

AN INTERNATIONAL LEGAL SYSTEM REGULATING THE TRADE IN THE PHARMACEUTICAL SECTOR AND SERVICES PROVIDED BY HUMAN SUBJECTS

Sarah Bahir*

I. INTRODUCTION

PHARMACEUTICAL COMPANIES BENEFIT from international trade not only to market their products, but also to obtain the services of human subjects for clinical trials. Clinical trial services in the pharmaceutical sector have revealed recurring breaches in ethical standards. To achieve speedy approval of their products, pharmaceutical companies conduct clinical trials in developing countries where “ethical standards may be lax and the impoverished sick abundant.”¹ As a result, clinical trials lacking ethical approval have emerged in countries where regulation is inadequate or where governments lack the resources or will required to enforce regulations.² Despite existing international guidelines on the ethical review of pharmaceutical testing, a survey conducted in 2004 by the United States National Bioethics Advisory Commission showed that a large number of clinical trials conducted in developing countries do not undergo ethical review.³ While the international market fuels an expanding trade in pharmaceuticals — providing incentive to invest in research and development — the market has failed to demand legally binding ethical standards regarding human testing. Human subjects in developing countries have been left unprotected against an industry accused of killing thousands of impoverished people in favour of those able to afford premiums attached to patents.

This paper begins with a short history of unethical research practices involving human subjects. It then discusses current unethical research practices committed by pharmaceutical companies in developing countries. Relevant international legal instruments and internationally recognized codes of ethics will then be considered. The suitability of the

* B.A. (Hons.) (UW), LL.B. (UM).

¹ Sonia Shah, “Globalization of Clinical Research by the Pharmaceutical Industry” (2003) 33:1 *International Journal of Health Services* 29 at 29.

² William Dubois, “New Drug Research, The Extraterritorial Application of FDA Regulations, and the Need for International Cooperation” (2003) 36 *Vand. J. Transnat'l L.* 168.

³ A.A. Hyder *et al.*, “Ethical Review of Health Research: A Perspective from Developing Country Researchers” (2004) 30 *Journal of Medical Ethics* 68.

World Trade Organization (WTO) and the United Nation's Global Compact (GC) are considered as possible organizations to implement ethical standards. This paper concludes that the existing instruments are inadequate to regulate transnational pharmaceutical research and suggests a legal instrument, enforced by an effective international organization, is required to solve the current problems.

II. HISTORY

AFTER WORLD WAR II, 23 GERMAN PHYSICIANS WERE tried for war crimes and crimes against humanity resulting from research conducted for Nazi Germany. The case of *U.S.A. v. Karl Brandt, et al.*,⁴ also known as the Doctors Trial, investigated these physicians for participating in Nazi German's "euthanasia program"⁵ and for performing medical experiments on human subjects without their consent.⁶ Prisoners of war and those in concentration camps were subjected to brutal experiments, including exposure to high levels of X-rays for sterilization research and freezing temperatures to investigate human recovery.⁷ Many prisoners had sections of their bones, muscles, and nerves removed for regeneration and transplantation studies.⁸ A number of research subjects were deliberately exposed to malaria, jaundice, and typhus viruses to investigate immunization and treatment for those diseases.⁹ In order to find a treatment for mustard gas, prisoners were exposed to lethal gas and drug treatments.¹⁰ One-hundred-and-twelve Jews were killed to complete a skeleton collection for the Reich University

⁴ *U.S.A. v. Karl Brandt, et al.*, online: Harvard Law School Library <http://nuremberg.law.harvard.edu/php/docs_swi.php?DI=1&text=medical>.

⁵ The "euthanasia" program of the Nazi German government involved systematic execution of mentally and physically impaired persons by gas, lethal injections, and other means in nursing homes, hospitals, and asylums. Such persons were regarded as "unworthy of life" and a burden to the German war machine. See "The Nuremberg Trials: The Doctors Trial," online: University of Missouri-Kansas City School of Law <<http://www.law.umkc.edu/faculty/projects/ftrials/nuremberg/NurembergDoctorTrial.html#COUNT%20ONE>>.

⁶ *Ibid.*

⁷ "The Doctors Trial (the Medical Case of the Subsequent Nuremberg Proceedings): Count Two – War Crimes" from National Archives Record Group 238, M887, online: The United States Holocaust Memorial Museum <<http://www.ushmm.org/research/doctors/twoa.htm>>.

⁸ *Ibid.*

⁹ *Ibid.*

¹⁰ *Ibid.*

of Strasbourg.¹¹ Before defleshing their corpses, the bodies were used for anatomical and pathological studies.¹² The trial lasted 140 days; 85 witnesses testified and almost 1,500 documents were introduced. Sixteen of the doctors were found guilty.

While the brutality of Nazi doctors remains unmatched, unethical research practices have occurred outside Nazi Germany as well. The Tuskegee Study of Untreated Syphilis, for example, was carried out in the United States.¹³ The study, which continued from 1932 to 1972, involved 399 black men with syphilis. The main purpose of the research was to determine the natural history of syphilis by leaving the subjects untreated. While the research subjects had agreed to examination and treatment, the main purpose of the study was deliberately concealed from them. The study continued despite the availability of penicillin in 1947 as the drug of choice for syphilis.¹⁴

III. CURRENT PROBLEMS

CURRENT UNETHICAL PRACTICES involving pharmaceutical clinical trials are concentrated in developing countries. National regulators in the developed countries have failed to police the activities of their pharmaceutical companies once they leave national boundaries to conduct their research. An award winning *Washington Post* investigative series into pharmaceutical testing in developing countries revealed “a booming, poorly regulated testing system that is dominated by private interests . . . that far too often betrays its promises to patients and consumers.”¹⁵ Developing countries are targeted because they

¹¹ *Supra* note 7, The United States Holocaust Memorial Museum, online: ushmm.org <<http://www.ushmm.org/research/doctors/two.htm>>.

¹² *Ibid.*

¹³ “The Tuskegee Timeline,” online: Department of Health and Human Services, Centers for Disease Control and Prevention <<http://www.cdc.gov/nchstp/od/tuskegee/time.htm>> [“The Tuskegee Timeline”]; also Marcia Angell, “The Ethics of Clinical Research in the Third World” (1997) 337:12 *N Eng. J. Med.* 847; also Baruch A. Brody, *The Ethics of Biomedical Research: An International Perspective* (New York: Oxford University Press, 1998) at 33.

¹⁴ “The Tuskegee Timeline,” *ibid.*

¹⁵ Joe Stephens, “Where Profits and Lives Hang in Balance; Finding an Abundance of Subjects and Lack of Oversight Abroad, Big Drug Companies Test Offshore to Speed Products to Market” *Washington Post* (17 December 2000) A01 (LexisNexis) [Joe Stephens]. *Washington Post* conducted an in-depth five part investigative series called “The Body Hunters: Exporting Human Experiments” in 2000. The series won the Malcolm Forbes Award for best business reporting from abroad in newspapers. This investigative series is regularly cited and relied upon in academic research regarding pharmaceutical testing in developing countries.

possess large numbers of ill people required for drug research.¹⁶ These people are also more likely to participate in research activities because they often lack access to adequate health care.¹⁷ Low research costs in developing countries provide incentives for drug companies to move clinical trials abroad. Inadequate regulations also accelerate the process of getting drugs to market. Consequently, clinical trials have become a lucrative business, where ethics are sidestepped in favour of profitability.

Drug companies conducting clinical trials abroad often fail to obtain adequate informed consent from subjects. In 1996, Pfizer was anxious to get the approval of the United States Food and Drug Administration (FDA) for its antibiotic, Trovan. Wall Street analysts had predicted Trovan would bring a yearly profit of one billion dollars to Pfizer if it received FDA approval for all its potential uses, including its effects on children.¹⁸ In the same year, Nigeria was hit with a meningitis epidemic affecting children. Pfizer researchers immediately planned clinical trials, and took only six weeks to prepare, not the year (or longer), which is common in the United States.¹⁹ The Washington Post investigated Pfizer's practices and found that the research proceeded with little independent oversight. Many of the poorly educated participants were treated (read tested) without realizing that they were guinea pigs.²⁰ While Pfizer claimed that local nurses explained the research to the families, the company did not have any signed consent forms to back their assertion.²¹ Scott Hopkins, one of Pfizer physicians, admitted that nurses did not translate the full consent form; only a general explanation was provided.²² Moreover, the availability of an alternative proven treatment at a nearby Doctors Without Borders' centre was not discussed with patients.²³

Pfizer researchers departed from research practices understood to be customary within the pharmaceutical industry. For example, one

See http://www.opcofamerica.org/opc_awards/archive/awards_2000.php online: OPC

¹⁶ *Ibid.*

¹⁷ Mary Pat Flaherty & Doug Struck, "Life by Luck of the Draw" *Washington Post* (22 December 2000) A01, online: [Washington Post <http://www.washingtonpost.com/ac2/wp-dyn/A37168-2000Dec21>](http://www.washingtonpost.com/ac2/wp-dyn/A37168-2000Dec21) [Flaherty & Struck]. See also Karen DeYoung & Deborah Nelson, "Latin America Is Ripe for Trials and Fraud: Frantic Pace Could Overwhelm Controls" *Washington Post* (21 December 2000) A01, online: [Washington Post <http://www.washingtonpost.com/ac2/wp-dyn/A31027-2000Dec20?language=printer>](http://www.washingtonpost.com/ac2/wp-dyn/A31027-2000Dec20?language=printer).

¹⁸ *Supra* note 2 at 163.

¹⁹ Joe Stephens, *supra* note 15.

²⁰ *Ibid.*

²¹ *Ibid.*

²² *Ibid.*

²³ *Ibid.*

Nigerian girl's condition deteriorated drastically after she was given her first dose of the antibiotic, and three days later she died. Pfizer's records showed that despite her frozen eye and declining health after the first dose, the researchers continued to give her the same dose of the experimental antibiotic. However, if a subject's condition does not improve within 24 hours, the common industry research practice demands either to change the experimental drug or its dosage.²⁴ For children in the control group, a proven anti-meningitis drug was administered, but at one-third of the recommended dosage. According to a spokesman for the comparison drug's manufacturer, "clinical failures . . . and perhaps deaths of children could have resulted from the low dosing."²⁵ Moreover, industry guidelines governing meningitis experiments were ignored. Specifically, guidelines suggested that researchers take a second spinal blood test one day after beginning treatment to determine if the medication is actually working.²⁶ In the case of the Nigerian girl, only one test was conducted before Trovan was administered; the required follow-up test was never performed.

Not only have pharmaceutical researchers ignored practices accepted in their industry, they have overlooked practices that any reasonable person would have considered. In 2004, for example, Gilead tested Tenofovir in Cameroon to study its effectiveness in reducing HIV transmission. Four hundred sex workers participated in the research. Most of the participants were illiterate and spoke limited French in addition to their local language. However, the initial consent forms and counseling documents given to the volunteers were only in English.²⁷ In fact, many of the sex workers innocently believed that they were receiving vaccines.²⁸ Gilead later corrected this problem, but only after huge criticism from aid organizations and other agencies.

Developing countries usually suffer from political and economic turmoil, which further aggravates unethical practices. Authoritarian regimes, corruption, and regulatory lacunas exasperate the problem. During Trovan research, for example, Nigerian physicians, who were aware of Pfizer's irregularities, failed to protest.²⁹ They feared the Nigerian military regime that had backed Pfizer's research in Nigeria.

²⁴ *Ibid.*

²⁵ *Ibid.*

²⁶ *Ibid.*

²⁷ "Cameroon: Clinical trial of anti-HIV drug on sex workers in question," online: Integrated Regional Information Networks (IRIN) <http://www.irinnews.org/report.asp?ReportID=45252&SelectRegion=West_Africa>.

²⁸ Jean-Philippe Chippaux, "Pharmaceutical Colonialism in Africa" *Le Monde diplomatique* (August 2005), online: Le Monde diplomatique <<http://mondediplo.com/2005/08/11pharma>>.

²⁹ Joe Stephens, *supra* note 15.

A common practice of Latin American pharmaceutical companies is to subcontract clinical trials to outside researchers who, in turn, fraudulently enroll patients into drug research. In one case, patients with heart disease were enrolled in a drug trial.³⁰ Prosecutors later determined that “signatures on at least 80 consent documents were forged.”³¹ Despite attempts by Latin American countries to create regulatory mechanisms, the pressure from pharmaceutical companies “to produce fast, high-volume results — and a willingness to pay for quantity over quality” — pervades the push for more appropriate regulations.³²

While drug research is not restricted to developing countries, the type of research conducted in these countries appears to be riskier than those performed elsewhere. Two research studies on preventing the transmission of HIV from pregnant mothers to their fetuses occurred simultaneously in the United States and Thailand.³³ While both studies researched the same kind of anti-viral drug, the study was designed in a way that the Thai group had greater opportunity to receive placebos. Two-thirds of American subjects received an anti-viral agent; a placebo was administered to the other one-third. On the other hand, only half of the Thai group received the real medicine. Furthermore, those who received the anti-viral drug in Thailand received it less frequently and in smaller doses than their American counterparts. In the American study, all of the newborn children were given anti-viral drugs, while none of the Thai children received such treatment.³⁴

Jagdish Bhagwati, the author of *In Defense of Globalization*,³⁵ would likely respond to the above by arguing that clinical research provides participants in developing countries with a choice between experimental treatment and no treatment at all. At the time, Nigeria was overwhelmed by a meningitis epidemic, and Thailand did not have the resources necessary to prevent HIV infections. As a result, people participated in the tests with the hope of at least receiving experimental treatment rather than no treatment. However, Bhagwati’s perspective neglects the fact that pharmaceutical companies are exploiting developing countries in order to make million dollar profits from the sale of the drugs once they are approved. The relationship between pharmaceutical companies and developing countries can be conceptualized in trade terms — trade in services of human subjects. As the *Washington Post* investigation shows:

³⁰ DeYoung & Nelson, *supra* note 17.

³¹ *Ibid.*

³² *Ibid.*

³³ Flaherty & Struck, *supra* note 17.

³⁴ *Ibid.*

³⁵ Jagdish Bhagwati, *In Defense of Globalization* (New York: Oxford University Press, 2004).

[R]ich countries have the drugs and hypotheses, while poor countries have vast numbers of patients. Yet the trade-offs made in experiments do not always distribute burdens and benefits evenly.³⁶

The benefit to pharmaceutical companies is invaluable. Not only do they get access to a ready pool of patients unavailable elsewhere, they also reduce research costs. In return for their services, research participants receive sub-standard care, unethical treatment, and unequal opportunity to benefit from prospective treatment.

Profit-driven drug companies frequently bargain with local authorities in a bid to maximize profit. In an HIV vaccine trial on drug addicts in Thailand, VaxGen negotiated a deal with Thai authorities that minimized research costs. Contrary to international guidelines, VaxGen refused to pledge care for subjects who became infected with HIV during its vaccine trial. Thai health authorities were required to pay for these HIV patients from government coffers.³⁷ VaxGen also refused to provide the vaccine, if proven to be effective, at a reduced price. It further rejected the Thai request for profit-sharing or a manufacturing plant to be located in that country. Its only commitment was too little, too late: if the drug was approved, VaxGen would provide free vaccinations for those volunteers who received the placebo.³⁸ By approval time, those volunteers would likely have been infected with HIV, and the vaccination would be of no help. VaxGen's program of providing free rice to addicts who brought five friends to participate in the study is a further insult to their desperate situation.³⁹

Developing countries' research participants are a valuable trade commodity in the pharmaceutical sector. It is this trade commodity that accelerates the approval of high-priced drugs and their sale in the international market. In fact, Julian Borger notes:

The combined worth of the world's top five drug companies is twice the combined GDP of all sub-Saharan Africa and their influence on the rules of world trade is many times stronger because they can bring their wealth to bear directly on the levers of western power.⁴⁰

³⁶ Flaherty & Struck, *supra* note 17.

³⁷ *Ibid.*

³⁸ *Ibid.*

³⁹ *Ibid.*

⁴⁰ Julian Borger, "Industry that stalks the US corridors of power" *The Guardian* (13 February 2001), online: [Guardian Unlimited <http://www.guardian.co.uk/international/story/0,3604,437212,00.html>](http://www.guardian.co.uk/international/story/0,3604,437212,00.html).

Pharmaceutical companies make enough money from research participants to afford to pay a fair fee for their valuable services. Contrary to VaxGen's corporate conscience, free rice is not enough. Research participants deserve a bigger piece of the pie.

The above cases testify that trade in pharmaceuticals products and clinical trials has indeed become a swift international enterprise. Maximizing profitability in the pharmaceutical trade requires compromise in the pharmaceutical research. The next section deals with the existing mechanisms intended to regulate such compromises.

IV. EXISTING MECHANISMS

International Legal Instruments

International human rights law recognizes the inherent dignity of every human being. The *United Nations Declaration on Human Rights* entitles individuals involved in medical research to the right not to be "subjected to torture or to cruel, inhuman or degrading treatment or punishment."⁴¹ Article 7 of the *International Covenant on Civil and Political Rights* adds that "[i]n particular, no one shall be subjected without his free consent to medical or scientific experimentation."⁴² International human rights law codifies standards for human protection and monitors the exercise of state power. The main shortcoming of this legal paradigm is its inability to control non-state human rights violators such as transnational corporations. It ultimately depends on the participating states to enforce national laws in conformity with human rights principles. The problem is that many developing nations are unable to effectively enact and enforce regulations that would bind transnational corporate actors. The usefulness of these existing international legal instruments, therefore, remains limited.

Other instruments that attempt to regulate research on human subjects are internationally recognized ethical codes. These include:

⁴¹ *The Universal Declaration of Human Rights*, 10 December 1948, art. 5, online: Office of the High Commissioner for Human Rights <<http://www.unhcr.ch/udhr/lang/eng.htm>>.

⁴² *International Covenant on Civil and Political Rights*, 16 December 1966, art. 7, online: Office of the High Commissioner for Human Rights <<http://www.ohchr.org/english/law/ccpr.htm>>.

1) **The Nuremberg Code, 1947**

In response to the Doctors Trial (1946-1947), the *Nuremberg Code* was designed to safeguard the rights of subjects in medical research.⁴³ Since the Nazi physicians subjected prisoners to medical testing without their consent, the Code identified voluntary consent as an essential part of clinical trials.⁴⁴ It also proposed that unnecessary pain and injury to participants should be avoided. The *Nuremberg Code* has historical significance; its current application has, however, waned as more expansive ethical codes have risen.

2) **World Medical Association Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects, 1964 (last amended in 2000)**

The Declaration of Helsinki, adopted in 1964 by the World Medical Association, is the most recognized set of guidelines in the area of biomedical research. Expanding on the Nuremberg principles, the Declaration of Helsinki recognizes that biomedical research extends beyond the exploitation of human subjects. Article 19 of the Declaration notes that medical research is only justified if the population on whom the research is carried out stands to benefit from the result.⁴⁵ It also requires researchers to provide research participants with the “best proven prophylactic, diagnostic and therapeutic methods” at the conclusion of the study.⁴⁶ The Declaration prioritizes the well-being of human subjects over the interests of science and society, and insists on providing special protection to economically and medically disadvantaged participants.⁴⁷ Physicians must provide the participants with adequate information about “the anticipated benefits and potential risks” of the research in order to obtain legitimate informed consent.⁴⁸ Participants should also be made aware that they can withdraw at anytime during the research.⁴⁹ The Declaration also proposes the establishment of

⁴³ The *Nuremberg Code*, 1947, online: The United States Holocaust Memorial Museum <http://www.ushmm.org/research/doctors/Nuremberg_Code.htm>.

⁴⁴ *Ibid.*

⁴⁵ *World Medical Association Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects*, June 1964, art. 19 (last amended October 2000), online: World Medical Association <<http://www.wma.net/e/policy/b3.htm>>.

⁴⁶ *Ibid.*, 30; also see Note of clarification on art. 30 added in 2004.

⁴⁷ *Ibid.*, arts. 5 & 8.

⁴⁸ *Ibid.*, art. 22.

⁴⁹ *Ibid.*

independent review committees to review research protocol and monitor ongoing trials.⁵⁰ The significance of this Declaration is evident as its principles have been followed in other international, regional, and national guidelines and regulations.⁵¹

3) Ethical Principles and Guidelines for the Protection of Human Subjects in Research (the Belmont Report), 1979

The Belmont Report⁵² was prepared in response to the Tuskegee Study, which exposed participants to syphilis despite an available treatment. The Report established three ethical principles to guide research: “respect for persons, beneficence and justice.”⁵³ Respect for persons requires informed consent of the participants based on information, comprehension, and voluntariness. The principle of beneficence is satisfied by protecting participants from harm as well as securing their welfare.⁵⁴ Justice demands fair distribution of both the burdens and benefits of the research. The Report particularly condemns research practices where the burdens of serving as research subjects fall upon poor, disadvantaged people, while the benefits of improved medical care flow to the rich. Although the Report is not an international instrument, it has become a standard reference for its “clarity and authority”. The Belmont Report has been included in U.S. legislation and has been referred to in the World Health Organization’s (WHO) guidelines.⁵⁵

⁵⁰ *Ibid.*, arts.13 & 26.

⁵¹ Delon Human & Sev S. Fluss, “The World Medical Association’s Declaration of Helsinki: Historical and Contemporary Perspectives” (24 July 01) at 7-11, online: World Medical Association <http://www.wma.net/e/ethicsunit/pdf/draft_historical_contemporary_perspectives.pdf>; also Delfosse M.-L., “Research Committees and The Principle of Justice: Putting Ethics and Law to The Test” in Weisstub DN, ed., *Research on human subjects: ethics, law and social policy* (Oxford: Elsevier Science 1998) 286.

⁵² *The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research*, (United States National Commission for the Protection Of Human Subjects of Biomedical and Behavioral Research, 18 April 1979), online: FDA <<http://www.fda.gov/oc/ohrt/IRBS/belmont.html>>.

⁵³ *Ibid.*

⁵⁴ *Ibid.*

⁵⁵ David Patterson, “Resolving Legal, Ethical, and Human Rights Challenges in HIV Vaccine Research” at 10, online: Canadian HIV/AIDS Legal Network <www.aidslaw.ca/durban2000/vaccinefinal.pdf>.

4) International Ethical Guidelines for Biomedical Research Involving Human Subjects (The CIOMS Guidelines) 1982, (last amended 2002)

The Council for International Organizations of Medical Sciences (CIOMS) is a non-governmental international organization that studies the implications of pharmaceutical research in resource limited countries.⁵⁶ The CIOMS was founded jointly by the WHO and the United Nations Educational Scientific and Cultural Organization (UNESCO) in 1949.⁵⁷ The CIOMS represents 48 international organizations in biomedical disciplines and 18 countries through membership of their national academies and medical research councils. The guidelines give elaborate directions to researchers who conduct their studies in developing countries, requiring them to ensure that their studies “[are] responsive to the health needs and the priorities of the population or community in which [they are] to be carried out.”⁵⁸ Similar to other guidelines, they require that any product or knowledge generated from the study “be made reasonably available for the benefit of that population or community.”⁵⁹ The guidelines also require equitable distribution of burdens and benefits of research when selecting subjects. Moreover, foreign researchers are under an ethical obligation to treat and compensate those participants who suffer injury as a consequence of the research.⁶⁰

5) The WHO Guidelines for Good Clinical Practice for Trials on Pharmaceutical Products, 1995

The WHO Guidelines for Good Clinical Practice are important for two reasons: they are published by an authoritative organization, and they specifically deal with pharmaceutical products. These guidelines adopt the ethical principles outlined in the Helsinki Declaration and the Belmont Report. The WHO guidelines emphasize the implementation of the ethical principles, which was lacking in previous guidelines. The guidelines propose that the 192 member states incorporate regulations

⁵⁶ *International Ethical Guidelines for Biomedical Research Involving Human Subjects* (2002), online: Council for International Organizations of Medical Sciences <http://www.cioms.ch/guidelines_nov_2002_blurb.htm>.

⁵⁷ “What is CIOMS?” online: Council for International Organizations of Medical Sciences <http://www.cioms.ch/what_is_cioms.htm>.

⁵⁸ *Supra* note 56, guideline 10.

⁵⁹ *Ibid.*

⁶⁰ *Ibid.*, guideline 12.

governing clinical trials in their national laws.⁶¹ Countries that lack proper regulations are advised to use the WHO guidelines. To oversee adherence to ethical guidelines and to ensure participants are protected, independent ethics committees are prescribed.

These guidelines are particularly important for their detail and clarity on the process of implementing ethical standards. Regarding informed consent, for example, the guidelines require that “information should be given in a language and at a level of complexity understandable to the subjects.”⁶² Consent is obtained only if

. . . a subject consents to participate after a full and comprehensive explanation of the study, this consent should be appropriately recorded. The explanation should include the aim of the study; the expected benefits for the subjects and/or others; the possibility of allocation to a reference treatment or placebo; the risks and inconveniences — e.g. invasive procedures; and, where appropriate, an explanation of alternative, recognized medical therapy. Consent must be documented either by the subject’s dated signature or in agreement with local laws and regulations by the signature of an independent witness who records the subject’s consent. In either case, the subject must be informed that signature confirms only that consent is based on the information provided, and that the subject has freely chosen to participate without prejudice to legal and ethical rights, while reserving the right to withdraw from the study at his or her own initiative at any time, without having to give any reason.⁶³

Similar detail is provided on the responsibilities of researchers, investigators and those who monitor the research.

The guidelines are also important because they are issued by the WHO, the United Nations specialized agency for health, whose broad objective is “the attainment by all peoples of the highest possible level of health.”⁶⁴ The WHO also provides other services that enhance the effectiveness of the guidelines. For example, it provides advisory groups to supply training, assistance, and advocacy to developing countries

⁶¹ World Health Organization, *Guidelines for Good Clinical Practice for Trials on Pharmaceutical Products* (1995), online: University of Minnesota Human Rights Library < <http://www1.umn.edu/humanrts/instree/clinicalpractice.html>>.

⁶² *Ibid.*

⁶³ *Ibid.*

⁶⁴ “About WHO,” online: WHO <<http://www.who.int/about/en/>>.

where research takes place.⁶⁵ In 2006, the WHO launched an International Clinical Trials Registry Platform.⁶⁶ The Registry Platform will record and publish the results of all clinical trials with human subjects without bias or selectivity in reporting. This will increase transparency and accountability on the part of companies and institutions that do clinical research.

6) ICH Harmonized Tripartite Guideline: Guideline for Good Clinical Practice, 1996

The International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) is currently working towards harmonizing regulatory requirements related to pharmaceutical testing and product registration.⁶⁷ This project brings together the regulatory authorities of Europe, Japan, and the United States to provide a unified standard of good clinical practices.⁶⁸ The three members have already agreed on a harmonized tripartite guideline and are currently in the process of implementing the guideline into their own national regulatory system. The regulatory bodies can enforce these standards by applying sanctions on researchers who fail to observe the governing principles.⁶⁹ The one shortcoming of ICH is that its applicability is limited only to the three members, Europe, Japan, and the United States. As a result, transnational companies that are not based in Europe, Japan or the United States may still escape liability.

V. PROBLEM WITH THE EXISTING MECHANISMS

INTERNATIONAL HUMAN RIGHTS LAW PROVIDES a legal instrument to protect the rights of human subjects in clinical trials. However, as mentioned earlier, its enforceability is limited to state actors. Private pharmaceutical companies escape liability if their countries are unable or unwilling to regulate the industry's operation outside their borders. Similarly, the guidelines provide elaborate ethical standards but fail to compel companies to abide by the rules. The Helsinki Declaration is

⁶⁵ "International Clinical Trials Registry Platform," online: WHO <<http://www.who.int/ictrp/about/details/en/index5.html>>.

⁶⁶ "International Clinical Trials Registry Platform (ICTRP)," online: WHO <<http://www.who.int/ictrp/about/details/en/index7.html>>.

⁶⁷ *ICH Harmonized Tripartite Guideline: Guideline for Good Clinical Practice* (10 June 1996), online: ICH <<http://www.ich.org/LOB/media/MEDIA482.pdf>>.

⁶⁸ *Ibid.*

⁶⁹ "The ethics of research related to healthcare in developing countries," online: Nuffield Council on Bioethics <<http://library.cph.chula.ac.th/downloads/Health-ethics/ethics%20of%20research.pdf>>.

recognized internationally but only imposes a moral obligation on countries and physicians. The CIOMS promotes transparency and the creation of review committees but “only binds members of the signatory organizations.”⁷⁰ The one exception to this general rule of unenforceability is the Belmont Report, which is incorporated into the United States *Code of Federal Regulations*. However, as noted above, American regulators did not have the capacity to police Pfizer’s practices outside the United States. Combating research irregularities beyond national borders requires a clear set of guidelines implemented by an organization with enforcement powers.

VI. AN INTERNATIONAL LEGAL SYSTEM REGULATING THE TRADE IN SERVICES PROVIDED BY HUMAN SUBJECTS

AS NOTED EARLIER, CLINICAL RESEARCH is ultimately a trade issue; namely the trade in services provided by human subjects. Unfortunately, such trade inherently advances the interests of pharmaceutical companies above vulnerable developing countries and their citizens. The trade in testing on human subjects is *laissez faire*; research conducted in the developing world encounters neither the same oversight nor the same ethical standards expected in the developed world. Human subjects who are desperate, impoverished, and sick let themselves to experimentation in lieu of treatment. This dynamic is further aggravated by globalization. Despite the serious ethical-, medical-, legal-, and trade-related problems identified above, the internationalization of trade has made it possible for pharmaceutical companies to conduct their trials in any country. While the market has borne trade in the biomedical sector, it has failed to sustain required regulations. Therefore, policy makers must take action that enables the trade in biomedical products to flourish in a safe and ethical manner.

Ideally, a system should exist to govern the international trade between pharmaceutical companies and the services provided by human subjects. This would ultimately balance the interests of the pharmaceutical sector with those of human subjects and developing countries. This system would comprise two key components working hand-in-glove: one, a well-crafted international legal instrument reflecting a universal ethical code; the other, a well-placed institution responsible for implementation.

A well-crafted international legal instrument would incorporate the virtues of the ethical codes discussed above. The WHO guidelines provide

⁷⁰ *Ibid.* at 65.

a particularly helpful starting point; they bring together the strongest principles of the Helsinki Declaration and the CIOMS guidelines' emphasis on the developing world. The WHO guidelines clearly define the rights and responsibilities of parties involved in clinical trials, while providing specific direction to researchers, monitors, and regulatory agencies.⁷¹ Moreover, these guidelines recommend an expansive implementation strategy.⁷² Building onto the WHO guidelines, an ideal instrument would include a responsibility for pharmaceutical companies to share the 'fruits of their research' with research participants. For example, Guideline 10 from the CIOMS guidelines reads:

Before undertaking research in a population or community with limited resources, the sponsor and the investigator must make every effort to ensure that:

- the research is responsive to the health needs and the priorities of the population or community in which it is to be carried out; and
- any intervention or product developed, or knowledge generated, will be made reasonably available for the benefit of that population or community.⁷³

Pharmaceutical companies would be obliged to provide the best available treatment to human subjects at the conclusion of the trial, including the experimental drug, should it demonstrate itself superior to its comparators. This instrument could also provide developing countries with the ability to formally negotiate the terms of trade in the services provided by their national human subjects, including national manufacturing agreements, preferential pricing, and testing terms.

An ideal institution would enforce this instrument directly onto pharmaceutical companies, preventing transnational companies from migrating to countries with the lowest regulatory standards. In so doing, the proverbial race to the bottom would end in a tie at a reasonable ethical standard. Currently, two possible international organizations exist to host such a system: the World Trade Organization (WTO) and the United Nations Global Compact.

The WTO is the main international organization dealing with the rules of trade between countries. Its objective is to create a secure trading environment for producers of goods and services through

⁷¹ *Supra* note 61.

⁷² *Ibid.*

⁷³ *Supra* note 56, guideline 10.

economic liberalization.⁷⁴ The WTO takes its legitimacy from legal agreements that are negotiated and ratified by trading nations. These agreements are binding on member countries and regulate their respective trade. In case of trade disputes, the WTO provides a dispute settlement process where resolution can be reached through bilateral consultations or expert panel rulings.⁷⁵ Failure to comply with the rulings may result in the imposition of sanctions by the WTO's dispute settlement body. The WTO regulates trades in services through its *General Agreement on Trade in Services (GATS)*.⁷⁶ This agreement obliges member countries to comply with general terms relating to the trade in services and specific commitments registered by certain member countries. *GATS* is a relevant instrument to advance trade agreements between countries hosting pharmaceutical companies and those providing clinical trial services to enhance the treatment of human subjects and shape the terms of this trade.

Unfortunately, there are three shortcomings preventing the WTO, in its current rendition, from acting as the implementing institution in regulating the trade in services provided by human subjects. First, the WTO is inherently about trade liberalization, not regulation. Second, *GATS* does not set ethical standards — so long as member countries abide by their trade agreements, the WTO does not concern itself with ethical or humanitarian issues. Even if the WTO engaged in regulatory work, its rulings are only enforceable on member states, not private corporations. Private transnational corporations can easily set up subsidiaries in countries with lower ethical standards and find a way to escape liability imposed by trade agreements.

For the WTO to implement an international legal instrument regulating the relationship between private pharmaceutical companies vis-à-vis developing countries and their nationals, fundamental changes are required. The WTO would have to evolve a corporate mandate enabling it to legitimately regulate private enterprise. It would also require a more multidimensional mandate, advancing its current core of trade liberalization in the context of other interests, like human rights. Such changes have been considered but not yet realized. In fact, the WTO has been discussed as a potential regulatory agency for the United Nations International Covenant on Economic, Social and Cultural

⁷⁴ "What is the WTO?" online: WTO <http://www.wto.org/english/thewto_e/whatis_e/whatis_e.htm>.

⁷⁵ "Understanding the WTO: Settling disputes – A unique contribution," online: WTO <http://www.wto.org/english/thewto_e/whatis_e/tif_e/displ_e.htm>.

⁷⁶ "General Agreement on Trade in Services," online: WTO <http://www.wto.org/english/docs_e/legal_e/ursum_e.htm#mAgreement>.

Rights.⁷⁷ Practically, however, the WTO may be reluctant to accept a more social mandate for fear that it might undermine its trade liberalization work. The WTO is an organization for trade liberalization. It provides a forum for countries to negotiate trade agreements and open their domestic markets to non-domestic consumers. It does not concern itself with trade regulation so long as the trading parties agree with the terms of their contracts. The WTO, therefore, is not the well-positioned institution required to implement such a legal instrument.

The Global Compact, however, may be the institution best suited to implement such a mandate. The Global Compact is a United Nations initiative intended to “safeguard open markets while at the same time creating a human face for the global economy.”⁷⁸ It promotes responsible corporate citizenship by challenging individual corporations to abide by nine key principles relating to human rights, labour, environment, and anti-corruption. On human rights, the Global Compact promotes two principles. First, “businesses should support and respect the protection of internationally proclaimed human rights,”⁷⁹ and second, corporations should “make sure that they are not complicit in human rights abuses.”⁸⁰

The Global Compact is a purely voluntary network of different United Nations agencies. The Global Compact is not a regulatory instrument and does not have enforcement powers, yet. It relies on “public accountability, transparency and the enlightened self-interest”⁸¹ of corporations in pursuing the principles of the Global Compact. During its launch, Secretary-General Kofi Annan stated:

Let us choose to unite the power of markets with the authority of universal ideals. Let us choose to reconcile the creative forces of private entrepreneurship with the

⁷⁷ George J. Andreopoulos, “Declarations and Covenants of Human Rights and International Codes of Research Ethics,” in Levine RJ, Gorovitz S, Gallagher J. eds., *Biomedical research ethics: updating international guidelines* (Geneva: Council for International Organizations of Medical Sciences, 2000) at 181-203.

⁷⁸ “The Global Compact: The UN’s New Deal with ‘Global Corporate Citizens’” *Corporate Europe Observer* (5 October 1999), online: Corporate Europe Observer <<http://www.corporateeurope.org/observer5/global.html>>.

⁷⁹ “About the Global Compact: The Ten Principles,” online: The Global Compact <<http://www.globalcompact.org/AboutTheGC/TheTenPrinciples/index.html>>.

⁸⁰ *Ibid.*

⁸¹ “About the Global Compact: What is the Global Compact?” online: The Global Compact <<http://www.globalcompact.org/AboutTheGC/index.html>>.

needs of the disadvantaged and the requirements of future generations.⁸²

The Global Compact promotes responsible corporate citizenship so that businesses include human rights considerations in their bottom line instead of mere monetary profits.

Unlike the WTO, the Global Compact directly applies to corporations rather than states. Moreover, it provides incentive for corporations to join voluntarily. Instead of corporations being viewed as exploiting human capital, the Global Compact places private enterprise in the United Nations system and begins to restore popular trust in business, services, and products. In fact, a number of pharmaceutical companies have already joined the Global Compact and participated in humanitarian projects.⁸³

The Global Compact is also a better choice than the WTO because it does not require fundamental changes to its structure and objective. Two modifications, however, could be made to the Global Compact to enhance its regulatory mandate in the pharmaceutical sector. First, the WHO must be added to the network of United Nations agencies. The WHO guidelines, with the adjustments discussed above, are an ideal starting point for an international legal instrument governing the pharmaceutical sector. Moreover, the WHO's pharmaceutical trial registry system is well-positioned to enhance the Global Compact's transparency goal.⁸⁴ Second, the Global Compact could take on a more regulatory profile, including mandatory membership for all pharmaceutical companies involved in the international trade in services provided by human subjects. It could also develop more regulatory levers, including a clearly defined UN mandate allowing for greater enforcement.

⁸² "Advancing Corporate Citizenship in the World Economy" Powerpoint Presentation, online: The Global Compact <http://www.globalcompact.org/docs/about_the_gc/gc_overview.pdf>.

⁸³ "Participants and Stakeholders," online: The Global Compact <http://www.globalcompact.org/ParticipantsAndStakeholders/search_participant.html?submit_x=page>; also "Global Compact – the United Nations' Corporate Initiative for a Sustainable World," online: Bayer <<http://www.bayer.com/about-bayer/social-responsibility/global-compact/page1188.htm>>.

⁸⁴ The WHO International Clinical Trials Registry Platform records and publishes the results of all clinical trials with human subjects without bias or selectivity in reporting. This would increase transparency and accountability on the part of companies and institutions that do clinical research.

VII. CONCLUSION

IN THIS PAPER, I HAVE IDENTIFIED MAJOR ETHICAL, medical, legal, and trade problems associated with the international trade in services provided by human subjects. I have reviewed the evolution of this subject, including specific cases where biomedical testing has egregiously violated human rights. Furthermore, I have considered the current international legal system and discussed relevant ethical codes concerning biomedical testing, none of which have proven adequate to protect human subjects from the harm perpetrated by pharmaceutical companies in the developing world. Therefore, it is clear that there is a need for a new, effective system to regulate the trade in services provided by human subjects. As such, I have proposed that such a system be comprised of two components: a well-crafted legal instrument built upon the Helsinki Declaration, the World Health Organization, the Guidelines for Good Clinical Practice for Trials on Pharmaceutical Products (1995), and the CIOMS International Ethical Guidelines for Biomedical Research Involving Human Subjects 1982. Moreover, the system would also require an enhanced and coordinated partnership between the UN Global Compact and the World Health Organization. Both of these organizations can jointly advance socially responsible trade and adopt a regulatory role over pharmaceutical companies that acquire services of human subjects outside their national borders. This ideal institution also requires a relatively enforceable mandate, including regulatory levers and an enforcement mechanism. Ultimately, such a system would ensure that trade in the pharmaceutical sector advances both the interests of pharmaceutical companies and those of developing countries and their nationals.