5] While WTO accepts that "patent protection stimulates development of needed new drugs," it argues that "countries must ensure a balance between the interests of the patent holders and the needs of society."[6] Advocating that "generic competition should begin promptly upon patent expiration" and that "preferential pricing is necessary for lower-income countries and should be actively pursued,"[7] and public involvement is necessary to "ensure development of new drugs for certain priority health problems."[8]

Problems in developing countries: Only economic and financial access do not guarantee the essential drugs; continuous training for health care professionals, dissemination of reliable pharmacological data, improvement of the management of drugs, research and development of an appropriate pharmaceutical agent, production, quality control, distribution, inventory control, reliable information for health care professionals and the

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1 TRIPS, 15 Apr. 1994, Marrakesh Agreement Establishing the WTO, Annex IC, Legal Instrument- Results of the Uruguay Round vol. 31, 33 I.L.M. 81 (1994).

2 WTO Doha Ministerial Declaration on the TRIPS Agreement and Public Health, WT/MIN (01)/DEC/2 (14 Nov. 2001); WTO Council for TRIPS, Implementation of Paragraph 6 of the Doha Declaration on the TRIPS Agreement and Public Health, Ip/C/W/405 (30 Aug. 2003).

3 Carlos Correa, "Implementing the TRIPS Agreement in the Patents Field- Options for Developing Countries", 1 J. World Intell. Prop. 75 (1998); C. Correa, "Intellectual Property Rights, The WTO and Developing Countries: The TRIPS Agreement and Policy Options", (Zed Books 2000). See also Frederick Abbott, "Managing the Hydra: The Herculean Task of Ensuring Access to Essential Medicines".

4 I. Kaul & R.U. Mendoza, "Advancing the Concept of Public Goods", in Providing Global Public Goods: Managing Globalization 78, 84 (Inge Kaul et al. eds., Oxford 2003).

5 Jonathan Mann et al., "Health and Human Rights, in Health and Human Rights", 7 (Routledge 1999), See Rebecca Cook, "Gender, Health and Human Rights", in Health and Human Rights 262 (J. Mann et al. eds., Routledge 1999).

6 Dr. M. Scholtz, "International Trade Agreements and Public Health: WHO's Role, Paper Presented at the Conference on Increasing Access to Essential Drugs in a Globalized Economy, at 1 (Amsterdam, 25-26 Nov. 1999); http://www.who.int/medicines/docs/WTO_Public_Health_Amsterdam_MS.html (last visited on 10-05-2009), at 3.

7 Id.

8 Id.

general public, diagnosis, prescription, financial accessibility, drug dispensing, observance, and pharmacovigilance are fundamental steps in improving the quality of care in the developing world. Compulsory license has long been recognized as the most important tool for addressing the adverse effects of the patent grant on public welfare.[1] Although Article 31 does not limit the grounds on which compulsory licensing is permissible[2] it refers to a number of circumstances for granting license where (a) situations of national emergency or extreme urgency,[3] (b) cases of public non-commercial use,[4] (c) there is a need to 'correct anti-competitive practices,'[5] and (d) the exercise of one patent is dependent on the infringement of another.[6] The conditions of Article 31 are not a significant restriction to the introduction and efficient operation of compulsory licensing regime.[7] No developing country to date has made use of compulsory licensing as a tool to address public health issues.[8] There are a number of economic and political reasons for this[9] that forbids granting compulsory license. For compulsory license, there must be an effort to obtain authorization from the right holder "within a reasonable period of time" on "reasonable commercial terms"

1 Frederick M. Abbott, "Compulsory Licensing for Public Health Needs: The TRIPS Agenda at the WTO after the Doha Declaration on Public Health", Quaker United Nations Office, Occasional Paper No. 9 (2002), available at http://www.geneva.quno.info/main/ search publication.php?loop=0# (last visited December 26, 2003); see Carlos Correa, Integrating Public Health Concerns into Patent Legislation in Developing Countries 93-94 at http://www.southcentre.org/publications/publichealth/publichealth.org (for compulsory licensing provisions in various national legislations, last visited on 15th June, 2009).

2 Robert Weissman, "A Long Strange TRIPs: The Pharmaceutical Industry Drive to Harmonize Global Intellectual Property Rules, and the Remaining WTO Alternatives Available to Third World Countries", 17 U. Pa. J. Int.'l Econ. L. 1069, 1113 (1996).

3 TRIPS, supra note 54, art. 31(b).

4 Id.

5 Id. art. 31(k).

6 Id. art. 31(l).

7 Weissman, supra note 75, at 1113.

8 F.M. Abbott, "The TRIPS Agreement, Access to Medicines and the WTO Doha Ministerial Conference", 11 (2002), available at http://www.geneva.quno.info/pdf/OP7Abbot1.pdf, (last visited on 15th April, 2009).

9 The International Federation of Pharmaceutical Manufacturers Association (IFPMA) has on its website the following reasons against the issuance of compulsory licenses: (a) they may reduce incentive to innovate. If a country adopts compulsory license measures, then a natural consequence is for fewer research funds to be allocated either to that country or disease area due to the resulting disincentives for research. (b) Generic drugs manufactured under a compulsory license in developing countries will be parallel exported to developed countries. (c) Governments tend to use compulsory licensing measures as industrial policy instead of using it as a pro-consumer tool. (d) There are safety reasons: developing countries do not have the infrastructure or administrative systems in place to ensure and monitor the correct supply and delivery of medication; see IFPMA, TRIPs, Pharmaceuticals and Developing Countries: Implications for Health care Access, Drug Quality and Drug Development (2002), available at http://www.ifpma.org/documents/NR86/TRIPS.pdf, (last visited on 1st April, 2009).

which is difficult to manage.[1] Less developed nations will have to issue their compulsory licenses mainly for importation rather than domestic production that require competitive global market supply sources exist.[2] Article 31 also requires judicial or other independent review of the decisions taken by the licensing authority,[3] which might take too long if examined from a pharmaceutical company's perspective.[4] The Agreement does not provide any guideline for the exact interpretation of significant terms such as "reasonable period of time,"[5] "reasonable commercial terms,"[6] "national emergency,"[7] "predominantly for the supply of the domestic market" and "adequate remuneration."[8] Thus, the text of Article 31 does not fully develop the factors required for the issuing of compulsory licenses under legitimate circumstances for less developing states.[9] In case of parallel importation GATT[10] and WHO support it in order to advance the principle of 'preferential pricing in poor countries'[11] in accordance with Articles 30 and 31 having been fulfilled the following conditions-(a) it would provide the simplest and most direct solution to the problem for developing countries.

(b) it could be limited to health problems the Doha Declaration seeks to address by restricting its application to exports of health products.

(c) it could allow the decision for a compulsory license to remain in

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1 TRIPS, supra note 75, art. 31(b).

2 Abbott, supra note 81, at 29.

3 F.M. Scherer & Jayashree Watal, Post-TRIPS Options for Access to Patented Medicines in Developing Countries 29 (Comm'n on Macroeconomics & Health, Working Paper No. WG4:1, 2001) available at http://www.cmhealth.org/docs/wg4paper1.pdf (last visited January 28, 2009) at 28-29.

4 The longer the issuance of compulsory licenses is delayed after patented drugs enter the marketplace, the less time licensees have to recover their start-up costs and the more difficult it is to achieve effective competition among multiple generic substitute suppliers.

5 Alan O. Sykes, "TRIPS, Pharmaceuticals, Developing Countries, and the Doha "Solution", 3 Chi. J. Int'l L. 47, 52 (2002)

6 Id.

7 Id. at 56.

8 According to Weissman, this condition creates a critical obstacle to adopting a compulsory licensing program for a developing nation. Weissman, supra note 75, at 1114.

9 Sara M. Ford, "Compulsory Licensing Provisions under the TRIPs Agreement: Balancing Pills and Patents", 15 Am. U. Int'L L. Rev. 941, 961 (2000)(citing Richard H. Marschall, Patents, Antitrust and the WTO/GATT: Using TRIPs as a Vehicle for Antitrust Harmonization, 28 Law & Pol'y Int'l Bus. 1165, 1188-89 (1997)).

10 Carlos Correa, "Integrating Public Health Concerns into Patent Legislation in Developing Countries", 93-94 athttp://www.southcentre.org/publications/publichealth/publichealth.org (for compulsory licensing provisions in various national legislations, last visited on 4th April, 2009) at 77.

11 Id. at 77 (WHO has stated that "in cases where drug prices are higher in poor countries than in richer ones, recourse to parallel imports in low-income countries in order to reduce prices might be appropriate, while preventing parallel exports to industrialized countries")

the country of consumption.

(d) it would allow compensation to be paid to the patent holder in the country of consumption, if a patent exists. If a patent does not exist in the importing country, then logically no compensation should be paid. Above all under compulsory license the The importing member country has to fulfill the following conditions: (A) the country should either be a least developed country or any other member that notifies the Council for TRIPS of its intention to use the waiver only in the case of a national emergency or other circumstances of extreme urgency or in cases of public non-commercial use;[1] (B) the notification from the importing country should:[2] (i) specify the names and expected quantities of the product; (ii) confirm that the member has established that it has insufficient or no manufacturing capacities in the pharmaceutical sector for that product;[3] and, (iii) also confirm that in case the imported product is already under a patent, a compulsory license has already been granted; (C) the importing country has to take reasonable measures to prevent re-exportation of the products that have actually been imported into their territory. They have to ensure that the imported products are used for public health purposes only;[4] (D) the importing country is not obliged to pay "adequate remuneration" as set out in Article 31 (h) of TRIPS if the exporting country has already done so with respect to the product imported. Other requirements are- (A) the compulsory license granted by exporting member has to meet the following requirements:[5] (i) no more than the amount required by the importing country may be manufactured and the entire production has to be sent to the importing country; (ii) the product to be exported under compulsory license should be clearly identified through specific labeling or marking. Such identification could be through special packaging or special coloring or shaping of the products, provided it does not impact the price significantly; (iii) the information related to the compulsory license and the product shall be publicly available on a website and the Council for TRIPS shall be notified about the compulsory license and conditions attached to it. (B) The exporting country should pay adequate remuneration to the patent holder taking into account the economic value to the importing country[6] which seems more

1 TRIPS Council Decision, P 1(b) (note 2 of the Decision also clarifies that the notification does not have to be approved by a WTO body in order to use this system set out in the Decision). See also TRIPS Council Decision, Doc. No. WT/L/540, available at http://www.wto.org/english/tratope/tripse/implement, (last visited on 25th May, 2009), para 6 e.htm, (the list of countries are: Australia, Austria, Belgium, Canada, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Italy, Japan, Luxembourg, Netherlands, New Zealand, Norway, Portugal, Spain, Sweden, Switzerland, United Kingdom and United States of America).

2 TRIPS Council Decision, Id. P 2(a).

3 This condition is not required for a least developing country. The Annex to the Decision provides two ways by which Assessment of Manufacturing Capacities in the Pharmaceutical Sector is to be done.

4 TRIPS Council Decision, supra note 95, at p. 4.

5 Id. P 2(b).

6 Id. P 3.

burdensome for developing states.

Poor quality: The prevalence of counterfeit and substandard drugs on the developing states market is increasing rapidly. Counterfeit drugs are those that mimic authentic drugs; substandard drugs are those produced with little or no attention to good manufacturing practices.[1] But drugs must be produced according to good manufacturing practices.[2] Poor quality may be accidental, with no intention to deceive, but oversights in manufacturing or neglected controls can have tragic consequences.[3]

Negative tendency: Commercial unprofitable drugs are being disappeared gradually from 1950 to date from developed states where as those drugs are still preventive in rare diseases in Africa region. For example, the trypanocidal activity of eflornithine hydrochloride was discovered in 1985.[4] It is the only treatment proven effective in cases in which African trypanosomiasis shows resistance to melarsoprol, and such resistance is becoming more frequent (20% in Omungo, Uganda).[5]

Patent-cost: Recently marketed rare drugs are patent protected and costly in developing states. For example, dysentery is extremely contagious and, without effective treatment, is lethal in 5% to 15% of cases.[6] Since 1979, this disease has been the cause of large epidemics in Africa (for example, in Malawi in 1992 and 1993[7] and in Burundi in 1994[8]). But treatment with these new drugs is 10 times more expensive than the traditional treatment using

1 Bernard Pécoul, Pierre Chirac, Patrice Trouiller, et al., "Access to Essential Drugs in Poor Countries: A Lost Battle?" JAMA. 1999;281(4):361-367 (doi:10.1001/jama.281.4.361), http://jama.amaassn.org/cgi/content/full/281/4/361 (last visited on 24th April, 2009).

2 World Health Organization, "WHO Expert Committee on Specifications for Pharmaceutical Preparations", Geneva, Switzerland: World Health Organization; 1996. WHO Technical Report Series 863.

3 O'Brien KL, Selanikio GD, Hecdivert C, et al., "Epidemic of pediatric deaths from acute renal failure caused by diethylene glycol poisoning", JAMA. 1998; 279:1175-1180. See Shakoor O, Taylor RB, Behrens RH., "Assessment of the incidence of substandard drugs in developing countries", Trop Med Int Health. 1997; 2:839-845.

4 Doua F, Boa FY, Schechter PJ, et al., "Treatment of human late-stage gambiense trypanosomiasis with adifluoromethylornithine, (eflornithine)", Am J Trop Med Hyg. 1987; 37:525-533.

5 Legros D, Enyaru JCK, Evans S, Maiso F., "An outbreak of relapses among patients treated for T. b. gambiense trypanosomiasis in Arua, Northern Uganda", Paper presented at: 24th International Scientific Council for Trypanosomiasis Response and Control (ISCTRC); September 1997; Maputo, Mozambique.

6 Centers for Disease Control and Prevention. Mortality From Dysentery in Africa: A Follow-up Study in Burundi. Atlanta, Ga: Centers for Disease Control and Prevention; 1993. CDC internal report.

7 Paquet C, Perea W, Grimont F, et al., "Aetiology of haemorragic colitis epidemic in Africa", Lancet. 1993; 342:175.

8 Paquet C, Leborgne P, Sasse A, Varaine F., "An outbreak of Shigella dysenteriae type 1 dysentery in a refugee camp in Rwanda", Sante. 1995;5:181-184. See Paquet C, Van Soest M., "Mortality and malnutrition among Rwandan refugees in Zaïre", Lancet. 1994; 344:823-824.

nalidixic acid (approximately $20 vs $2).[1] Ceftriaxone treatment is also 10 times more expensive than chloramphenicol treatment.[2] Vaccines for hepatitis B, a disease predominantly found in eastern Asia and sub-Saharan Africa[3] are approximately 10 times more expensive than other vaccines included in the Expanded Program on Immunization promoted by UNICEF[4] because of prohibitive and steep price raised by patent.

Lack of R&D for Orphan drug: After 1960 pharmaceutical companies adopted complete different strategy[5] to innovate and commercialize only updated rare drugs for tropical diseases[6] abandoning R&D for following reasons-

Cost and risk of R&D relative to the low purchasing power of developing countries:

Profit in commerce: After 1980 pharmaceutical companies consolidated and merged to cope with large investment and reduce duplicate spending with a view to focusing on the most profitable segments of the market leaving orphan drugs largely out of the equation.

Patent Infringement: Developing states are reluctant of patent protection and usually have developed less expensive manufacturing process.[7] In addition to copies of drugs resulting from a different notion of intellectual property rights, there are cases of pure and simple piracy that are frequent in countries where informal markets play a significant role.[8]

High Quality Standard: Various quality standards[9] for orphan drug production make the drug expensive where the drug companies discontinued its reproduction for fear of nonprofit. Free trade system gives the rare drugs different price among countries or set unique world-wide price which jeopardizes the access to drugs for LDC people.

New Research: After 1995, directors of pharmaceutical companies in the developed world have stated repeatedly that the reason for not

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1 Essential Drugs Price List. Copenhagen, Denmark: UNICEF Supply Division; 1995.

2 Varaine F, Keita M, Kaninda AV, et al., "Long acting chloramphenicol versus ceftriaxone for treatment of bacterial meningitis in children aged 2-35 months", Paper presented at: Eighth International Congress on Infectious Diseases; May 15-18, 1998; Boston, Mass.

3 Tandon BN, Acharya A, Tandon A., "Epidemiology of hepatitis B virus infection in India. Epidemiol Infect'', 1996;117:313-325.

4 Kaddar M., 'La mutation du marche' mondial des vaccins', Rev Prescrire. 1995;157:844-847.

5 Trouiller P., 'Recherche et de' veloppement pharmaceutiques en matie' re de maladies transmissibles dans la zone intertropicale'', Sante. 1996;6:299-307.

6 Trouiller P, Rey JL, Olliaro P., "Analysis of drug development patterns of six tropical diseases between 1975 and 1997", Paper presented at: Eighth International Congress on Infectious Diseases; May 15-18, 1998; Boston, Mass.

7 International Strategies for Tropical Diseases Treatments: Experiences with Praziquantel. Boston, Mass: Harvard School of Public Health; 1996.

8 World Health Organization, "Counterfeit Drugs: Report of a WHO/IFPMA Workshop. Geneva, Switzerland": World Health Organization; 1992. WHO/ DMP/CFD/92.

9 World Health Organization, "Recommendations from the ICDRA reinforce the mission of regulatory authorities". WHO Drug Information, 1996; 4:182-185.

conducting research on tropical diseases is the lack of protection for innovations in some developing countries, which would also explain their limited investments in the countries concerned.[1] Manufacturing companies in developing countries may actually be motivated to invest more in research for new drugs, but such investments will essentially respond to the need to shift their innovation capacity away from finding ways to copy the patented drugs of developed countries and toward discovering new drugs.[2] After 1994, 1994, strategies for product R&D have not produced any convincing results[3] and no real impact has been seen with respect to tropical diseases.[4] Especially from 1990, the change in the organization[5] of drug research leads to decrease the number of 'new molecular entities'[6] of orphan drug because of results from a greater emphasis on developing products for chronic and complex indications; the growing size of clinical trials; difficulties recruiting and retaining patients; increased regulatory and political pressures, especially in the United States, where the Food and Drug Administration is requiring more extensive safety data sets for new drug applications; increasing clinical development costs; and poor returns on expensive discovery technologies.[7]

Further for developing countries seeking improved access to essential medicines, implementation of policies and legislation that would facilitate resort to compulsory and government use licensing provides the principal counterbalance to the adverse impact of patent monopolies.[8] Other Other following solutions for ensuring essential medicines to cure orphan diseases in case of patent problems are important to consider-

Compulsory licensing and government use: It serves functions by-

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1 Intellectual Property: Patents and Pharmaceuticals. Geneva, Switzerland: International Federation of Pharmaceutical Manufacturers Associations; 1997.

2 Lanjouw JO., "The Introduction of Pharmaceutical Product Patents in India: Heartless Exploitation of the Poor and Suffering?", Cambridge, Mass: National Bureau of Economic Research; 1998.

3 Tropical Disease Research, "From Investigation to Eradication: Tropical Diseases Research Twelfth Program Report", Geneva, Switzerland: World Health Organization; 1995:9-36.

4 Olliaro P., "Will the fight against tropical diseases benefit from orphan drug status?", Trop Med Int Health. 1997; 2:113-115.

5 Cockburn IM., "The changing structure of the pharmaceutical industry", Health Aff (Millwood). 2004; 23:10-22.

6 Tufts Center for the Study of Drug Development. Outlook 2003. Available at: http://www.csdd.tufts.edu (last visited on 14th May, 2009). See US Food and Drug Administration. Challenge and Opportunity on the Critical Path to New Medical Products. Washington, DC: US Food and Drug Administration; 2004.

7 Tufts Center for the Study of Drug Development. Outlook 2004. Available at: http://www.csdd.tufts.edu, (last visited on 19th May, 2009). See Pammolli F, Riccaboni M. Market structure and drug innovation. Health Aff (Millwood). 2004; 23:48-50.

8 Frederick M. Abbott, "Compulsory Licensing for Public Health Needs: The TRIPS Agenda at the WTO after the Doha Declaration on Public Health", Quaker United Nations Office Occasional Paper 9, (Feb. 2002), http://www.quno.org (last visited on 19th January, 2009).

(i) Providing a favorable background for all price and licensing negotiations with patent holders;
(ii) Serving as critical bargaining levers in specific negotiations;
(iii) Allowing the realization of production by persons other than patent holder.

Paragraph 7 and Least Developed Countries: Until 2016 LDC are waived to apply TRIPS provisions for pharmaceutical product as well as obligation regarding "exclusive marketing rights" but in case or orphan drugs this opportunity is useless as the LDC are unable to invent new orphan drugs due to lack of resources.

Differential Pricing: Paragraph 5(d) of Article 6 of TRIPS Agreement allows WTO members to adopt a rule of international exhaustion of IPRs, and thus to permit parallel importation of medicines where the LDC are allowed to seek the lowest priced of medicines but it is also ineffective as the availability and amount of orphan drugs are the exclusive matter of developed countries R&D.

PATENT BASED ORPHAN DRUGS

In intellectual property circles the notion of the orphan has been deployed to great effect in the field of patent law, where the notion of the "orphan drug" is conceived as a means of making investment in a research project a more financially realistic proposition: where an "orphan disease" is suffered by an insufficiently large number of patients to constitute a viable market, an enhanced period of exclusivity may be conferred—both in the USA and in Europe—during which the developer of a drug treatment may market its new product.[1] Pharmaceutical industries faced substantial criticism on continued high profits using patents masking growing difficulties in developing new pharmaceuticals and the lack of incentives for products addressing diseases in developing countries.[2] Criticism based on the high costs and cost increases of drugs promote drug development, they also significantly restrict access.[3] From 1992 to 2002, retail prices for prescription pharmaceuticals in the United States increased 7.3% annually, greatly exceeding the 2.5% annual inflation rate.[4] In 2002, drug costs accounted for 10.5% of all health expenditures, nearly twice the level of 5.8% a decade

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1 Jeremy Phillips, "Killing the Orphans", editorial speech, Journal of Intellectual Property Law & Practice, 2007, Vol. 2, No. 10, p. 633.

2 Angell M., "The Truth About the Drug Companies— How They Deceive Us and What to Do About It", New York, NY: Random House; 2004. See Médécins Sans Frontières, "MSF Puts Drug Patents Under the Spotlight", May 22, 2003.Availableat:http://www.accessmedmsf.org/prod/publications.asp?scntid=22520031 14784 (last visited on 13th May, 2009) & contenttype=PARA &. Accessibility verified September 9, 2005. See Greider K. The Big Fix: How the Pharmaceutical Industry Rips Off American Consumers. Cambridge, Mass: Public Affairs; 2003.

3 Scherer FM., "The pharmaceutical industry—prices and progress", N Engl J Med. 2004; 351:927-932.

4 Kaiser Family Foundation, "Prescription Drug Trends", May 2003. Available at: http://www.kff.org. Accessibility verified May 9, 2009.

earlier.[1] Many of these pharmaceutical expenditures improve quality of life and save money by substituting for more expensive interventions.[2] Combined with the withdrawal of medications because of adverse effects, efforts to thwart the dissemination of negative research results, and conflicts of interest with academic researchers have generated considerable worldwide public hostility toward the pharmaceutical industry and pressure for political responses, including calls for drug reimportation or price controls, tighter regulation, and international agreements permitting the override of drug patents.[3] Patent rationale[4] is justified as recognition of the inventor's creativity by means of enhancing innovation. A patent is a right to exclude others; it is a right to a temporary monopoly, permitting a higher price to be charged for the product, which in turn is supposed to stimulate innovation.[5] To obtain a patent, an invention must be (1) novel—meaning that it has not been published more than a year before the patent application; (2) not obvious; (3) useful; and (4) adequately disclosed in the patent application to enable a scientist to practice the invention.[6] Patent right excludes others from making, using, selling, offering for sale, or importing products that derive from or incorporate the protected invention[7] granting on a country-

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1 Centers for Medicare & Medicaid Services National Health Expenditures Available at http://www.cms.hhs.gov review/supp/ (last visited on 5th April, 2009).

2 Cutler DM, McClellan M. "Is technological change in medicine worth it?", Health Aff (Millwood). 2001; 20 11-29. See Lichtenberg FR, "Availability of new drugs and Americans' ability to work", J Occup Environ Med. 2005; 47: 373-380. See Pharmaceutical Research and Manufacturers of America. Pharmaceutical Industry Profile 2005 Available at http://www.phrma.org (last visited on 24-01-2009)

3 Barton JH., "TRIPS and the global pharmaceutical market", Health Aff (Millwood). 2004; 23:146-154.

4 Penrose ET., "The Economics of the International Patent System. 'Baltimore", Md: Johns Hopkins University Press; 1951.

5 John H. Barton and Ezekiel J. Emanuel. "The Patents-Based Pharmaceutical Development Process: Rationale. Problems. and Potential Reforms", JAMA. 2005; 294 (16); 2075-2082 (doi: 10.1001 jama.294.16.2075), http://jama.ama-assn.org/cgi/content/full/294/16/2075 (last visited on 6th May, 2009). Similar view can be found in the Constitution of the United States. Article 1,§8. which gives Congress the power "to promote the progress of science and useful arts, by securing for limited times to authors and inventors the exclusive right to their respective writings and discoveries."Available at: http://www.constitutioncenter.org/explore/TheU.S.Constitution/index/html (last visited on 7th April, 2009).

6 35 USC §§101, 102, 103, 112.

7 Y. Taylor, ed., Battling HIV/AIDS: A Decision-Maker's Guide to the Procurement of Medicines and Related Supplies (Washington, D.C.: The World Bank, 2004) at 106 [World Bank Procurement Guide]. In exchange for this temporary grant of monopoly (usually 20 years from the date of filing), the patent holder must make full disclosure of his or her invention such that others skilled in the same art are able to put the invention into practice once the patent expires. Additional important requirements for the grant of a patent are that the invention must be new, non-obvious, and useful (otherwise described as "capable of industrial application" in some jurisdictions). See Commission on Intellectual Property Rights, Integrating Intellectual Property Rights and

by-country basis or on a regional basis.[1] Though some authors treat patent under the rubric of natural rights,[2] without it private investment into R&D would be sub-optimal or non-existent.[3] Development of patent based orphan drugs are enormous expensive because of high attrition rate of potential product process, laboratory and trial cost. The pharmaceutical industry recovers its expenses through charging a high price for the drug, typically based on exclusivity rights under a patent. When the patent expires, the price normally decreases through competition with generic drugs.[4] The newly developed orphan drug includes the huge research cost as a first generation and covers not only 20 years of patent monopoly rights but some cases more than it. Because to preempt competitors, companies will have to apply earlier of development process and at the same time, before completing 20 years patent, it is possible to reapply for the same. Consequently patent process jeopardizes easy access to orphan drugs. For example in U.S.A. under the 1983 Orphan Drug Act,[5] a shorter additional

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Development Policy: Report of the Commission on Intellectual Property Rights (London: Commission on Intellectual Property Rights, 2002) at 12, online: Commission on Intellectual Property Rights www.iprcommission.org/papers/pdfs/final_report/CIPRfullfinal.pdf (last visited on 25th March, 2009). With respect to new medicines, patent claims can be filed for new pharmaceutical products, new processes to make pharmaceuticals, new formulations of pharmaceuticals, new combinations of separate pharmaceuticals, and new uses of known pharmaceutical compounds.

1 Examples include the Organisation Africaine de la Propriété Intellectuelle (OAPI), which comprises 16 French West-African countries, and the African Regional Intellectual Property Office (ARIPO), which comprises 15 English-speaking African countries. See World Bank Procurement Guide, ibid. at 106. The implication of the country-by-country, or regional, granting of patents is that an invention may be patented in one country and not another, depending on various factors such as an owner's decision not to apply for a patent in a given country, or differing standards of patentability across jurisdictions (though the latter will become less of a factor once the WTO TRIPS Agreement is fully implemented).

2 Michael J. Trebilcock and Robert Howse, The Regulation of International Trade, 2nd ed. (New York: Routledge, 1999) at 308.

3 Because it is difficult to prevent others from copying information, free-riders, in the absence of a patent, could easily copy a new invention and market it. Under such conditions, rational investors would not devote sufficient private resources to innovative activity because they would not be able to recoup the substantial fixed costs associated with R and D and because they would not be adequately compensated for assuming the inherently high risks involved.

4 US Office of Technology Assessment, "Pharmaceutical R&D: Costs, Risks, and Rewards", February 1993. Publication OTA H-522; at: http://www.wws.princeton.edu/~ota/ns20/pubs_f.html (last visited on 10-01-2009).

5 Villarreal MA., "Orphan Drug Act: background and proposed legislation in the 107th Congress: Congressional Research Service Report for Congress", July 25, 2001. Available at: http://www.law.umaryland.edu/marshall/crsreports/crsdocuments/RS20971.pdf (last visited on 16th March, 2009). See US Food and Drug Administration. The Orphan Drug Act. 1983. Available at: http://www.fda.gov/orphan/oda.htm (last visited on 15th May, 2009).

period of exclusivity may be given to a firm for use of a known product to treat an orphan disease, and amendments to the Food, Drug, and Cosmetic Act[1] provide for 6 months of additional exclusivity for certain drugs if extra testing is performed for pediatric applications.

Patent based orphan drugs creates some practical problems, like-

i. high cost in research and recovery by patent monopoly intensify the tension between research goals and accessibility goals;

ii. absence of noncommercial market for recovery of development cost of orphan drugs in developing states influences research priorities;

iii. a misallocation of resources exists between research and marketing[2]i.e., the production process expenditure is more than real recovery for rare drugs;

iv. payment for drugs without patent monopoly is not an ideal market, for example, about 67% of expenditures for drugs in the United States are covered by private insurance and the government.[3] Third-party payments distort market incentives and preclude traditional economic analyses;[4]

v. from 1070 to 2003 the total investment in orphan drug development is low, given the profits;

vi. there is an imbalance of pharmaceutical investment of orphan drug production among the USA, Canada, Australia, Newzealand and European Countries which makes hindrance of inventing new orphan drug.

To address these problems, the following steps may act as its solution for appropriate dissemination of orphan drugs throughout the world-

a. the price of orphan drugs should have to be controlled, although the down price bargaining is prohibited under Medical pharmaceutical benefit,[5] it may have short-term political appeal[6] to maintain the same level of research and development everywhere;

b. tiered pricing, i.e., having higher drug prices in developed countries and lower prices in developing countries—is efficient, equitable, and enhances utility[7] to compel the surrender of patent rights in developing countries;[1]

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1 US Food and Drug Administration. Federal Food, Drug, and Cosmetic Act. 2004. Available at: http://www.fda.gov/opacom/law/fdcact/fdctoc.htm (last visited on 20th March, 2009).

2 Pharmaceutical Research and Manufacturers of America. Pharmaceutical Industry Profile 2002. Washington, DC: PhRMA; 2002.

3 Kaiser Family Foundation. Prescription Drug Trends. November 2001. Available at: http://www.kff.org (last visited on 7th May, 2009). See Price Waterhouse Coopers, "The Value of Pharmacy Benefit Management and the National Cost Impact of Proposed PBM Legislation", 2004. Available at: http://www.pwchealth.com/cgi-local/hcregister.cgi?link=pdf/savings.pdf, (last visited on 5th February, 2009).

4 John H. Barton and Ezekiel J. Emanuel, Supra at note 133.

5 Pub L No. 108-173, §101, 42 USC §1869D-11(i) (2003).

6 HHS Task Force on Drug Importation, "Report on Prescription Drug Importation", Washington, DC: US Dept of Health and Human Services; 2004.

7 Scherer FM, Watal J., "Post-TRIPS options for access to patented medicines in

c. although 'buy-out' pricing requires political will of government[2] it may spread the cost of drug development across all of society and make pharmaceutical products available to patients at the lowest possible price, while giving industry substantial research incentives;
d. push arrangements may be used by foundation- supported Public Private Partnerships such as the International Aids Vaccine Initiative to develop drugs for specific diseases of concern to developing nations. Likewise market-pull arrangements are proposed under the World Bank to promise to pay for vaccines meeting the needs of developing countries for some rare diseases.[3]

PATENT VERSUS ACCESS TO MEDICINE: U.S.A., CANADA, AND EUROPEAN UNION PERSPECTIVE:

USA: On January 4, 1983, President Ronald Reagan signed the Orphan Drug Act[4] into law in order to encourage the development of drugs for orphan diseases having incentives of: (i) seven-year market exclusivity for firms that developed orphan drugs; (ii) tax credits equal to half of the development costs -- later amended to offer a fifteen-year carry-forward provision and a three-year carry-back stipulation that can be applied in profitable years; (iii) drug development grants; (iv) fast-track development and approvals of drugs indicated for rare diseases; (v) expanded access to the Investigational New Drug Program, which allows patients access to pre-approved orphan drugs; and (vi) fee reductions, whereby the US FDA waives its drug application fees.[5] The seven year market exclusivity period incentive creates an attractive monopolistic market for companies interested in developing a product for any given rare disease.[6] Before ODA-1983, only ten products for the treatment of rare diseases were approved for use in the

developing nations", J Int Econ Law. 2002;5:913-939.

1 Lanjouw JO., "A new global patent regime for diseases: U.S. and international legal issues", Harv J Law Technol. 2002;16:2-40.

2 Grabowski H., "Alternatives to the patent system: perspectives from economics", Presented at: Innovation in the Life Sciences: Intellectual Property and Public Investment for Pharmaceuticals and Agriculture; May 21, 2004; New York, NY. Available at: http://www.earthinstitute.columbia.edu/cgsd/events/life_sciences_agenda.html (last visited on 18th May, 2009).

3 Kremer M., "Creating markets for new vaccines. In: Jaffe AB, Stern S, eds. Innovation Policy and the Economy", Vol 1. Cambridge, Mass: MIT Press; 2001. See Barton JH., "Financing of vaccines", Lancet. 2000; 355: 1269-1270.

4 John Henkel, "How TV Launched the Orphan Drug Law" FDA Consumer 33:3 (May-June 1999) 34 at 34.

5 Marlene E. Haffner, "Orphan Drugs: the United States Experience" (1999) 33 Drug Information Journal 565.

6 Carson R. Reider, "The Orphan Drug Act: Provisions and Considerations" (2000) 34:1 Drug Information Journal 297 [Reider]; Lisa Ruby Basara & Michael Montagne, "Searching for Magic Bullets", (New York: Pharmaceutical Products Press, 1994) at 144-146 [Basara].

US.[1] Since then, over 1,100 medicinal products have received orphan status in the US, with 248 of these products gaining approval by the FDA.[2] This drug development has improved the quality of life of orphan diseases patients and extended life expectancies. Not only has this legislation helped patients, but it has also benefitted the health care system through cost-savings because many of the treatments help to avoid expensive surgeries and their incidental costs.[3] In 2002, President George W. Bush signed the Rare Diseases Act into law given the concerned office federal power.[4] The Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred as the 'Hatch-Waxman Act' is the model to develop regulatory systems in developing and poor nations.[5] The Orphan Drug Act is a valuable policy change to complement the U.S. patent system to encourage R&D investment for rare diseases.[6] But the promise and problems of pharmaceutical innovation for orphan diseases in USA are difficult to reconcile. Economist Patricia Danzon summarizes the situation as follows:

"Overall, the relatively unregulated, more competitive structure of the United States market seems to result in relatively high prices for on-patent originator products and relatively high use of new products, but strong generic competition, high generic share and low generic prices once patents expire, and a relatively large share of the total public price that goes to manufacturers rather than to intermediaries. By contrast, more regulated markets have lower originator prices but larger post-patent sales for originators and less generic competition. The United States structure appears more favorable to innovation."[7]

Canada: The Doha Ministerial Declaration[8] and the Doha Declaration on TRIPS and Public Health[9] have binding effects on WTO members, and

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1 Marlene E. Haffner, Janet Whitley & Marie Moses, "Two Decades of Orphan Product Development" (2002) 1.10 Nature Reviews 821, at 824.

2Carol Rados, "Orphan Products: Hope for People with Rare Diseases" FDA Consumer 37.6 (November-December 2003), online: U.S. Food and Drug Administration <www.fda.gov/fdac/features/2003/603_orphan.html> (last visited on 17th May, 2009).

3Thomas Maeder, "The Orphan Drug Backlash" (2003) 288:5 Scientific American 80 at 81.

4Alexander Iribarne, "Orphan Disease and Adoptive Initiatives" (2003) 290:1 Journal of the American Medical Association 116.

5 William Haddad, "Generic Medicines: The Solution or the Problem?", 21 October 2004, p. 8, http:// www.cptech.org/ip/health/generic/haddad10212004.doc (last visited on 17th July, 2009) .

6 Grabowski, H., "Increasing R&D incentives for neglected diseases: lessons from the Orphan Drug Act", In International Public Goods, and Transfer of Technology under a Globalized Intellectual Property Regime (eds. Maskus, K.I. & Reichman, J.H.) 457–480 (Cambridge University Press, Cambridge, UK, 2005)

7 Danzon P, Furukawa MF., "Prices and Availability of Pharmaceuticals: Evidence From Nine Countries", Health Affairs Web exclusive. Available at: http://www.healthaffairs.org/WebExclusives/Danzon_Web_Excl_102903.htm (last visited on 10th May, 2009).

8 Doha Ministerial Declaration, WT/MIN (01)/DEC/1, Doha, 14 November 2001.

9 Doha Declaration, WT/MIN (01)/DEC/2, Doha, 14 November 2001.

therefore must guide the interpretation and implementation of the TRIPS Agreement[1] which are the basis for Canada's Act to amend the Patent Act and the Food and Drugs Act of 1985[2]. This Act gives effect to Canada's pledge to Africa by facilitating access to pharmaceutical products to address public health problems afflicting many developing and least developing countries for AIDS and orphan diseases. Therefore Canada is using compulsory licensing for balancing patent protection and universal access to orphan medicines. "From 1969 to 1992, Canada issued more than 600 compulsory licenses on medicines. In nearly every case, the compensation to the patent owner was a standard 4% royalty applied to the generic competitor's sale price".[3] In practice, the Canadian court are free on lower royalties in compulsory licenses for orphan medicines. In Beecham Group Ltd V. Franch W. Horner Ltd.,[4] the Federal Court of Appeal unanimously upheld the Commissioner's decision to award a 1% royalty on the selling price of a pharmaceutical product. Canadian generic pharmaceutical companies, through compulsory licenses issued by the Canadian government, are now able to manufacture patented pharmaceutical, for the purpose of exporting them to developing countries that do not have the required infrastructures and technical knowledge to produce them the pharmaceuticals needed to respond to their public health problems.[5] Bill C-9 gives benefit to non-WTO members in case of extreme urgency of health crisis.[6] In 2004, the Health Ministers of Canada established a Task Force of F/P/T Ministers to create a National Pharmaceuticals Strategy with a report to the Ministers of Health by June 2006 that includes, among other things:

- **drug trial registration designed to accelerate access to breakthrough drugs;**
- **drug purchasing strategies;**
- **national formulary and catastrophic drug coverage;**

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1 Vienna Convention on the Law of Treaties, section 31(3), and TRIPS, on 15 April 1994.

2 An Act to Amend the Patent Act and the Food and Drugs Act, Bill C-9, sanctioned on May 14th, 2004, Third Session, Thirty-seventh Parliament, 52-53 Elizabeth II, 2004, section 21.04.

3 Canadian HIV/AIDS Legal Network, Global Access to Medicines: Will Canada Meet the Challenge?", February 26th, 2004, p. 11 , http://www.aidslaw.ca (last visited on 25th March, 2009), with further reference to: F.M. Sherer, "The Economic of Compulsory Drug Patent Licensing" (2003); Jerome H. Reichman and Catherine Hasenzahl, "Non-voluntary licensing of patented inventions: The Canadian experience" (2002); UNCTAD/ICTSD Capacity-building Project on Intellectual Property Rights and Sustainable Development; Joel Lexchin, "Pharmaceuticals, patents and politics: Canada and bill C-22" (1993); 23 International Journal of Health Services, 47-60; Joel Lexchin, "After compulsory licensing: coming issues in Canadian pharmaceutical policy and politics" (1997), 40 Health Policy, 69-80.

4 1974, 1 F.C. 9.

5 Bill C-9, sanctioned on May 14th, 2004, Third Session, Thirty-seventh Parliament, 52-53 Elizabeth II, 2004, section 21.04.

6 Bill C-9, section 21.03(1) (d)(ii).

There must be specific provision for orphan drugs within this strategy, including:[1]

- tax incentives for R&D that will make Canadian-based companies competitive with those in the USA and other countries;
- market exclusivity for a specified period of time to be facilitate appropriate Return on Investment (ROI);
- protocol assistance in the design and development of clinical trials suitable for rare diseases and disease subgroups;
- expedited reviews;
- assessments for reimbursement (drug plan coverage) that are pre-planned with manufacturers but also with input from clinical experts and patient groups to assure appropriate costs and benefits are included;
- funding for post-market research and patient registry to collect outcomes and safety data;
- catastrophic drug coverage for orphan drugs that includes all patients within an indication, with deductibles and co-payments that do not limit access for any patient, regardless of income or age;
- requirements for coverage within private drug plans (with no annual or life-time capitation).

An Orphan Drug Policy[2] in Canada will-

- provide a registry maintained at the national level that contains statistical information, medications, drug trials and everything known about orphan diseases in order to better assist patients, doctors and researchers to diagnosis orphan diseases;
- detail the appropriate method for fast tracking evaluation processes and funding of orphan drugs and treatments;
- ensure federal funding to assist provinces when faced with a disproportionate number of patients, as many orphan diseases are hereditary. Provincial and local ratios of people afflicted with these diseases are particularly high in given areas;
- promote and support development, research, studies and create jobs in Canada as it provides pharmaceutical and biotechnology companies and institutions incentive to develop orphan drugs in Canada;
- it is clear that all stakeholders including governments, patients/families, doctors, researchers and industry will benefit from a national Orphan Drug Policy in Canada.

European Union: EU believes that adequate protection is to be enacted

1 DePaulsen N., "Working Paper: Abandonment or access: Canada's Orphan Drug Policy", University of Toronto Health Law and Policy Group. 2004. http://www.law.utoronto.ca/healthlaw/studentpapers_content.html (last visited on 28th May, 2009).

2 Canadian Organization for Rare Disorders, "Towards A Canadian Orphan Drug Policy", Guiding Documents, Prepared by the Canadian Organization for Rare Disorders, August 2005.

through WTO in order to encourage investment in research and development of new medicines and particularly those targeted at the major communicable diseases.[1] The 953 regulation allows exporters of life saving pharmaceuticals to deliver their products at a sharply reduced price to developing nations.[2] Since the WTO General Council Decision of 30 August 2003 on the Implementation of paragraph 6 of the Doha Declaration on the TRIPS Agreement and Public Health was finally adopted, the European Parliament and the Council formulated a proposal for a regulation allowing compulsory licensing of patents for developing countries with public health problems.[3] This regulation encourages pharmaceutical companies to reduce the price of orphan drugs in a number of poor countries by preventing their re-importation in the market of rich countries. Under section 4, only the WTO members (especially LDCs) will be able to seek cheap medicines manufactured under a compulsory license.

Incentives for orphan drug development

USA	EU
Tax credit for the costs of clinical research	Access to the centralized procedure for marketing authorization
Annual grant funding to defray the costs of qualified clinical testing expenses	EU-funded research grants from Community and member states programs
Assistance in clinical-study designs	Protocol assistance to optimize development
Seven-year period of exclusive marketing after an orphan drug is approved	Ten-year period of exclusive marketing after an orphan drug is approved
Waiver of Prescription Drug User Fee Act filing fees	100% fee reduction for protocol assistance 50% fee reduction for marketing authorization 100% fee reduction for pre-authorization inspections

1 "European Union, TRIPS: Council Discussion on Access to Medicines", paper submitted by the EU to the TRIPS council, for the special discussion on intellectual property and access to medicines, IP/C/W280, 12 June 2001, (01-2903).

2 Council Regulation (EC) No 953/2003 of 26 May 2003 to avoid trade diversion into the European Union of certain key medicines, Official Journal L 135, 03/06/2003, p. 0005-0011.

3 Commission of the European Communities, "Proposal for a Regulation of the European Parliament and of the Council on compulsory licensing of patents relating to the manufacture of pharmaceutical products for export to countries with public health problems", Brussels, November 2004; http://www.europa.eu.int/comm/internal_market/en/indprop/patent/draft_en.pdf (last visited on 29th April, 2009).

PHARMACEUTICAL PATENT LAW IN BRAZIL, RUSSIA, INDIA, CHINA AND SOUTH AFRICA (BRICS):

Brazil: Brazil, which having the world's fifth largest population is the poster child of the use of compulsory licenses to promote access to essential orphan medicines. In April 2007 Brazil granted compulsory licenses for the non-commercial public use of the patented orphan (especially AIDS) drug.[1] Over the years, Brazil has also developed a very successful program to provide free, universal access to the treatment of HIV including some rare diseases. Its National STD/AIDS Programme "has reduced AIDS-related mortality by more than 50 percent between 1996 and 1999. In two years, Brazil saved $472 million in hospital costs and treatment costs for AIDS-related infections."[2] The Programme has been widely recognized as a model for the less developed world.[3] For decades, Brazil has been a leading voice for less developed countries. During the TRIPs negotiations, it was one of the ten hardliner countries that refused to expand the mandate of the General Agreement on Tariffs and Trade ("GATT") to cover substantive intellectual property issues.[4] During the Fifth WTO Ministerial Conference in Cancún in 2003, Brazil choreographed the G-20,[5] whose demands and resistance led to

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1 Press Release, Brazilian Ministry of Health, Brasil decreta licenciamento compulsório do Efavirenz (May 5, 2007), available at: portal.saude.gov.br/portal/aplicacoes/noticias/noticias_detalhe.cfm?co_seq_noticia=29717 (last visited on 16th May, 2009). As Robert Bird and Daniel Cahoy have noted, "it is likely that the move was at least partially sparked by the desire to obtain the same price Thailand secured following its successful issuance of several compulsory licenses for AIDS and heart drugs." Robert C. Bird & Daniel R. Cahoy., "The Emerging BRIC Economies: Lessons from Intellectual Property Negotiation and Enforcement", 5 Nw. J. Tech. & Intell. Prop. [illegible] (2007).

2 Ellen't Hoen, "TRIPS, Pharmaceutical Patents, and Access to Essential Medicines: A Long Way from Seattle to Doha", 3 Chi. J. Int'l L. 27, 32 (2002)

3 See id. (Noting that "[t]he Brazil AIDS program serves as a model for some developing countries that are able to produce medicines locally"); Comm'n on Intellectual Prop. Rights, Integrating Intellectual Property Rights and Development Policy: Report of the Commission on Intellectual Property Rights 43 (2003) (noting that the National STD/AIDS Programme in Brazil "has been widely acclaimed as a possible model for other countries"); John S. Odell & Susan K. Sell, "Reframing the Issue: The WTO Coalition on Intellectual Property and Public Health", 2001, in Negotiating Trade: Developing Countries in the WTO and NAFTA 85, 96 (John S. Odell ed., 2006) (observing that "[d]eveloping countries looked to Brazil as a beacon of hope in strategies to combat the HIV/AIDS crisis").

4 Jayashree Watal, "Intellectual Property Rights in the WTO and Developing Countries", 19 (2001). The other countries were Argentina, Cuba, Egypt, India, Nicaragua, Nigeria, Peru, Tanzania, and Yugoslavia.

5 The current members of the G-20 are Argentina, Bolivia, Brazil, Chile, China, Cuba, Ecuador, Egypt, Guatemala, India, Indonesia, Mexico, Nigeria, Pakistan, Paraguay, Peru, Philippines, South Africa, Tanzania, Thailand, Uruguay, Venezuela, and Zimbabwe. The website of the G-20 is available at www.g-20.mre.gov.br (last visited on 5th May, 2009). Notably, the G-20 includes all BRICS countries that are members of the WTO. G-20, G-20 Members, www.g-20.mre.gov.br/members.asp (last visited 5th May, 2009).

[illegible] Organization [illegible] Brazil remains the only [illegible] developed country that has [illegible] requested consultations [illegible] WTO [illegible] settlement process [illegible] developed country [illegible] of intellectual property laws with the TRIPS agreement. [illegible] Brazil's aggressive public health positions [illegible] developed world, the United States Trade [illegible] in its Influence [illegible] countries [illegible] major barriers to U.S. intellectual property [illegible] which is another barrier [illegible] orphan drugs by passing [illegible] compulsory [illegible] Article 68 of the 1996 [illegible] principle of IP protection [illegible] population to [illegible] the spirit of TRIPS [illegible] is [illegible] patent.[6] [illegible] Brazil has put pressure on pharmaceutical companies to reduce their drug prices by threatening to make generic copies locally if they did not oblige and announced to import generic medicines from China and India.[7] In 2005 Brazilian public and private companies are producing 7 out

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1 Elizabeth Becker, "Poorer Countries Pull Out of Talks Over World [illegible]", N.Y. Times, Sept. 15, 2003, at A1; Editorial, The Cancun Failure, N.Y. Times, Sept. 16, 2003, at A24.

2 Press Release, World Intellectual Prop. Org. [WIPO], Member States Agree to Further Examine Proposal on Development (Oct. 4, 2004), [illegible] www.wipo.int/edocs/prdocs/en/2004/wipo_pr_2004_390.html (last visited on [illegible] 2009).

3 Press Release, WIPO, Member States Adopt a Development Agenda for WIPO (Oct. [illegible] 2007), available at www.wipo.int/pressroom/en/articles/2007/article_0071.html (last visited on 7th July, 2009).

4 Request for Consultations by Brazil, United States--US Patents Code, WT/DS224/1 (Feb. 7, 2001). It is important to note that the request was made in response to the United States' challenge of Brazil's patent laws before the WTO. As Gregory Shaffer lamented, "Brazil ... never seriously pursued their claims to advance commercial interests, but rather searched for bargaining chips for a potential settlement of the US and EC complaints." Gregory Shaffer, "Recognizing Public Goods in WTO Dispute Settlement: Who Participates? Who Decides? The Case of TRIPS and Pharmaceutical Patent Protection," [illegible] (2004).

5 Government of Brazil, Press Communique by the Government of Brazil [illegible] 2001, [illegible] (last visited on [illegible] 2009).

6 [illegible]

7 Mario Osava, IPS: Brazil: Imports Generic AIDS Drugs from India and China, September 6th, 2003, [illegible] (last visited [illegible])

of 16 drugs that are used in the tri-therapy while there is capacity to produce all of the needed medicines.[1]

Russia: As a major military power with nuclear capabilities, it has an enviable status in world politics and is of great political importance to the European Communities and the United States.[2] It also has very high research-and-development capabilities and a considerable amount of technology-related human capital--two critical elements for the successful development of indigenous intellectual property industries. But its technological development relates to the nuclear improvement rather than orphan or conventional drug and medicine. Although Russia's piracy and counterfeiting problems are as serious as, if not more than, those of China,[3] the country's limited economic growth has made Russia a less attractive market for Western businesses. For the same reason Russia is not paying attention to improved drugs for orphan diseases as well as it is not an active participant for R&D or cure of neglected diseases in developing state of the world.

India: In case of India and other developing countries TRIPS always bears controversial debates between developed and developing countries. One side, strong business interests in the developed world claimed that illegitimate use of their innovation was being made in the developing world, and that this was leading not only to important financial losses for the industry in the developed countries, but also distinctive for foreign investment, technology transfer and greater domestic research and development.[4] India adopted Patent Act in 1970 that prohibited product patents for medicines, restricting the scope of patentability of medicines only for the production processes and not for the end product itself. The 1970 Patent Act brings lower price for drugs through independent drug manufacturers who make generic copies of drugs that are originally developed and patented in the west. This trend leads India to be one of the main suppliers of cheap drugs to developing countries for both common and orphan diseases. The general provisions for compulsory licensing become more relevant since TRIPS has started to be implemented in India from March 2005, therefore modifying India's patent law. Section 83 of the Patent

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on 18th May, 2009).

1 Group De Trabalhosobre Propriedade Intelectual, "Declaration of Civil Society regarding the Brazilian Negotiations for Voluntary Licenses for AIDS drugs", GTPI-da Rde Brazilaira pela Integracao dos Povos- Rebrip, Rio de Janeiro, May 5th, 2005.

2 Bird & Cahoy, "The Emerging BRIC Economies", supra note 140, at 409 (noting that "India lacks the economic power of China and the political importance of Russia in the eyes of the United States").

3 Int'l Intellectual Prop. Alliance, 2007 Special 301 Report 115 (2007) (noting that "Russia's current copyright piracy problem remains one of the worst of any country in the world").

4 J. O. Lanjouw, "The Introduction of Pharmaceutical Product Patents in India: Heartless Exploitation of the Poor and Suffering", WP 07/99, OIPRC Electronic Journal of Intellectual Property Rights; http://www.oiprc.ox.ac.uk/EJWP0799.html (last visited on 13th June, 2009).

Act No. 39 of 1970 provides principles for working of a patent in India stating that without prejudice to other provisions, "that patents are granted to encourage inventions and to secure that the inventions are worked in India on a commercial scale and to the fullest extent that is reasonably practicable without undue delay"; and "that they are not granted merely to enable patentees to enjoy a monopoly for the importation of the patented article". Section 84 allows the issuance of a compulsory license if an invention is not made available to the public in India at a reasonable price after three years since the invention has started to be commercialized. On January 1, 2005, India introduced a new patent law[1] which is likely to have a major impact on the development and availability of cheap, generic drugs and related ingredients without affecting the production of drugs that have already been developed and 'it includes specific provisions to allow generic manufacturers to continue to sell drugs that are already developed by paying reasonable royalties to patent holders'.[2]But the impact of the new law on the global supply of generic drugs is matter of concern because India "makes more than a fifth of the world's generic drugs." [3]

China: In 2001 China became the 143rd member of WTO[4] having piracy and counterfeiting problems in pharmaceutical sectors also.[5] As a result, the country catches the attention of the United States Priority of Section 301 Watch List. Notwithstanding the considerable piracy and counterfeiting problems in China, there has been noticeable improvement of intellectual property protection in the country's major cities and the coastal areas.[6] Although China has hitherto maintained a relatively low profile in the WTO,[7] it is likely to become a very important player in the WTO, even if

1 For a comprehensive discussion of the recent changes in Indian patent law, see generally Janice M. Mueller, "The Tiger Awakens: The Tumultuous Transformation of India's Patent System and the Rise of Indian Pharmaceutical Innovation", 68 U. Pitt. L. Rev. 491 (2007).

2 Peter K. Yu, "The International Enclosure Movement", 82 Ind. L.J. 863 (2007).

3 Kamal Nath, "India's Century 110 (2008); see also Colleen Chien., "HIV/AIDS Drugs for Sub-Saharan Africa: How Do Brand and Generic Supply Compare?", 2 PLOS ONE e278 (2007) (reporting that India provided 85% of generic HIV/AIDS antiretrovirals in Sub-Saharan Africa), available at ssrn.com/abstract=1009287.

4 Symposium, China and the WTO: Progress, Perils, and Prospects, 17 Colum. J. Asian L. 1, 2 (2003).

5 For discussions of piracy and counterfeiting problems in China in the 1980s and 1990s, see Peter K. Yu, From Pirates to Partners: Protecting Intellectual Property in China in the Twenty-First Century, 50 Am. U. L. Rev. 131 (2000); Peter K. Yu, "Piracy, Prejudice, and Perspectives: Using Shakespeare to Reconfigure the U.S.-China Intellectual Property Debate", 19 B.U. Int'l. L.J. 1 (2001).

6 Peter K. Yu, "From Pirates to Partners (Episode II): Protecting Intellectual Property in Post-WTO China", 55 Am. U. L. Rev. 901, 975-99 (2006) (examining the progress China has made in the intellectual property arena).

7 Henry S. Gao, "China's Participation in the WTO: A Lawyer's Perspective", 11 Sing. Yb. Int'l L. 1, 29-30 (2007) (explaining why "China has consistently taken a low profile in all WTO activities"); see also Yan Li, "Faint Silhouette: Can China Be a WTO Leader?", Wash. Observer, Dec. 14, 2005, www.washingtonobserver.org/en/topic.cfm?topicid=29&charid=3, (reporting an

it does not become as vocal a leader as Brazil or India in case of orphan drug innovation and research.

South Africa: Although economy is powerful,[1] South Africa has been cited as an example of the wider socio-economic and public health problems caused by high intellectual property standards required by the TRIPS Agreement.[2] Along with Brazil and India, South Africa was prominently involved in the negotiations[3] that led to the Decision on the Implementation of Paragraph 6 of the Doha Declaration on the TRIPS Agreement and Public Health.[4] It has also been instrumental in putting the access-to-medicines issue on the human rights and public health agendas.[5] South Africa remains now very active in the access-to-medicines debate especially in the field of orphan drugs as the prevalence of rare diseases there is more than others.

In retrospect, one could argue that the campaign on access to drugs, to which South Africa made an important contribution, provides a major turning point in the TRIPS debate.[6] When South Africa enacted a law to allow for compulsory licenses used in the manufacture of generic HIV/AIDS drugs including some orphan drugs in December 1997, the South African Pharmaceutical Manufacturers Association brought suit to challenge the law before the Pretoria High Court.[7] The United States government backed the industry by putting South Africa on the Section 301 Watch List and announcing the suspension of its Generalized System of Preferences (GSP) benefits.[8] But the South African government received considerable support

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interview with the Author on China's potential leadership in the WTO) (last visited on 4th May, 2009).

1 Dominic Wilson & Roopa Purushothaman., "Dreaming with BRICs: The Path to 2050", www.goldmansachs.com/ideas/global-growth/99-dreaming.pdf (last visited on 7th July, 2009), at 11.

2 Susan K. Sell, "Private Power, Public Law: The Globalization of Intellectual Property Rights", 146-62 (2003); Debora Halbert., "Moralized Discourses: South Africa's Intellectual Property Fight for Access to AIDS Drugs", 1 Seattle J. Soc. Just. 257 (2002); Ellen't Hoen., "TRIPS, Pharmaceutical Patents, and Access to Essential Medicines: A Long Way from Seattle to Doha", 3 Chi. J. Int'l L. 27, 32 (2002).

3 Sonia E. Rolland, "Developing Country Coalitions at the WTO: In Search of Legal Support", 48 Harv. Int'l L.J. 483, 496 (2007)

4 General Council, Implementation of Paragraph 6 of the Doha Decaration on the TRIPS Agreement and Public Health, WT/L/540 (Sept. 1, 2003), 43 I.L.M. 509 (2004).

5 See Yu, The International Enclosure Movement; supra note 191, at 865-66.

6 Susan K. Sell, "Private Power, Public Law: The Globalization of Intellectual Property Rights", 146-62 (2003); Debora Halbert., "Moralized Discourses: South Africa's Intellectual Property Fight for Access to AIDS Drugs", 1 Seattle J. Soc. Just. 257 (2002); at 181 (observing that "[t]he HIV/AIDS pandemic was a contingency that sped up the revelation of the negative consequences of TRIPS"); Ruth Mayne., "The Global Campaign on Patents and Access to Medicines: An Oxfam Perspective, in Global Intellectual Property Rights: Knowledge, Access and Development", 244, 249 (Peter Drahos & Ruth Mayne eds., 2002) (noting that "the South African government's decision to fight the case was a critical factor in generating global media interest").

7 id, at 151.

8 id. at 152.

from advocacy and minority groups who are concerned about rare disease and drugs.[1] South Africa is now trying to innovate drugs for rare disease and government is proceeded to do R&D on tropical diseases also.

TRIPS AND PHARMACEUTICAL PATENT: ACCESS TO MEDICINE IN NATIONAL LEVEL:

Patients in the developing world suffer from same global orphan diseases having limited access to currently existing treatments[2] as the current system of pharmaceutical innovation ignores neglected diseases entirely or predominantly afflicting those poor[3] and market-exclusivity protection are insufficient to recoup the high costs and justify the high risk associated with pharmaceutical research and development.[4] In case of neglected diseases, though fostering access to currently existing medicines is imperative, the primary policy concern is stimulating R&D into new and improved treatments appropriate for resource-limited settings.[5] Neglected diseases can broadly be defined as seriously disabling or life-threatening diseases for which treatment options are inadequate or do not exist,[6] and for which the

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1 id. Sell, at 152-53; see also Halbert, id, at 270.

2 According to the World Health Organization [WHO], at the beginning of the 21st century an estimated one-third of the world population still lacked regular access to even essential medicines, with this figure rising to over 50 per cent in Africa and Asia. WHO, WHO Medicines Strategy 2000-2003: Framework for Action in Essential Drugs and Medicines Policy (Geneva: WHO, 2000) at 2, online: WHO whqlibdoc.who.int/hq/2000/WHO_EDM_2000.1.pdf. (last visited on 15th May, 2009)

3Illustrative is Africa, which accounts for only 1.3 per cent of the world pharmaceutical market by sales. IMS Health, "Market Report: Global Pharmaceutical Market Forecasts", online: IMS Health www.ims-global.com, (last visited on 17th June, 2009).

4 www.insight/report/global/report.htm, (last visited on 29th May, 2009) [IMS Market Report] cited in C. Correa, "Patent Law, TRIPS, and R and D Incentives: A Southern Perspective" in Commission on Macroeconomics and Health Working Paper Series (Geneva: WHO, 2001) Paper No. WG2:12 at 21, online: Commission on Macroeconomics and Health www.cmhealth.org/docs/wg2_paper12.pdf, (last visited on 29th May, 2009). Innovator pharmaceutical companies are unlikely to allocate research and development capital to conditions localized to such a small and impoverished market because expected future sales would be unlikely to provide sufficient return on investment.

5 Developing countries have unique disease epidemiologies and very different drug needs compared to the developed world that are not taken into account in pharmaceutical R and D expenditures. See J.O. Lanjouw and I. Cockburn, "New Pills for Poor People? Empirical Evidence after GATT" (2001) 29:2 World Development 265, cited in Correa, supra note 5 at 19. For example, for most neglected diseases (other than perhaps tuberculosis), 99 per cent of the global disease burden is localized to low-income developing countries and LDCs.

6Treatments for some of these diseases do exist and are included on the WHO Model List of Essential Medicines, but are often antiquated, very difficult to administer, ineffective due to drug resistance, and/or cause severe side effects. See Drugs for Neglected Diseases Initiative, "DNDi: An Innovative Solution (DNDi Introductory Brochure)" (April 2004) at 6, online: Drugs for Neglected Diseases Initiative www.dndi.org-www.dndi.org/cms/public_html/images article/268/An%20Innovative%20Solution.pdf,

potential market is insufficient to attract a private sector response.[1] R&D is urgently needed to offer a wider range of safe and effective treatments for conditions such as malaria,[2] tuberculosis,[3] African sleeping sickness,[1] and

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(last visited on 16th April, 2009), [DNDi Brochure] at 7.

1C. Milne, K. Kaitlin and E. Ronchi, "Orphan Drug Laws in Europe and the US: Incentives for the Research and Development of Medicines for the Diseases of Poverty" in Commission on Macroeconomics and Health Working Paper Series (Geneva: WHO, 2001) Paper No. WG2:9 at 42, online: Commission on Macroeconomics and Health www.cmhealth.orgwww.cmhealth.org/docs/wg2_paper9.pdf (last visited on 13th June, 2009), at 2.

2 Malaria infects 300-500 million people (almost 90 per cent of whom reside in Africa) and kills one to three million people each year. See Milne, Kaitlin and Ronchi, supra note 211 at [illegible] and Kremer, supra note 150 at 10. Currently existing malaria drugs, such as chloroquine and mefloquine, are not well suited to treating those infected in the developing world and widespread resistance is rendering them ineffective. New artemisinin derivatives offer the most promise, but are urgently needed in fixed-dose combinations (FDCs) to ensure adherence and prevent resistance. So far, Coartem (produced by Novartis) is the only FDC in existence, but is expensive, has serious side-effects, and must be taken with a fatty meal (an impossibility for many patients in developing countries). See Drugs for Neglected Diseases Initiative, "FACT Sheet: The Drugs for Neglected Diseases Initiative (DNDi) Fixed-dose Artesunate Combination Therapy (FACT) Project", online: Drugs for Neglected Diseases Initiative www.dndi.org/cms/public_html/insidearticleListing.asp?categoryid=164&articleid=304 &templateid=2, (last visited on 6th May, 2009) A further problem is that new artemisinin-based treatments continue to be as much as 20 times more expensive than chloroquine. See Médecins Sans Frontières, "Will the Lifeline of Affordable Medicines be Cut?" (Geneva: Médecins Sans Frontières, February 2005) at 2, online: Campaign for Access to Essential Medicines www.accessmedmsf.org/upload/ReportsandPublications/23520051143836/India%20briefing%20note%20Feb%2024%20FINAL.doc(last visited on 6th May, 2009), [MSF, "Lifeline"]. Though outdated, price constraints mean that many African countries continue to rely on chloroquine for their treatment programs.

3 Tuberculosis kills 1.7 million people each year, 98 per cent of them in the developing world. See M. Kremer, "Public Policies to Stimulate Development of Vaccines and Drugs for the Neglected Diseases" in Commission on Macroeconomics and Health Working Paper Series (Geneva: WHO, 2001) Paper No. WG2:8 at 12, online: Commission on Macroeconomics and Health www.cmhealth.orgwww.cmhealth.org/docs/wg2_paper8.pdf, (last visited on 6th May, 2009) at 10. The accepted regimen, directly-observed-treatment-short-course (DOTS), involves a cocktail of old, off-patent drugs that were developed 40-60 years ago and which need to be administered over a period of months with supervision to ensure compliance. See Médecins Sans Frontières, "R and D System is Failing to Meet Health Needs in Developing Countries, MSF Briefing Note" (Geneva: Médecins Sans Frontières, 2005) at 8, online: Campaign for Access to Essential Medicines www.accessmed-msf.org/documents/MexicoR&Dbriefing.pdf,(last visited on 6th May, 2009) [MSF, "R and D System Failure"]. They are inexpensive, typically costing in the range of $10 per patient. See H. E. Bale, Jr., "Consumption and Trade in Off-Patented Medicines" in Commission on Macroeconomics and Health Working Paper Series (Geneva: WHO, 2001) Paper No. WG4:3 at 5, online: Commission on Macroeconomics and Health www.cmhealth.org/docs/wg4_paper3.pdf, (last visited on 6th May, 2009). However, only 21 per cent of patients received DOTS worldwide as of 1998. See Milne,

leishmaniasis;[2] yet current efforts are paltry.[3] This has led to an appalling dearth of new drug development, with only 13 of 1,393 new drugs registered worldwide between 1975 and 1999 being indicated for the treatment of tropical diseases (including malaria), and an additional three being indicated for tuberculosis.[4] This absence of innovative activity persists despite an environment in which public sector R&D has generated a substantial amount of basic knowledge about these diseases, which could be used for promising drug development leads.[5]

Kaitlin and Ronchi, supra note 211 at 37. DOTS is also very poorly suited for the developing world and is becoming increasingly ineffective due to resistance. An alarming number of infections, termed multi-drug resistant tuberculosis (MDRTB), are resistant to two or more of the major anti-tubercular drugs. No new drugs for MDRTB are in the pipeline and fixed-dose combinations of currently-existing drugs are needed. See Milne, Kaitlin and Ronchi, ibid. at 37-38. A vaccine does exist but is largely ineffective. See M. Kremer, supra note 150 at10.

1 African sleeping sickness, which is entirely confined to tropical Africa, killed 150,000 people in 1996, with 60 million people at constant risk. There are only four drugs in existence to treat this disease, and only 10 per cent of patients have access. The first-line treatment, melarsoprol, induces fatal reactive encephalopathy in 5 per cent of patients, and 30 per cent of patients do not respond to it at all. See C. Milne, K. Kaitlin and E. Ronchi, "Orphan Drug Laws in Europe and the US: Incentives for the Research and Development of Medicines for the Diseases of Poverty" in Commission on Macroeconomics and Health Working Paper Series (Geneva: WHO, 2001) Paper No. WG2:9 at 42, online: Commission on Macroeconomics and Health www.cmhealth.orgwww.cmhealth.org/docs/wg2_paper9.pdf, (last visited on 5th May, 2009), at 43-44.

2 Leishmaniasis is fatal without treatment and affects 12 million worldwide, with 200 million at risk. See DNDi Brochure, supra note 210 at 18. The most widely prescribed drug, pentavalent antimony, was discovered a century ago, has serious side effects, requires prolonged treatment, and is losing efficacy due to widespread resistance. See Drugs for Neglected Diseases Initiative, DNDi's R and D Portfolio: 2003-2004 (First Quarter) (June 2004), online: Drugs for Neglected Diseases Initiative www.dndi.org/cms/public_html/images/article/284/DNDiRDStrategyMay2004.pdf, (last visited on 6th May, 2009), [DNDi R and D Portfolio].

3 Kremer, supra note 150 at 10. For example, as of 2001, only three pharmaceutical companies world-wide were undertaking any R and D for malaria, and only two for all other tropical diseases. See Milne, Kaitlin and Ronchi, supra note 211 at 14. Research from the 1990s indicated that, while $3,800 was being spent on research per cancer-related death and $1,000 per heart disease death, only $84 was being spent per malaria death, which was the best funded of tropical diseases. Further, in 2001, total worldwide health R and D funding was $60 million for malaria and $19-33 million for tuberculosis, compared to approximately $985 million for HIV/AIDS (ibid. at 35).

4 P. Trouiller et al., "Drug Development for Neglected Diseases: A Deficient Market and a Public-Health Policy Failure", (2002) 359, The Lancet 2188 at 2189. These figures suggest that adequate capital resources are currently being allocated to R and D on these conditions, at 2189.

5 B. Pecoul, "New Drugs for Neglected Diseases: From Pipeline to Patients" (2004) 1:1 PloS Medicine 19 at 19, online: PLoS Medicine at http; //www.medicine.plosjournals.org/archive/1549-1676/1/1/pdf/10.1371_journal.pmed.0010006-S.pdf, (last visited on 7th May, 2009).

PATENT AND TRIPS:

Patent makes an important contribution to stimulating R&D in the developed world pharmaceutical sector,[1] spurs local innovative activities[2] for neglected disease and ultimately brings investment resources and transfer technologies for developing states. IP protection for a given country is thus related to its level of economic development and its level of indigenous technological capacity, with stricter protection becoming rational over time as innovative capacity evolves.[3] Global efficiency arguments state that the worldwide protection of intellectual property rights will increase global revenues to innovators and thus yield greater amounts of innovation, which will in turn benefit consumers everywhere.[4] The Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPs) came into force on 1 January 1995 by setting minimum uniform standards of IP protection and enforcement in all Member States. Instead of being based on sound economic principles, the conclusion of TRIPS is better understood as the product of global political forces.[5] TRIPS requires that all WTO Member States

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1 E. Mansfield, "Patents and Innovation" (1986) 32:2 Management Science 173.

2 Trebilcock and Howse, "The Regulation of International Trade", 2nd ed. (New York: Routledge, 1999) at 310.

3India provides an apt example. After 1970, and until 2005, India did not allow patents on pharmaceutical products, which allowed a flourishing domestic generic drug industry to develop by imitating and adapting technologies from abroad (by 2005, India was home to over 20,000 generic drug companies, producing 60,000 generic brands in 60 therapeutic categories). With the introduction of pharmaceutical product patenting in 2005, experts say that Western companies will now ramp up investments and begin launching new products in India. Further, some of the larger local generic companies will begin investing more into R and D as well. Ultimately, the Indian pharmaceutical industry is expected to grow 8-9 per cent annually. See R. Mayer, "A Passage for India: Following the Adoption of the TRIPS Agreement, India's Generic Pharmaceutical Sector will Contract, but Western Companies and Some Indian Companies that have Expanded their Focus to Original Research will Benefit" (1 February 2009) 24:2 Med Ad News 4 (Lexis). However, this sort of economic stimulus from the introduction of pharmaceutical patenting would not have been possible without a substantial period of lax IP protection in which technology transfer occurred due to the absence (not presence) of pharmaceutical patenting. India's economy grew substantially under these conditions, with a current middle class of over 300 million, giving it a large degree of latent innovative capacity waiting to be unleashed by a pharmaceutical patenting regime. Conditions are not similar in many other developing countries, where introducing pharmaceutical patenting would have no impact on local innovation. Also, it is not clear that the increased level of innovation in India can justify the attendant expected contraction in the local generic industry, and thus the increased prices and reduced access that will follow.

4 Trebilcock and Howse, supra note 220 at 310.

5 Powerful producer interests such as the brand name pharmaceutical industry and powerful Western countries with comparative advantage in innovation, such as the United States, were a significant driving force behind the adoption of TRIPS. The overall American goal in negotiating TRIPS was clear: to obtain rules that would ensure that US innovators' IP rights were as extensively protected abroad as domestically. See Trebilcock and Howse, supra note 220 at 320. Despite strong opposition among

provide patent protection for any inventions, whether products or processes, in all fields of technology, including pharmaceuticals, provided they are new, involve an inventive step and are capable of industrial application.[1] Protection must be granted for a minimum of 20 years from the date of filing[2] and must confer on the patent holder the exclusive right to prevent third parties from making, using, offering for sale, selling, or importing for such purposes, a product that is the subject of his or her patent.[3] A separate requirement of the TRIPS Agreement is that Members, when requiring the submission of undisclosed test data as a condition of granting regulatory approval to a drug incorporating a new chemical entity, must protect such data against "unfair commercial use".[4] Further, Members must protect such data against disclosure except where necessary to protect the public or unless steps are taken to ensure that the data is protected against unfair commercial use.[5] The extent to which this provision prevents national drug regulatory authorities (NDRAs) from registering generic drugs on the basis of bio-equivalence is unclear, though negotiators directly rejected proposals to include concrete pharmaceutical data exclusivity provisions, which would have completely prevented the use of originator clinical trial data in registering generics during a period of five to 10 years.[6] TRIPS provides certain flexibilities in an attempt to balance conflicting national perspectives with respect to intellectual property protection.[7] Under Article 31 it allows

developing country Members to the negotiation of IP rights within the WTO Global Agreement on Tariffs and Trade (GATT), they eventually succumbed to the pressure of American and other Western governments, in part because of promised concessions on agricultural and textile tariffs which to date have not materialized.

1 WTO, Agreement on Trade-Related Aspects of Intellectual Property Rights, Being Annex 1C to the Final Act and Agreement Establishing the World Trade Organization, 33 I.L.M. 81, 15 December 1993, art. 27(1), online: WTO www.wto.org/english/docs_e/legal_e/27-trips.pdf (last visited on 15th June, 2009), [TRIPS].

2 Ibid., art. 33.

3 Ibid., art. 28(1).

4 Ibid., art. 39(3).

5 Ibid.

6 Despite the absence of a concrete provision of this nature, countries such as India have been under international pressure to implement strict data exclusivity provisions under TRIPS. See S. Narrain, "Patents and Public Health Concerns" The Hindu (15 November 2005).

7 Trebilcock and Howse, supra note 220 at 322. For example, Article 7, which sets out the objectives of TRIPS, acknowledges that a balance of competing interests must be struck. According to that article, "the protection and enforcement of intellectual property rights should contribute to the promotion of technological innovation and to the transfer and dissemination of technology, to the mutual advantage of producers and users of technological knowledge and in a manner conducive to social and economic welfare, and to a balance of rights and obligations". Particularly relevant to pharmaceuticals, the Principles articulated in Article 8 recognize that "Members may, in formulating or amending their laws and regulations, adopt measures necessary to protect public health... provided that such measures are consistent with the provisions of this Agreement". See TRIPS, supra note 19, arts. 7-8.

Member states to grant compulsory licenses and to permit parallel importation of patented products sold abroad. Compulsory licensing, which is defined as an authorization "permitting a third party to make, use, sell, [or import] a patented invention without the patent holder's consent".[1] Though Members theoretically have unlimited scope to make use of compulsory licensing, TRIPS imposes certain procedural and substantive requirements. Prior to issuing a compulsory license, the proposed user must have made efforts to negotiate authorization from the patent holder on reasonable commercial terms, and such efforts must not have been successful within a reasonable period of time.[2] This requirement can be waived in the case of national emergency or other circumstances of extreme urgency or in cases of non-commercial public use.[3] This language is ambiguous and its precise meaning has not been clarified in WTO dispute settlement resolution. Article 31 further requires that the permitted use must be limited in scope and duration to the purpose for which it was authorized,[4] and must be liable to termination when the circumstances which led to it cease to exist and are unlikely to recur.[5] In all cases, the patent holder must be paid adequate remuneration, taking into account the economic value of the authorization.[6] Finally, and perhaps most controversially, Article 31(f) requires that use authorized under a compulsory license must be "predominantly for the supply of the domestic market".

Under Article 31 conditions are relaxed where a Member determines that a compulsory license is required to remedy an anti-competitive practice.[7] The requirements of prior negotiation with the patent holder in Article 31(b) and predominantly supplying the domestic market in Article 31(f) are not applicable in such a circumstance, and the need to correct the anti-competitive practice may be taken into account in determining the amount of remuneration required under Article 31(h). Article 6 of TRIPS allows countries to permit parallel importation, which occurs when a patented product is sold abroad by the patent holder and then imported without his or her consent[8] i.e., any country may adopt the doctrine of international exhaustion of rights. This doctrine prevents a patentee who has sold a product from exercising any determination over the conditions of resale of the same product abroad.[9] Article 2 recognizes the so-

1 Scherer and J. Watal, "Post-TRIPS Options for Access to Patented Medicines in Developing Countries" in Commission on Macroeconomics and Health Working Paper Series (Geneva: World Health Organization, 2001) Paper No. WG4:1 at 4, online: Commission on Macroeconomics and Health www.cmhealth.org/docs/wg4_paper1.pdf., (last visited on 17th June, 2009), at 13.

2 TRIPS, supra note 54, art. 31(b).

3 Ibid.

4 Ibid., art. 31(c).

5 Ibid., art. 31(g).

6 Ibid., art. 31(h).

7Ibid., art. 31(k).

8 Scherer and Watal, supra note 231 at 30. Incentives for this sort of trade materialize when there is a sufficient price differential between two countries.

9 Ibid. at 31.

called right of priority for patent applications where an inventor who files for a patent in one Member country has one year to file for patents in all other Members before the subject matter of his or her patent application will be considered publicly disclosed and thus not eligible for protection in those other Members.[1] TRIPS permitted certain transitional arrangements with respect to its implementation.[2] All Members were given one year following the entry into force of TRIPS to apply its provisions domestically (until January 1996), with developing country and transition economy Members being given an additional four years (until January 2000).[3] Further, to the extent that a developing country Member was obliged to extend product patent protection to areas of technology not previously protectable in its territory, it was permitted an additional five years for those areas of technology (until January 2005).[4] In practice, this extension was of little value as most developing countries already granted pharmaceutical product patents. One key exception was India, whose full use of the extension ensured access to low cost generic ARVs both domestically and in other developing countries up to now.[5] The Indian Parliament passed an amendment to its Patents Act in 2005 to become TRIPS compliant and is currently in the process of fully implementing pharmaceutical product patenting.[6] The passage of this amendment has been a central focus of advocates for access to essential medicines, who are concerned that the developing world's primary source of cheap generic versions of on-patent medicines will be cut off.[7] An additional extension was also granted for least-developed country Members (LDCs).[8] These countries were granted a blanket 10-year exemption from the TRIPS Agreement from the date of its entry into force, with the understanding that the Council for TRIPs[9] could extend this period upon

1 World Intellectual Property Organization (WIPO), Paris Convention for the Protection of Industrial Property, 20 March 1883, as rev. 14 July 1967 and as am. 28 September 1979 revised, 828 U.N.T.S. 305, art. 4, online: WIPO www.wipo.int/treaties/en/ip/paris/pdf/trtdocs_wo020.pdf, (last visited on 16th June, 2009).

2 See TRIPS, supra note 54, Part VI.

3 Ibid., art. 65.

4 Ibid., art. 65(4).

5 Health Gap Global Access Project, Press Release, "Fact Sheet: Changes to India's Patents Act and Access to Affordable Generic Medicines After January 1, 2005" (16 December 2004), online: Health Gap Global Access Project www.healthgap.org/press_releases/04/121404_HGAP_FS_INDIA_patent.pdf, (last visited on 17th May, 2009), [Health Gap India].

6 The amendment passed in both houses of Parliament and was given presidential assent on 6 April 2005. Elizabeth Engdahl, "India Alters Patent Views" Legal Times (11 July 2005) at 6.

7 See Health Gap India, supra note 244.

8 For a list of least-developed countries, see World Trade Organization, "Understanding the WTO-Least-Developed Countries", online: World Trade Organization www.wto.org/english/thewto_e/whatis_e/tif_e/org7_e.htm., (last visited on 8th March, 2009).

9 TRIPS created a new institution, the Council for TRIPS, charged with monitoring

request from an LDC Member.[1] Despite this arrangement, most LDCs already grant patents for all inventions, including pharmaceutical products.[2] After 1995, where a developing Member, such as India, decided to avail itself of the flexibility to delay the implementation of pharmaceutical product patent protection until 2005, that Member was required to provide a means by which patent applications for such inventions could be filed[3] according to mailbox patent applications.[4] Upon implementation of pharmaceutical product patenting, the Member would then be required to review these mailbox applications, and grant patents where warranted from the date of filing until the remainder of the patent term expired.[5] The potential for the TRIPS Agreement to impede effective responses to public health problems of orphan diseases, the WTO Fourth Ministerial Conference in Doha, Qatar issued the Doha Declaration on the TRIPS Agreement and Public Health in November 2001.[6] The Declaration affirmed that "the TRIPS Agreement does not and should not prevent Members from taking measures to protect public health" and that "the Agreement can and should be interpreted and implemented in a manner supportive of WTO Members' right to protect public health and, in particular, to promote access to medicines for all."[7] It further resolved certain ambiguities with respect to some of the flexibilities available under TRIPS. First, it affirmed that Members have the right "to grant compulsory licenses and the freedom to determine the grounds upon which such licenses are granted."[8] Second, it clarified that Members have the right to determine what constitutes a national emergency or other circumstances of extreme urgency, it being understood that public health crises... can represent a national emergency or other circumstances of extreme urgency.[9] Under Article 31(f) the obligations of a potential exporting

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domestic compliance. See TRIPS, supra note 54, art. 68.

1 Ibid., art. 66.

2 C. Correa, "Patent Law, TRIPS, and R and D Incentives: A Southern Perspective" in Commission on Macroeconomics and Health Working Paper Series (Geneva: WHO, 2001) Paper No. WG2:12 at 21, online: Commission on Macroeconomics and Health www.cmhealth.org/docs/wg2_paper12.pdf, (last visited on 6th March, 2009), at 20.

3 For a general discussion of the mailbox application process, see Médecins Sans Frontières, "The Effects of the 2005 TRIPS Implementation Deadline on Access to Medicines" (Geneva: Médecins Sans Frontières, February 2005) at 2, online: Campaign for Access to Essential Medicines www.accessmed-msf.org/documents/technical%202005.doc, (last visited on 16th April, 2009), [MSF, "Effects of TRIPS Implementation"].

4 TRIPS, supra note 54, art. 70(8)(a).

5 Ibid. art. 70(8)(b)-(c).

6 Draft Declaration on the TRIPS Agreement and Public Health, Ministerial Conference, Fourth Session, Doha, 9-14 14 November 2001, WT/MIN(01)/DEC/W/2, online: WTO www.wto.org, (last visited on 5th June, 2009), [Doha Declaration].

7 Ibid. at para. 4.

8 Ibid. at para. 5(b).

9 Ibid. at para. 5(c). This clarification is important because it allows Members, in dealing with public health problems such as HIV/AIDS, tuberculosis, and malaria, to take advantage of the TRIPS Article 31(b) exception to the obligation to negotiate with the

Member are waived to the extent necessary to produce pharmaceutical products and export them to eligible importing Members so long as certain procedural requirements are met.[1] Members are eligible to be an exporter having limitations of which countries are eligible to import pharmaceutical products. Eligible importers include any LDC Member and any other Member that has made a notification to the Council for TRIPS of its intention to use the system as an importer.[2] Such a Member must, however, confirm in its notification that it has established that it has insufficient or no manufacturing capacities for the pharmaceutical product in question.[3] Non-LDC importing Members are free to make a determination of insufficient or no manufacturing capacities on their own, so long as they comply with the notification requirements subjected to review by the Council for TRIPS.[4] The Council states "insufficient manufacturing capacities" to include situations where it is economically infeasible to produce the pharmaceutical products in question, instead of limiting the scope of this provision to situations where the technical capacity is insufficient.[5] But developed states disagreed to be importers.[6] Though the Agreement is not limited to specific diseases or pharmaceutical products, it imposes several procedural hurdles that may ultimately render it ineffective.[7] TRIPS is reinforced and expanded

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patent holder prior to issuing a compulsory license.

1 WTO, General Council, Implementation of Paragraph 6 of the Doha Declaration on the TRIPS Agreement and Public Health, 2003WTO Doc. WT/L/540 Dec. of 30 August 2003, 2 September 2003, online: WTO www.wto.org/English/tratop_e/trips_e/implem_para6_e.htm, (last visited on 25th June, 2009), [August 30th Agreement],at para. 2.

2Ibid. at para. 1(b).

3 Ibid. at para. 2(a)(ii).

4 See WTO, Minutes of Meeting (held on 25, 26 and 30 August 2003), WTO Doc. WT/GC/M/82, 13 November 2003, at para. 29, online: WTO: www.wto.org/english/news_e/news03_e/ trips_stat_28aug03_e.htm.

5 It is undesirable from a global efficiency standpoint to require poor countries lacking comparative advantage in pharmaceutical manufacturing to invest scarce resources in producing generic drugs domestically as this is economically wasteful and inhibits the realization of economies of scale through trade. A more balanced and efficient approach is for developing countries such as India, Brazil, China, and others with substantial domestic manufacturing capacity, as well as developed countries with vibrant generic industries, to produce and export generic pharmaceuticals to the plethora of developing countries and LDCs in which it would be overly burdensome and inefficient to manufacture drugs. This is not to devalue arguments for increased technology transfer to developing countries. It must be recognized, however, that technology transfer is a gradual process. See discussion of pharmaceutical patenting in India, supra note 47. In the interim, it is more desirable for poor countries to import products, such as pharmaceuticals, that they cannot efficiently produce domestically.

6 August 30th Agreement, supra note 258 at note 3.

7 The procedure envisaged under the Agreement is as follows: a Member desiring to import under the system must first examine the pharmaceutical product in question to determine its patent status and, in the case of a non-LDC Member, to determine that there is insufficient or no domestic capacity to manufacture it. If a patent does exist on the product, the Member must first negotiate with the patent holder to seek a voluntary

by the Doha Declaration and the August 30th Agreement, it is essential that developing countries frame their patent legislation in a way that fully incorporates these flexibilities so as to minimize the potential adverse affects of universal IP protection.[1] This will require unbiased technical assistance from developed countries and institutions such as the World Intellectual Property Organization (WIPO).[2] Some have called for the WHO or WIPO to develop "a model TRIPS-compliant law that makes maximum use of TRIPS flexibilities to achieve public health goals."[3] Further, though the upfront costs involved with introducing generic substitutes are much less than those for originator pharmaceutical R&D, generic entry is more likely when anticipated sales are high enough to provide sufficient returns on investment.[4] Access to medicines in developing countries is constrained by inadequate infrastructure, drug regulatory hurdles, insufficient financing,

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license on reasonable commercial grounds unless it declares a public emergency or other situation of extreme urgency, or intends to make only public non-commercial use of the product in accordance with TRIPS Article 31(b). See TRIPS, WTO, Agreement on Trade-Related Aspects of Intellectual Property Rights, Being Annex 1C to the Final Act and Agreement Establishing the World Trade Organization, 33 I.L.M. 81, 15 December 1993, art. 27(1), online: WTO www.wto.org/english/docs_e/legal_e/27-trips.pdf (last visited on 4th July, 2009),[TRIPS].. If this negotiation is not successful within a reasonable time, it may then issue a compulsory license for importation of the pharmaceutical product. The potential importer must then submit a notification to the Council for TRIPS listing the name and expected quantity of the pharmaceutical product needed, declaring its assessment of insufficient or no manufacturing capacity, and confirming either the non-existence of a patent in its territory or the issuance or intention to issue a compulsory import licence (ibid. at para. 2(a)). A potential exporting Member must then seek a voluntary license from the patent holder, and if this fails within a reasonable time period, may issue a compulsory license for export to an interested generic manufacturer within its borders. Such a licence must be limited to production of the amount necessary to meet the needs stipulated by the eligible importing Member, and must require the entirety of the amount produced to be exported to that Member (ibid. at para. 2(b)(i)). An exporting Member must then provide notification to the Council for TRIPS of the conditions of this licence (ibid. at para. 2(c)). Further, it must ensure adequate remuneration to the patent holder in accordance with Article 31(h) of the TRIPS Agreement, though this requirement is waived in the eligible importing Member to prevent duplication of royalty fee payments (ibid. at para. 3).

1 Maxwell R. Morgan, "Medicines for the Developing World: Promoting Access and Innovation in the Post-TRIPs Environment", 2006, 64 U.T. Fac. L. Rev. 45 – 11.

2See Pascale Boulet, Christopher Garrison and Ellen 't Hoen, "Drug Patents Under the Spotlight: Sharing Practical Knowledge About Pharmaceutical Patents", (Geneva: Médicins Sans Frontières, June 2004) at 11, online: Campaign for Access to Essential Medicines www.accessmed-msf.org/documents/Patent%20report%20.pdf, (last visited on 17th June, 2009), [MSF, "Patents"].

3 Access to Medicines in Underserved Markets: What are the Implications of Changes in Intellectual Property Rights, Trade and Drug Registration Policy? (London: UK Department for International Development Health Systems Resource Center, 2004) at 28, online: UK Department for International Development Health Resource Centre www.dfidhealthrc.org/shared/publications/issues_papers/ATM/DFID_synthesis_aw.pdf, (last visited on 8th May, 2009), [Underserved Markets].

4 Scherer and Watal, supra note 231 at 6.

and high drug prices.[1] Sometimes developing countries and LDCs often lack the requisite infrastructure to deliver medicines to that in need.[2] Improving infrastructure will be a key component of any strategy to scale-up access to medicines in developing countries and will entail significant costs.[3] Drug registration refers to the process by which "a national drug regulatory agency (NDRA) confirms a medicine's safety, quality and efficacy, in order to approve its use domestically"[4] but in reality generic ARV registration status in each state is a significant barrier to accessing drugs in several countries.[5] TRIPS-plus provisions in bilateral and regional Free-Trade Agreements (FTAs) threaten to create more barriers to NDRA generic drug approval in developing countries. Again developing states finance inadequately in public health[6] seeming a barrier and enormous gap[7] to accessing medicines. At present many poor countries apply duties and tariffs to imported pharmaceutical products as a means of raising tax revenue that can be higher than 10-30 per cent in countries such as Kenya, Nigeria, Ghana, India, and Burkina Faso.[8] Absence of competition in market is another barrier to accessing cheap drugs. Patents are an insignificant

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1 Y. Taylor, ed., "Battling HIV/AIDS: A Decision-Maker's Guide to the Procurement of Medicines and Related Supplies", (Washington, D.C.: The World Bank, 2004) at 106 [World Bank Procurement Guide], at xii.

2 Problems of infrastructure can include a lack of distribution and supply systems, inadequate access to health care generally (including a lack of access to appropriately trained medical personnel who can diagnose and prescribe proper treatment), and insufficient laboratory facilities, which are particularly important for monitoring the administration of ART for HIV/AIDS.

3 For example, even assuming access to the lowest cost first-line ART regimen, currently $140 per person per year, the World Bank projects the total cost of scaling up ART in Burkina Faso to be $620 per person per year due to additional costs associated with biological monitoring, personnel and equipment. See World Bank Procurement Guide, supra note 63 at 97.

4 Underserved Markets, supra note 267 at 7.

5 See generally Surmounting Challenges: Procurement of Antiretroviral Medicines in Low- and Middle-Income Countries (Geneva: Médecins Sans Frontières, November 2003), online: Campaign for Access to Essential Medicines www.accessmed-msf.org/documents/procurementreport.pdf, (last visited on 19th July, 2009), [MSF, "Surmounting Challenges"].

6 A. Attaran, "How Do Patents and Economic Policies Affect Access to Essential Medicines in Developing Countries?" (2004) 23:3 Health Affairs 155 at 159.

7 C. Grace, "Equitable Pricing of Newer Essential Medicines for Developing Countries: Evidence of the Potential of Different Mechanisms" (London: London Business School, 2003) 1 at 17, online: UK Department for International Development Health Resource Centre www.dfidhealthrc.org/shared/publications/Issues_papers/equitable_pricing_essential_med.pdf, (last visited on 13th June, 2009).

8 H. E. Bale, Jr., "Consumption and Trade in Off-Patented Medicines" in Commission on Macroeconomics and Health Working Paper Series (Geneva: WHO, 2001) Paper No. WG4:3 at 5, online: Commission on Macroeconomics and Health www.cmhealth.org/docs/wg4_paper3.pdf, (last visited on 7th July, 2009), however, only 21 per cent of patients received DOTS worldwide as of 1998, at 21, Annex 2.

limitation on access to currently existing medicines.[1] For example, MSF (Médicins Sans Frontières) has documented how Kenyan implementation of TRIPS through the Kenyan Industrial Property Act 2001 could prevent it from importing generic drugs from India for use in its local ARV treatment programs.[2] MSF reports that access to low-cost generic ARVs is still severely lacking in South Africa due to this widespread patenting.[3] Continued scale-up of cheap and effective ART in developing countries will become increasingly dependent on the successful importation of generic versions of second-line ARVs.[4] As of June 2005, in LDCs and sub-Saharan Africa, second-line drugs were still six to 12 times more expensive than first-line treatments.[5] Even new medicines developed from 2005 onward, when

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1 Despite the fact that ARVs were developed according to the needs of patients in rich countries, the WHO, as part of its strategy to have three million people on ART in the developing world by the end of 2005, has been able to develop a set of ARV treatment guidelines that are appropriate and effective for use in resource-limited settings. See WHO, "Scaling UP Antiretroviral Therapy in Resource-Limited Settings: Treatment Guidelines for a Public Health Approach, 2003 Revision" (Geneva: WHO, 2004) at 5, online: WHO www.who.int/3by5/publications/documents/arv_guidelines/en, (last visited on 7th July, 2009), [WHO Treatment Guidelines]. Because of simplicity in terms of numbers of pills per day, dietary requirements, and monitoring, and because of low incidence of side effects, the WHO recommends a first-line regimen composed of two nucleoside reverse transcriptase inhibitors (NRTIs): stavudine (d4T) or zidovudine (AZT), and lamivudine (3TC); plus a non-nucleoside reverse transcriptase inhibitor (NNRTI): nevirapine (NVP) or efavirenz (EFV) (ibid. at 13). It also suggests that countries adopt a second-line regimen for those who cannot tolerate, or who develop resistance to, the first-line regimen (P. Trouiller et al., "Drug Development for Neglected Diseases: A Deficient Market and a Public-Health Policy Failure" (2002) 359 The Lancet 2188 at 2189). This second-line regimen should include two NRTIs: tenofovir (TDF) or abacavir (ABC), and didanosine (ddI); plus a protease inhibitor (PI): ritonavir (RTV)-enhanced lopinavir (LPV/r) or ritonavir-enhanced saquinavir (SQV/r). Thus, as a minimum, all countries should have access to at least 11 (five first-line and six second-line) ARVs. A. Attaran, "How Do Patents and Economic Policies Affect Access to Essential Medicines in Developing Countries?" (2004) 23:3 Health Affairs 155 at 159.

2 Pascale Boulet, Christopher Garrison and Ellen 't Hoen, "Drug Patents Under the Spotlight: Sharing Practical Knowledge About Pharmaceutical Patents", (Geneva: Médicins Sans Frontières, June 2004) at 11, online: Campaign for Access to Essential Medicines www.accessmed-msf.org/documents/Patent%20report%20.pdf, (last visited on 7th July, 2009), [MSF, "Patents"] at 8.

3 See generally Surmounting Challenges: Procurement of Antiretroviral Medicines in Low- and Middle-Income Countries (Geneva: Médecins Sans Frontières, November 2003), online: Campaign for Access to Essential Medicines www.accessmed-msf.org/documents/procurementreport.pdf, (last visited on 7th July, 2009), [MSF, "Surmounting Challenges"] at 39.

4 Second-line ARVs become more important over time as viral resistance to first-line treatment emerges.

5 Médecins Sans Frontières, Untangling the Web of Price Rreductions: A Pricing Guide for the Purchase of ARVs for Developing Countries, 8th ed. (Geneva: Médecins Sans Frontières, June 2005) at 12-14, online: Campaign for Access to Essential Medicines www.accessmed-msf.org/documents/untanglingtheweb%208.pdf, (last visited on 17th July, 2009), [MSF, "Prices"] at 4.

pharmaceutical product patents will be available in virtually all Member states of the WTO, the supply of low-cost versions of such new products in developing countries will be threatened by the greatly reduced possibility of generic substitution during the life of the patent.[1]

Steps are being taken to increase the access to medicines in poor countries; such as, under Article 6 of TRIPS states disallow parallel importation of medicines from abroad, i.e., Argentina, Thailand, and South Africa have each adopted laws permitting parallel imports of pharmaceuticals,[2] but many developing countries have not.[3] The pharmaceutical industry fix the drug price arbitrarily accounting R&D and other cost which makes a difference in national drug markets between developed and developing states. To minimize this variation drugs should be high rated in developed states market than the poor[4] under 'Accelerated Access Initiative (AAI)' regime. Drug donation through giant pharmaceutical industries in poor states is another easy access. The use vigorous generic substitution to supply poor markets while maintaining patent exclusivity and thus monopoly pricing in rich markets may be other alternative. The "Decision of the WTO General Council on the Implementation of paragraph 6 of the Doha Declaration on the TRIPS Agreement and public health"[5] was adopted to allow especially the least developing countries but also the developing countries facing a national or an extreme emergency situation, to import generic drugs when they do not have the manufacturing capacities to produce these drugs, or when these current capacities are insufficient to meet their needs.[6]

Where patents are blocking access, additional strategies beyond efficient regulatory procedures and increased financing are needed to foster cheap generic supply. State may go ahead to foster –Compulsory licensing: It reduces domestic price of drugs where under TRIPS Article 31, developing countries should use the national emergency and public non-commercial use exceptions in the context of public health to take advantage of the simplified licensing procedures.

Voluntary Licensing: Generic substitution of patented medicines could be achieved if originator firms would agree to grant voluntary licenses to developing world generic companies for local production and export.[7] Voluntary licenses negotiates directly with originator firms that delimit the

1Grace, supra note 275 at 18.

2 Scherer and Watal, supra note 231, at 33.

3 Underserved Markets, supra note 267 at 15.

4 World Health Organization and World Trade Organization Secretariats, Report of the Workshop on Differential Pricing and Financing of Essential Drugs, (Report on Workshop convened by the WHO and WTO Secretariats. Hbsjr, Norway, 8-11 April 2001) at 8, online: whqlibdoc.who.int/hq/2001/a73725.pdf (last visited on 27th July, 2009), [Hbsjr Report] at 10.

5 WTO Decision WT/L.540 on the implementation of paragraph 6 of the Doha Declaration on TRIPS Agreement and public health, WTO General Council, 1 September 2003.

6 Ibid, annex, Assessment of Manufacturing Capacities in the Pharmaceutical Sector.

7 Grace, supra note 275 at 41.

scope of permissible importing countries will offer a degree of certainty to potential generic entrants.

Patent waivers: It facilitates access to generic versions of patented medicines by filing a patent for a new drug, it must acquire a foreign filing license from own country's Patent and Trademark Office (PTO) on the same invention in other jurisdictions and the PTO should require the applicant to promise that permission to file abroad will not be used to restrict the sale or manufacture of the new drug in a set list of developing countries.[1] This would allow for generic companies in those countries to produce the new drug for domestic consumption and/or for export to any of the other listed countries. It has two benefits -(i) because of its transparency and predictability, it would provide a level of security from litigation to potential developing world generic producers that does not exist under the current compulsory licensing regime;[2] and (ii) it is entirely consistent with TRIPS, and if implemented unilaterally by only the US, EU, and Japan, it would largely abrogate the negative effects of TRIPS implementation in developing countries on pharmaceutical access.[3]

Bulk Purchasing: It combines with differential-pricing mechanisms and rely funding of public treatment programs by involving pooling demand for drugs from multiple developing world sources and then use the resultant negotiating power to induce lower price offers from suppliers. Here long-term market certainty reduces capital investment risks, increases economies of scale, and reduces demand-forecasting costs, costs associated with individual country-level operation including costs of negotiating, monitoring, and enforcing contracts.

Price control: It the advantage of being entirely compliant with TRIPS[4] and pharmaceutical patenting, and of being able to induce lower prices for both on-patent and off-patent medicines. Usually the developed states are free to control the price of drug but the developing states can take effort to do the same in case of necessity.

Public + Private Partnership (PPP) for R&D: Although the recent market system has generated many innovative therapies, it cannot cater for diseases for which commercial incentives are insufficient to trigger private sector investments in R&D.[5] In less developed countries, many diseases can affect

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1 Grace, ibid at 54-58 and Lanjouw, supra note 155, at 10.

2 Grace, ibid at 241.

3Lanjouw, supra note 189 at 12-13. Because of the concentration of pharmaceutical innovation in these areas, their adoption of patent waivers alone would create secure market entry for developing world generic firms in a substantial proportion of newly developed pharmaceutical products.

4R. Rajkumar, "The Central American Free Trade Agreement: An End Run Around the Doha Declaration on TRIPS and Public Health" (2005) 15 Alb. L.J. Sci and Tech. 433 at 444.

5 Trouiller, P. et al., "Drugs development for neglected diseases: a deficient market and a public health policy failure", Lancet 359, 2188–2194 (2002). See also Mrazek, M. F. & Mossialos, E., "Stimulating pharmaceutical research and development for neglected diseases", Health Policy (New York) 64, 75–88 (2003).

millions of patients, but their lack of ability to pay for market-financed innovative products means there is still no market for drug developers to exploit.[1] The 'neglected diseases'[2] include diseases such as malaria, tuberculosis, African trypanosomiasis (sleeping sickness), Chagas disease, dengue, leishmaniasis, schistosomiasis, onchocerciasis and lymphatic filariasis.[3] Additional factors that further depress the market for innovative new drugs for these diseases include poor regulatory infrastructure in many countries and competing counterfeit drugs.[4] The net effect is that only 10% of global R&D resources are directed at diseases accounting for 90% of the global disease burden.[5] The governance systems put in place for public–private partnership (PPP) organizations is particularly important when one considers the policy debate underway relating to intellectual property rights, innovation and access to essential medicines.[6] However, the disengagement of most pharmaceutical companies from tropical disease R&D in the 1970s left a huge gap in the development of new and affordable drug.[7] The few existing drugs often fail due to the emergence of resistance, have significant compliance and safety issues, or are inaccessible due to lack of affordability and/or appropriate infrastructure.[8] A partnership-oriented approach to

1 Trouiller, P. et al., "Drugs for neglected diseases: a failure of the market and public health failure", Trop. Med. Int. Health 6, 945–951 (2001). See Sachs, J., "The link of public health and economic development", Office of Health Economics, London (2001).

2 Kettler, H. E. & Modi, R., "Building local research and development capacity for prevention and cure of neglected diseases: the case for India", Bull. World Health Organization 79, 742–747 (2001). See Medecins Sans Frontieres, "Access to Essential Medicines Campaign: Fatal imbalance, the crises in research and development for drugs for neglected diseases", (2001). See Reich, M. R., "The global drug gap", Science 287, 1979–1981 (2000).

3 Remme, J. F. H. et al., "Strategic emphasis for tropical disease research. A TDR perspective", Trends Parasitol. 18, 421–426 (2002). See Nossal, G. J., "Modern medicine and global communicable diseases: new partnerships for progress", Aust. NZ J. Med. 30, 267–271 (2000). See Yamey, G., "Public sector must develop drugs for neglected diseases", BMJ 324, 698 (2002).

4 Kettler, H. & Towse, A., "Public–private partnerships for research and development: medicines and vaccines for diseases of poverty", Office of Health Economics, London (2002). See Bruneton, C. et al., "The drug trade between European countries and developing countries", Med. Trop. (Mars) 57, 375–379 (1997).

5 Global Forum for Health Research. The 10/90 report of research 2001–2002. Global Forum for Health Research, Geneva (2002). See Widdus, R., "Public–private partnerships for health: their main targets, their diversity, and their future directions", Bull. World Health Organization 79, 728–734 (2001).

6 Macroeconomics and Health: Investing in Health for Economic Development. Report of the Commission on Macroeconomics for Health, World Health Organisation, Geneva (2001).

7 Veekan, H. & Pecoule, B., "Drugs for 'neglected diseases': a bitter pill", Trop. Med. Int. Health 5, 309–311 (2000). See Froese, E. H., "Meeting the pharmaceutical needs of a developing country", World Health Forum 12, 25–28 (1991).

8 Bryceson, A., "Current issues in the treatment of visceral leishmaniasis", Med. Microbiol. Immunol. (Berl.) 190, 81–84 (2001). See Legros, D. et al., "Treatment of human African trypanosomiasis: present situation and needs for research and

drug discovery and development by international organizations has rapidly accelerated since the late 1990s, for example, through the creation of the Medicines for Malaria Venture (MMV)[1] and other organizations, which are now called PPPs.[2] Another example is the MMV (Medicines for Malaria Venture) which is the first organization to put the theory of PPP-driven virtual drug discovery into practice in a concerted manner, and has initiated several virtual drug discovery projects.[3] At present in public-private partnership R&D development the costs of compounds that do not make it to the market are considered, the cost of development is calculated to be in the range of US $0.5–1 billion.[4] Although cost is all-time high, PPP in R&D for rare diseases are continuing and the recent creation of the European Developing Countries Clinical Trial Partnership[5] is going to have a major impact in this area of activity, as will the creation of the Strategic Initiative to Develop Capacity for Ethical Review.[6] Similarly The European Rare Disease Task Force has surveyed the existing reference centers in Europe[7] likewise the National Organization of Rare Disorders (NORD) in the USA is instrumental in the approval of the Orphan Drug Act.[8] Rather the public-

development", Lancet 2, 437–440 (2002). See Seawort, B. J., "Multidrug-resistant tuberculosis", Infect. Dis. Clin. North Am. 16, 73–105 (2002). See Rosenthal, P "Antimalarial Chemotherapy: Mechanisms of Action, Resistance, and New Direc ons in Drug Discovery" (Humana, Totowa, 2001).

1 Ridley R. G., "Putting the partnership into public–private partnerships", Bull. World Health Organization 79, 694 (2001). See Ridley, R. G., "Medical need, scientific opportunity and the drive for antimalarials", Nature 415, 686–693 (2002). See TDR News. MMV: New Medicines for Malaria Venture. February (1999).

2 Wheeler, C. & Berkley, S., "Initial lessons from public–private partnerships in drug and vaccine development", Bull. World Health Organization 79, 728–734 (2001). See Ridley, R. G. et al., "Round table. A role of public–private partnerships in controlling neglected diseases", Bull. World Health Organization 79, 771–777 (2001).

3 Medicines for Malaria Venture. Annual Report (2002). See Medicines for Malaria Venture. Business Plan (2003).

4 DiMasi, J. A. et al., "Cost of innovation in the pharmaceutical industry", J. Health Econ. 10, 107–142 (1991). See Murray D. M. & Shinket, R., "Discovery and development of a genomic drug", Curr. Drug Disc. June, 27–33 (2003). See Mattieu, M. P., "Parexel's pharmaceutical R&D statistical sourcebook", Parexel International Corp. Waltham, MA (2002/2003). See DiMasi, J. A., Hansen, R. W. & Grabowski, H. G., "The price of innovation: new estimates of drug development costs", J. Health Econ. 22, 157–185 (2003).

5 Medaglini, D. & Hoeveler, A., "The European research efforts on HIV/AIDS, malaria and tuberculosis", Vaccines 21, S116–S120 (2003).

6 Dickson, D. WHO and industry combine to form ethics body. Nature Med. 8, 645 (2002).

7 Overview of current Centres of Reference on rare diseases in the EU. Report to the High Level Group on Health Services and Medical Care, and Annexes. September 2005. http://ec.europa.eu/health/ph_information/implement/wp/morbidity/keydocs_morbidity_en.htm, (last visited on 8th July, 2009).

8 Haffner ME., "Adopting orphan drugs: two dozen years of treating rare diseases", N Engl J Med 2006; 354: 445-47.

private collaboration and partnership[1] is insufficient to solve rare diseases problem as the investment and public-private partnership is less than it demand. So future will say how successful PPP initiative will be.[2]

USA has taken some extra PPPs measures to promote R&D for neglected diseases; some of them are as follows--

USA Universities affiliation: Capital investments by universities such as the $30million committed to found the Duke Global Health Institute—an interdisciplinary initiative combining education, research, and service missions for advancing R&D for orphan diseases.[3] Even simple structural changes, such as the creation of a Center for Neglected Diseases, and marketing of neglected-disease research capacity can help attract talented researchers and new sources of funding, as seen in the cases of the George Washington University and the University of California at Berkeley.[4] Another 18 research institutions called for ensuring access to university innovations in the developing world.[5] The AAMC and collaborating universities joined committees of the World Health Organization[6] with the American Association of Arts and Sciences[7] and the Gates Foundation.[8] These virtual-type organizations, funded by groups such as the Gates and Rockefeller foundations, engage in a variety of risk- and reward-sharing arrangements to advance R&D portfolios dedicated to particular orphan diseases.[9] It is estimated that worldwide R&D spending on diseases of poverty concentrated in these public–private partnerships could reach $500 million by the end of this decade.[10]

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1 Buse K, Walt G., "Global public-private partnerships", part II: what are the health issues for global governance? Bull World Health Organ 2000; 78: 699-709. Also part I: a new development in health? 78: 549-61.

2 Wheeler C, Berkley S., "Initial lessons from public-private partnerships in drug and vaccine development", Bull World Health Organ 2001; 79: 728-34.

3 Haynes B., "Global health and reducing disparities: the role of the university.", Presented at: Institute of Medicine Regional Meeting; Durham, NC; May 4, 2005.

4 Hotez P., "The George Washington University Neglected Tropical Diseases Initiative", Washington, DC: George Washington University Center for Neglected Diseases; 2005. See Coloma J, Harris E., "Open-access science", PLoS Pathog. 2005; 1(2):e21.

5 Stanford University Web site. In the public interest: nine points to consider in licensing university technology, March 6. http://news-service.stanford.edu/news/2007/march7/gifs/whitepaper.pdf, (last visited on 5th July, 2009).

6 Commission on Innovation; Intellectual Property Rights, and Public Health of the World Health Organization. Public Health, Innovation and Intellectual Property Rights. Geneva, Switzerland: World Health Organization; 2006.

7 Brewster A, Chapman A., "Facilitating humanitarian access to pharmaceutical and agricultural innovation", Innovation Strategy Today. 2005;1(3):14.

8 Moran M, Ropars A, Guzman J, Diaz J, Garrison C., "The New Landscape of Neglected Disease Drug Development. London", England: Welcome Trust; 2005.

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PART THREE:

RIGHT TO HEALTH PRINCIPLE AS A MEANS OF ACCESS TO MEDICINE: INTERNATIONAL HUMAN RIGHTS LAW PERSPECTIVE:

Health has been part of the modern human rights rhetoric dating back to the end of World War II.[1] As the post-War world considered the crimes against individuals and the genocide committed during the War, there arose a general consensus that human rights norms should be codified and set forth as a common standard to which all nations should aspire to and ultimately achieve.[2] Out of this general consensus, the United Nations was founded and included in its Charter the statement and agreement that all people are "born free and equal in dignity and rights"[3] and the Universal Declaration of Human Rights-1948 adopted all word of human rights. The preamble of the WHO Constitution states:

"[T]he enjoyment of the highest attainable standard of health is one of the fundamental rights of every human being without distinction of race, religion, political belief, economic or social condition."[4]

The right to health is described in Article 25 of the UDHR:

Everyone has the right to a standard of living adequate for the health and well-being of himself and of his family, including food, clothing, housing and medical care and necessary social services, and the right to security in the event of unemployment, sickness, disability, widowhood, old age or other lack of livelihood in circumstances beyond his control.[5] As is evidenced by this language, the concept of health was broadly defined and holistic, encompassing virtually all of what we now know as the "social determinants" of health and well-being.[6]

The Constitution[7] of the World Health Organization first recognized

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Financing Strategies for Product Development and the Potential role of Public–Private Partnerships", (London, 15–16 April 2004).

1 Stephen P. Marks, "The Evolving Field of Health and Human Rights: Issues and Methods", 30 J. L. Med. & Ethics 739, 739 (2002) ("The Second World War was the defining event for the internationalization of human rights"); see also Sofia Gruskin, "SARS, Is There a Government in the Cockpit: A Passenger's Perspective or Global Public Health: The Role of Human Rights", 77 Temp. L. Rev. 313, 319-20 (2004).

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4 Constitution of the World Health Organization, opened for signature July 22, 1946, reprinted in World Health Organization, Basic Documents (40th ed. 1994), at 1; for a full discussion of the Preamble of the WHO Constitution, David P. Fidler, "Caught Between Paradise and Power: Public Health, Pathogenic Threats and the Axis of Illness", 35 McGeorge L. Rev. 45, 73 (2004), at 60-64.

5 Universal Declaration of Human Rights, art. 25.

6 Sofia Gruskin, supra note 320, at 326; Hoda Rashad, "Promoting Global Action on the Social Determinants of Health", 51 Diabetes Voice 33 (2006).

7 Preamble to the Constitution of the World Health Organization as adopted by the International Health Conference, New York, 19-22 June, 1946; signed on 22 July 1946 by the representatives of 61 States (Official Records of the World Health Organization, no. 2, p 100) and entered into force on 7 April, 1948. The Preamble states as follows,

the concept of standard of health; later the Universal Declaration of Human Rights[1] and International Covenant on Economic, Social and Cultural Rights[2] made the right to medical care and treatment obvious for all. These international law instruments create obligations both on national and foreign states to respect, protect and fulfill of ensuring right to attainable standard[3] health towards its entire population. Rio Declaration has provision of immunization and essential drugs for all.[4] Article 7 and 8 of TRIPS Agreement support the recognition of the right to access to essential medicines stating as follows:

Professor Paul Hunt affirms that, "Intellectual property protection can affect the enjoyment of the right to health, and related human rights, in a number of ways custom."[5] He establishes a link between the right to health and the right to essential medicines stating that, "Given that the right to health includes an obligations on states to provide affordable medicines according to the WHO essential drugs list, intellectual property protection can lead to negative effects on the enjoyment of the right to health."[6] He then extends this state obligation to other states when he reaffirms that, "- - - protected negotiations that led to (the Decision of the WTO General Council on the Implementation of paragraph 6 of the Doha Declaration on the TRIPS Agreement and Public Health) should have been informed by the human rights responsibility of rich states to engage in international assistance and cooperation in relation to the right to health. The special

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"The enjoyment of the highest attainable standard of health is one of the fundamental rights of every human being without distinction of race, religion, political belief, economic or social conditions."

1 Article 25 of Universal Declaration of Human Rights states, "Everyone has the right to a standard of living adequate for the health and of his family, including food, clothing, housing and medical care and necessary social services."

2 Article 12 states, "1. The States Parties to the present Covenant recognize the right of everyone to the enjoyment of the highest attainable standard of physical and mental health.

2. The steps to be taken by the States Parties to the present Covenant to achieve the full realization of this right shall include those necessary for: (a) The provision for the reduction of the still birth-rate and of infant mortality and for the healthy development of the child; (b) The improvement of all aspects of environmental and industrial hygiene; (c) The prevention, treatment and control of epidemic, occupational and other diseases; (d) The creation of conditions that would assure to all medical service and medical attention in the event of sickness."

3 Economic And Social Council Of The United Nations, "The Right to the highest attainable standard of health", substantive issues arising from the implementation of the International Covenant On Economic, Social And Cultural Rights, E/C 12?2000?4, 11 August 2000, paragraph 8.

4 Agenda 21, United Nations Conference on Environment and Development (UNCED), Rio de Janeiro, June 1992, paragraph 6.3.

5 Economic and Social Council Of The United Nations, Addendum to the Report of the Special Rapporteur, Paul Hunt – Mission to the World Trade Organization, Commission on Human Rights, 16th Session, item 10 of the provisional agenda, E/CN.4?2003/58, 13 February 2003, par. 42.

6 Ibid, par. 43.

Rapporteur underlines the effectiveness of the Decision will depend on the extent to which it actually does lead to increased access to medicines for the poor".[1] But in reality there are no established central legislatures comparable to those existing in national systems, no compulsory or even widely used judicial system, and no effective machinery to enforce international law and its obligations on states.[2] Sometime states disobey the obligation because of lack of resources although right to access to essential medicines is one of the fundamental components of human rights provisions.[3] Generally TRIPS is characterized as to (a) promote technological innovation, transfer and dissemination of technology in a manner conducive to social and economic welfare;[4] (b) allow the member states (i) adopt measures necessary to protect public health and nutrition,[5] (ii) promote the public interest in sectors of vital importance to their socio-economic and technological development,[6] (iii) prevent the abuse of intellectual property rights,[7] (iv) restrict practices which unreasonably restrain trade or adversely affect the international transfer of technology[8] and (v) take action against anti-competitive practices;[9] (c) provide an exception for (i) the commercial exploitation to protect public order or morality, including to protect human, animal or plant life or health or to avoid serious prejudice to the environment[10] and (ii) diagnostic, therapeutic and surgical methods for the treatment of humans or animal[11] to the promotion and protection of human rights by maintaining the balance sought under Article 27 of UDHR and Article 15 of ICESCR. Further TRIPS provisions are commercially innovated[12] subjected to human right notion which (i) alludes to the responsibilities of patent holders that should balance

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1 Ibid. par. 43.

2 David Freestone, "The Road from Rio: International Environmental Law after the earth summit", 1994, 6 Journal of Environmental Law, No. 2, p. 195.

3 Philippe Cullet, "Patents and Medicines: The Relationship between TRIPS and the Human Right to Health", in Sofia Grushin, Michael A. Grodin, Georges J. Annas, and Stephen P. Marks, "Perspectives on Health and Human Rights", Taylor and Francis Group, New York, 2005, p. 182.

4 Agreement on Trade Related Aspects of Intellectual Property Rights, Apr. 15, 1994, Marrakesh Agreement Establishing the World Trade Organization, Annex 1C, Legal Instruments- Results of the Uruguay Round vol. 31, 33 I.L.M. 81 (1994) art. 7.

5 19. Id. art. 8(1).

6 Id.

7 Id. art. 8(2).

8 Id.

9 Id. art. 31(k).

10 Id. art. 27(2).

11 Id. art. 27(3)(a).

12 Report of the High Comm'r of the Human Rights Comm'n, The Impact of the Agreement on Trade-Related Aspects of Intellectual Prop. Rights on Human Rights, P 20-28, U.N. Doc. E/CN.4/Sub.2/2001/13 (2001) available at http://www.unhchr.ch/Huridocda/Huri_doca.nsf/E.CN.4.Sub.2.2001.13.En?, (last visited on 14th June. 2009).

those rights in accordance with its own objectives.[1] (ii) removes a degree of autonomy from the States.[2] (iii) focuses on the forms of protection that have developed in industrialized countries.[3]

The Evolving Right to Health in International Law: Potential links between human rights and TRIPS are indicated by the Articles 7, 8, 29 and 31. (A) Promoting technological innovation, transfer and dissemination of technology in a manner conducive to social and economic welfare;[4] (B) allowing the member states (i) to adopt measures necessary to protect public health and nutrition,[5] (ii) to promote the public interest in sectors of vital importance to their socio-economic and technological development,[6] (iii) to prevent the abuse of intellectual property rights,[7] (iv) to restrict practices which unreasonably restrain trade or adversely affect the international transfer of technology[8] and (v) to take action against anti-competitive practices;[9] (C) providing an exception for (i) the commercial exploitation to protect public order or morality, including to protect human, animal or plant life or health or to avoid serious prejudice to the environment[10] and (ii) diagnostic, therapeutic and surgical methods for the treatment of humans or animal[11] are measures that - at least in theory - are conducive to the promotion and protection of human rights and seek to maintain the balance sought under Article 27 of UDHR and Article 15 of ICESCR. Certainly all human beings in any place of the world have the right of getting medicine and treatment if he/she is suffering from any orphan disease or other common disease. The "right to health" is contained and detailed in the International Covenant on Economic, Social and Cultural Rights (ICESCR).[12] Article 12(1) of this Covenant echoes the preamble of the WHO

1 Id. P 23.

2 Theresa Beeby Lewis, Patent Protection for the Pharmaceutical Industry: A Survey of the Patent Laws of Various Countries, 30 Int'l Law 835 (1996).

3 Report of the High Comm'r of the Human Rights Comm'n, The Impact of the Agreement on Trade-Related Aspects of Intellectual Prop. Rights on Human Rights, P 20-28, U.N. Doc. E/CN.4/Sub.2/2001/13 (2001) available at http://www.unhchr.ch/Huridocda/Huridoca.nsf/E.CN.4.Sub.2.2001.13.En?, (last visited on 14th June, 2009). p.25.

4 Agreement on Trade Related Aspects of Intellectual Property Rights, Apr. 15, 1994, Marrakesh Agreement Establishing the World Trade Organization, Annex 1C, Legal Instruments- Results of the Uruguay Round vol. 31, 33 I.L.M. 81 (1994), TRIPS Agreement art. 7.

5 Id. Art. 8(1).

6 Id.

7 Id. Art. 8(2).

8 id

9 Id. Art. 31 (k).

10 Id. Art. 27(2)

11 Id. Art. 27(3)(a).

12 Siracusa Principles on the Limitations and Derogation Provisions in the International Covenant on Civil and Political Rights, U.N. ESCOR Sub-Commission on the Prevention and Protection of Minorities, Annex, 41st Sess. Agenda Item 18, U.N. Doc. E/CN.4/1985/4 (1985).

s to the present Covenant recognize the right of
ment of the highest attainable standard of physical and
icle 12(2) details some of the metrics used to assess the

be taken by the States Parties to the present covenant to
ration of this right shall include those necessary for:
or the reduction of the stillbirth rate and of infant
lthy evelopment of the child;
f aspects of environment and industrial hygiene;
n l control of epidemic, endemic, occupational

ions which would assure to all medical service and
vent of sickness.[2]
CR are not non-derogable because of the differences
terms of development, economic - financial- health
ditions, but are subject to progressive realization:
to the present Covenant undertakes to take steps,
through international assistance and co-operation,
mic and technical, to the maximum of its available resources,
achieving progressively the full realization of the rights
the present Covenant by appropriate means, including
e adoption of legislative measures.[3] Progressive realization
y to embrace the rights and duties of the treaty or covenant,
they are not able to affect them immediately and the
purposeful movement toward full realization.[4]
erally government obligations with respect to the right to health
ee categories of action: to respect, to protect, and to fulfill.[5]
he right to health means that the government must refrain from
ons that inhibit or interfere with people's ability to enjoy their
esting the right to health means that the state must seek to
ple from having their rights infringed by third parties, such
industry, pharmaceutical companies, researchers, health care
or vendors.[7] Fulfilling the right to health means that the
nt is required to take positive action to implement the right to
adopting a national health policy that allocates public resources to

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ional Covenant on Civil and Political Rights, Dec 19, 1966, 000 U.N.T.S. 171
after ICCPR]; International Covenant on Economic, Social and Cultural Rights,
, 1966, 933 U.N.T.S. 3 [hereinafter ICESCR] art. 12(1).
CR, art. 12(2).
R, art. 2(1).
Asher, "The Right to Health: A Resource Manual for NGOs", 9 (2004), at 35.
h Asher, ibid at 35-37; Michael J. Dennis & David P. Stewart, "Justiciability of
onomic Social and Cultural Rights: Should There be an International Complaint
Mechanism to Adjudicate the Rights to Food, Water, Housing and Health?", 98
A.M.J.I.L. 462, 478 (2004), at 490-91.
Judith Asher, ibid at 35-37; Michael J. Dennis & David P. Stewart, id. at 490-91.
Judith Asher, id. at 35-37; Michael J. Dennis & David P. Stewart, id. at 490-91.

correct deficiencies in health facilities, goods and services.[1] At the present time, most of the obligations are effectively at the "respect" or "protect" stage of realization rather than the more positive rights-oriented "fulfill" stage. The right to health must be understood as a right to the enjoyment of a variety of facilities, goods, services and conditions necessary for the realization of the highest attainable standard of health.[2] Formulating national health policy, governments must adopt an epidemiologically sound and population-relevant public health strategy.[3]

The ICESCR differs from the ICCPR in terms of enforcement capacity. The ICCPR has an Optional Protocol, which allows for individual or group complaints to be heard and considered by the Human Rights Committee.[4] While the country is subject to this complaint process only if it has signed on the Optional Protocol, this individual complaint process provides a forum for adjudication of human rights violations.[5] There is no parallel Optional Protocol and individual complaint process for the ICESCR.[6] Thus an aggrieved individual or group will be unable to seek validation and enforcement of their rights, unless they can do so collaterally, by alleging a violation of the right to life,[7] or through a national forum in a country that has incorporated the right to health into its Constitution or public health legislation.[8]

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1 Judith Asher, id. at 35-37; Michael J. Dennis & David P. Stewart, id. at 490-91.

2 Committee on Economic, Social and Cultural Rights, general comment 14, The Right to the Highest Attainable Standard of Health. E/C.12/2000/4, para. 9.

3 Id. at para 9. General Comment 14 also emphatically states that states have an immediate obligation to ensure non-discrimination. Governments must abolish any laws or policies that allow discrimination that affects the right to health, refrain from engaging in any discriminatory practice in implementing laws and policies, and implement measures to counter-balance past discrimination against those previously subjected to discrimination. See id. para. 18.

4 International Covenant on Civil and Political Rights, G.A. Res. 2200A (XXI), GAOR, U.N. Doc. A/6316 (1966).

5 Dina Bogecho, "Putting It to Good Use: the International Covenant on Civil and Political Rights and Women's Right to Reproductive Health", 13 S. Cal. L. & Women's Stud. 229, 345 (2004). The Human Rights Committee is the treaty monitoring body for the ICCPR. One of its prerogatives is to issue clarifying comments interpreting various provisions of the Convention, at 239.

6 Michael J. Dennis & David P. Stewart, supra note 361 at 465.

7 Ms. Yekaterina Pavlovna Lantsova v. The Russian Federation, Communication No. 763/1997 (July 22, 1996), CCPR/C/74/D/763/1997 (before the UN Human Rights Committee).

8 For example, South Africa has included a number of human rights in its Constitution. including a broad and far-reaching right to health. See Constitution of South Africa (adopted May 8, 1996, amended Oct 11, 1996), http://www.polity.org.za/html/govdocs/constitution/saconst.html?rebookmark=1. South Africa has also passed legislation to control drug prices with the aim of improving access to antiretroviral drugs for the treatment of HIV/AIDS. A challenge by multinational pharmaceutical companies followed in which they alleged violation of WTO intellectual property agreements; however, as a result of significant negative public media attention, the challenge was ultimately dropped. See Leslie London, "Human Rights and Public

Proponents of a complaint mechanism for the ICESCR argue that the absence of enforcement capacity has marginalized economic, social and cultural rights and limited movement toward full realization.[1] Others note that the reason for the absence of enforcement is obvious and appropriate given that economic, social and cultural rights are so complex and dependent upon so many determinants that justifiability would be impossible.[2] Despite the lack of a formal individual complaint process, the right to health has enjoyed significant attention and advocacy through pressure exerted by NGOs, the media, and a variety of local, national and international commissions.[3] In addition, the U.N. appointed a Special Rapporteur to monitor and assess efforts of governments to progressively realize the highest attainable standard of physical and mental health.[4]

Disease spreads quickly, wreaking havoc and endangering populations regardless of development or relative wealth.[5] International law has gained new prominence as a tool for multilateral cooperation in the public health field as states increasingly realize the need to complement domestic action in the health sector with cross-sector and cross-border action to protect the health of their populations.[6]

The present expanded international trade and the increasing role of WTO treaties provide links between health, human rights and trade law. For example, access to pharmaceutical drugs and the health implications have been a dominant issue in the Trade Related Aspect of Intellectual Property Rights (TRIPS) agreement.[7] Under the TRIPS agreement, WTO members have the capacity to grant compulsory patent licenses without the patent holder's consent.[8] The TRIPS agreement was further clarified in 2001 by the Doha Declaration, which clarified that TRIPS was to be implemented with an eye to protecting public health and, in particular, to promote access to medicine for all.[9] The Doha Declaration was adopted by the WTO in 2003 and, although it remains embattled, it represents a multilateral trade decision that attempts to balance the rights of patent holders with the profound health needs of the developing world for affordable access to

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Health: Dichotomies or Synergies in Developing Countries? Examining the Case of HIV in South Africa", 30 J.L. Med. & Ethics 677, 678 (2002).

1 Michael J. Dennis & David P. Stewart, supra note 361, at 453

2Michael J. Dennis & David P. Stewart, id. at 496.

3 Sofia Gruskin, supra note 320, at 321.

4U.N. Comm'n on Human Rights, Res. 2002/31, 49th mtg, (2002). See also Judith Asher, supra note 360, at 128-30 (discussion of role of the Special Rapporteur).

5 Laurie Z. Asher, "Confronting Disease in a Global Arena", 9 Cardozo J. Int'l & Comp. L. 135, 138 (2001), at 141.

6 Allyn L. Taylor, "Governing the Globalization of Public Health", 32 J. L. Med. & Ethics 500, 500 (2004), at 501.

7 Allyn L. Taulor, id at 501; Frederick M. Abbott, "The WTO Medicines Decision: World Pharmaceutical Trade and the Protection of Public Health", 99 Am. J. Int'l L. 317, 317 (2005).

8 Frederick M. Abbott, id. at 319.

9 Declaration on the TRIPS Agreement and Public Health (Nov 14 2001), http://www.wto.org, (last visited Feb 13, 2009).

essential medications.[1]

Global health and human rights have been conspicuously linked over the last several years with the United Nations system paying increasing attention to the interrelationship of the two as the ICCPR and ICESCR have matured and tailored rights instruments have addressed the rights of particular vulnerable populations.[2] Human rights work is shifting from a narrow, legalistic focus on civil and political rights to a broader rights approach encompassing economic, social and cultural rights.[3] The role of human rights in achieving global health is recognized by global governance efforts such as the recently issued International Health Regulations.[4]

FINDINGS, RECOMMENDATIONS AND CONCLUSION

The vast majority (more than 70%) of orphan drug producers are small companies, with R&D activity focused on biotechnology.[5] Several factors have promoted this trend. First of all, research grants, fiscal subsidies, technical assistance, and the fast-track approval process included in the orphan drug laws have reduced the financial risks of R&D investments and facilitated the entry of small companies into the market.[6] Second, small biotech companies seem more willing than big pharmaceutical firms to take on risky and innovative projects as such companies are usually financed by a restricted group of risk-taking investors and venture capitalists. The most successful orphan drug producers (such as Amgen, Genentech, and Genzyme) have become financially profitable even with small markets, by exploiting the incentives of the Orphan Drugs Legislation (ODL). All three companies were born from university scientists with expertise in newly developed techniques and therapeutic skills. The companies then pursued different strategies on three orphan drugs allowing them to avoid direct competition in market. "In addition one of the critical aspects of Genentech's success, despite its small markets, has been the capacity to create long-term business relationships with big pharmaceutical companies, first Eli Lilly and more recently Roche. These arrangements supported Genentech's R&D activities and allowed it to re-fill its drug pipeline, while allowing the biotech company more time to learn from failures, accumulate capabilities, and exchange expertise, aspects of great

1 Frederick M. Abbott, supra note 378, at 358; see also Allyn L. Taulor, supra note 377, at 502.

2 Allyn L. Taylor, supra note 377, at 502.

3 Paul Farmer & Nicole Gastineau, "Rethinking Health and Human Right: Time for a Paradigm Shift", 30 J. L. Med. & Ethics 655, 656 (2002).

4 David P. Fidler, "From International Sanitary Conventions to Global Health Security: The New International Health Regulations", 4 Chinese J. Int'l L. 325, 369-70 (2005), at 386.

5 Haffner ME., "Orphan drug development update", 1996, Drug Inf J 30: 29–34. Also from 2006, Adopting orphan drugs—two dozen years of treating rare diseases. N Engl J Med 354(5): 445–447.

6 Borgman RJ., "Development of an orphan drug by a start-up company", 1992, Int J Techno l Assess Health Care 8(4): 566–572.

value as such a risky business."[1] In recent years new orphan drug designations suggest a new trend in using these laws for neglected tropical diseases.

In 2005, the Institute of OneWorld Health, a nonprofit pharmaceutical company mainly supported by the Bill & Melinda Gates Foundation, received orphan drug designation with off-patent status which represents an exception more than the rule thanks to a unique business model that combines some characteristics of a convential for-profit pharmaceutical company with innovative ways of creating not-for-profit partnerships, leveraging existing products and promoting social entrepreneurship.[2] The 2005 orphan designation in Europe of a tuberculosis vaccine developed by Oxford University represents a second interesting case.[3] In Europe this is the first time orphan drug status has been granted for a product developed by a university and to an organization that clearly stated its intention of making the product available in developing countries. Austrian biotech company, Intercell aims at developing vaccines where there is "substantial unaddressed medical need" especially in Japan, Korea and China. These three cases show that small companies and universities, rather than big pharmaceutical companies, are the more common drivers in the development of new orphan drug products. All three firms have taken advantage of the incentives of orphan drug laws in the US and Europe. Similarly, as with successful biotech companies involved in rare diseases, these organizations have sought benefits or could potentially benefit by establishing very early on long-term partnerships with venture philanthropists, national governments, and international organizations.[4]

The success of orphan drug designation for neglected rare diseases shows that, first, drug companies using orphan drug programs can still generate profits and recoup their R&D investments even with relatively small markets in the developed world. Second, the orphan drug designation mainly encourages investments and initiatives by small science-oriented companies. For the future, the followings steps are urgent to sufficiently cure the orphan problems-

(i) A strong commitment to demonstrating value on the part of the biotech and pharmaceutical sectors. Dedicated and focused teams are required in order to embed principles of reimbursement and market access throughout the discovery and development process.

(ii) The Medical Research and Development Treaty (MRDT)[5] among both

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1 Pisano GP. 2006. Science Business. Harvard Business School Press: Cambridge.

2 Hale VG, Woo K, Lipton HL., "Oxymoron no more: the potential of nonprofit drug companies to deliver on the promise of medicines for the developing world", 2005, Health Aff 24(4): 1057–1063.

3 Lang T, Hill AV, McShane H, et al., " New TB vaccine granted orphan drug status", 2005, BMJ 331(7530): 1476.

4 Kettler HE, Marjanovic S., "Engaging biotechnology companies in the development of innovative solutions for diseases of poverty", 2004, Nat Rev Drug Discovery 3: 171–176.

5 Medical Research and Development Treaty (MRDT)

developed and developing countries would agree to a treaty that commits them to contribute a fixed portion of their GDP year after year to fund medical R&D.

(iii) The concept of an Advanced Market Commitment (AMC) is another approach to incentivize R&D for diseases of poverty.[1] An AMC is a financial commitment to subsidize the future providers of vaccines or pharmaceuticals that meet targeted technical specifications and demand requirements in developing countries. It is estimated that a vaccine meeting the AMC criteria could save the lives of 5.4 million children by 2030.

(iii) Market incentive must be significant enough to overcome barriers to innovators and also insure broad access in poorer countries. To focus this, three policy options are to be considered-

- Purchase funds
- Transferable patent exclusivity
- Transferable priority review by FDA

Purchase Funds: A purchase fund with a guaranteed price to companies will produce a new vaccine for malaria, TB, or AIDS which would require sizeable purchase funds for each disease area - $500 million or more and countries would provide a small co-payment to insure new vaccine met a market test.

Transferable Patent Exclusivity Rights: it includes the idea as follows-

- firms would obtain a transferable patent right in developed countries market as an incentive for developing a new drug for a neglected disease;
- could provide powerful stimulus to firms with established blockbuster products in developed states;
- but cost of market exclusivity add-ons would be borne by consumers and payers of these products through higher prices.

Transferable Priority Review Rights: It includes the following measures-

- firm would receive a transferable right of priority state's review for a new drug application as an incentive for developing new product for a neglected disease;
- shortening review times from 18 months to 6 months would be worth an estimated $300 million for a top deciles compound and
- program would need to be structured so it doesn't slow down approval of products with high unmet needs.

(iv) Drug Donation Programs: These programs have made strong contributions to particular orphan diseases in poorer countries where the participants are the biggest pharmaceuticals industries.

(v) Lead global and regional efforts to promote, coordinate and formulate a

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http://www.cptech.org/workingdrafts/rndtreaty4.pdf, (last visited on 14th June, 2009), (2005). See Love, J., "Measures to enhance access to medical technologies, and new methods of stimulating medical R&D", U.C. Davis Law Rev. 40, 679–715, 2007.

1 Kremer, M., "Pharmaceuticals and the developing world", J. Econ. Persp. 16, 67–90 (2002). See Berndt, E.R. et al., "Advanced Purchase Commitments for a Malaria Vaccine: Estimating Costs and Effectiveness", National Bureau of Economic Research, NBER Working Paper No. 11288 (2005).

model for applying the integrated approach in the context of eco-systems that facilitate transmission of orphan diseases;
(vi) Provide guidelines on establishing national health project to identify and solve the neglected diseases that are uncommon to all;
(vii) Promote advocacy to emphasize the burden of orphan disease on society and to create demand at all levels of society for control them;
(viii) Develop or update guidelines for surveillance, prevention and control of specific orphan diseases and conduct, maintain and report inventories of activities and tools to control them effectively;
(ix) Develop guidelines for implementing activities to integrate surveillance, prevention and control of unknown orphan diseases.

The greatest intellectual achievements of human being are the religion and science where the full realization will only come when it is placed in the service of man and women. The modern world is long way from that. Unless these two are putted in the service of closing the gap between the rich and the poor worlds, particularly in the delivery of critical medicines and health services, our scientific achievements will provide, 'naught for our comfort'.[1] The rich world must recognize its moral and economic responsibilities and put up the necessary money and support; otherwise failure will result in both humanitarian and security crisis for the rich world.

1 Huddlestone T., "Naught For Your Comfort", 1956, New York: Doubleday.

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- European Social Charter of 1961, European Treaty Series- No 163, Strasbourge 3, v. 1996.
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- Memorandum of Understanding On The Access To Medicines For Poor Countries, USTR, San Antonio, Texas, 16th July Of 2004.
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