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# Beyond Nuremberg: A Critique of Informed Consent in Third World Human Subject Research

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# BEYOND NUREMBERG: A CRITIQUE OF "INFORMED CONSENT" IN THIRD WORLD HUMAN SUBJECT RESEARCH

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*The hidden Yes in you is stronger than all Nos and Maybes that afflict you and your age like a disease. – Friedrich Nietzsche*[1]

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[1] FRIEDRICH NIETZSCHE, THE GAY SCIENCE 340 (Walter Kaufman trans., Vintage Books 1974).

## I. INTRODUCTION: FROM NUREMBERG TO KANO

### *A. The Birth of Informed Consent*

The principle of "informed consent" forms one of the "basic ethical protections for research involving human participants."[2] Informed consent requires that a human subject of scientific research "willingly verif[y] his/her willingness to participate in a particular treatment, after having been informed of all aspects which are pertinent to that treatment and relevant to the subject's participation."[3] Governments around the world have adopted a variety of regulations[4] that articulate and enforce this "oldest and most universally accepted ethical standard in research."[5] In the United States, the Federal Food, Drug, and Cosmetic Act (FD&C) mandates that scientists who test new drugs first inform human subjects about the experimental nature of the studies and obtain their consent.[6] The U.S. Food and Drug Administration (FDA), the federal agency charged with administering and enforcing the FD&C,[7] has promulgated a series of regulations to implement this requirement.[8]

The informed consent requirement originated in the Nuremberg Trials following World War II.[9] Under the Third Reich in Germany, Nazi scientists conducted a variety of involuntary and often fatal medical experiments on concentration camp inmates,[10] mainly Jews, Roma, and Slavs.[11] After the war ended, the United States

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[2] Maxwell J. Mehlman & Jessica W. Berg, *Human Subjects Protections in Biomedical Enhancement Research*, 36 J. L. MED & ETHICS 546, 552 (2008).

[3] Jennifer J. Couture, *The Changes in Informed Consent in Experimental Procedures: The Evolution of a Concept*, 1 J. HEALTH & BIOMEDICAL L. 125, 126 n.6 (2005).

[4] *See id.* at 133-60.

[5] SONIA SHAH, THE BODY HUNTERS: TESTING NEW DRUGS ON THE WORLD'S POOREST PATIENTS 147 (2006).

[6] *See* 21 U.S.C. § 355(i)(4) (2008).

[7] *See* PETER BARTON HUTT ET AL., FOOD AND DRUG LAW 4 (3d ed. 2007).

[8] *See* 21 C.F.R. §§ 50.20-50.27, 312.120(a) (2010).

[9] *See* Abdullahi v. Pfizer, Inc., 562 F.3d 163, 177 (9th Cir. 2009); *see also* Couture, *supra* note 3, at 128-129.

[10] *See* SHAH, *supra* note 5, at 69. A brief description can only begin to convey the horror of these studies:

> Eager to understand how the human body functioned at high altitudes, [Nazi scientists] encased subjects in decompression chambers, pumped all the air out, and then dissected the subjects while still alive to study their lungs. To see firsthand the effects of dehydration they starved subjects and forced them to drink only saltwater. They injected children with gasoline. They removed their subjects' bones and limbs . . . Inmates were injected with phenol to see how long it would take them to die.

*Id.*

[11] George J. Annas, *The Changing Landscape of Human Experimentation: Nuremberg, Helsinki, and Beyond*, 2 HEALTH MATRIX 119, 121 (1992). By performing these "medical atrocities," Nazi doctors sought to aid the German war effort, eliminate what they regarded as inferior races, and gain "scientific insight." Couture, *supra* note 3, at 127-28.

prosecuted twenty Nazi scientists[12] before the International Military Tribunal in Nuremberg, Germany for war crimes and crimes against humanity.[13] Ultimately, seven of the Nazi scientists were sentenced to death and eight to varying prison terms.[14] As part of its final judgment, the Tribunal promulgated a set of ten principles, later known as the "Nuremberg Code," that provided the first international rules for scientific research on human subjects.[15] The Nuremberg Code's first and most important principle[16] directed:

> The voluntary consent of the human subject is absolutely essential. This means that the person involved should have legal capacity to give consent; should be so situated as to be able to exercise free power of choice . . . and should have sufficient knowledge and comprehension of the elements of the subject matter involved as to enable him to make an understanding and enlightened decision.[17]

Later international guidelines, such as the World Medical Association's 1964 "Declaration of Helsinki,"[18] provided further direction for medical researchers. Nevertheless, the Nuremberg Code "remains the most authoritative legal and ethical document governing international research standards."[19] Supreme Court Justice William Brennan once remarked, "[t]he medical trials at Nuremberg in 1947 deeply impressed upon the world that experimentation with unknowing human subjects is morally and legally unacceptable."[20]

### *B. Global Challenges to Informed Consent*

The globalization of the pharmaceutical industry, especially the clinical testing process for new drugs,[21] has undermined enforcement of the informed consent requirement. When the FDA first began to regulate clinical studies in the 1960s, it hesitated to approve new drugs based on research conducted abroad, which caused pharmaceutical companies to rarely sponsor overseas trials.[22] But as the FDA

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[12] SHAH, *supra* note 5, at 69.

[13] *See Abdullahi*, 562 F.3d at 177-78.

[14] *See Abdullahi*, 562 F.3d at 178.

[15] *See* Couture, *supra* note 3, at 129.

[16] *See id.*; SHAH, *supra* note 5, at 71.

[17] *The Nuremberg Code*, THE NAZI DOCTORS AND THE NUREMBERG CODE: HUMAN RIGHTS IN HUMAN EXPERIMENTATION 3 (George J. Annas & Michael A. Grodin eds., 1992).

[18] *Declaration of Helsinki Recommendations Guiding Doctors in Clinical Research*, THE NAZI DOCTORS AND THE NUREMBERG CODE: HUMAN RIGHTS IN HUMAN EXPERIMENTATION 331-42 (George J. Annas & Michael A. Grodin eds., 1992).

[19] Annas, *supra* note 11, at 121.

[20] United States v. Stanley, 483 U.S. 669, 687 (1987) (Brennan, J., concurring in part and dissenting in part).

[21] *See* Ileana Dominguez-Urban, *Harmonization in the Regulation of Pharmaceutical Research and Human Rights: The Need to Think Globally*, 30 CORNELL INT'L L.J. 245, 245 (1997).

[22] PETER BARTON HUTT ET AL., FOOD AND DRUG LAW 650 (3d ed. 2007).

gradually liberalized this policy, especially in its 1994 decision to allow new drug applications based entirely on foreign research data,[23] the industry responded by moving its experiments offshore. The number of foreign investigators seeking FDA approval for new drugs increased sixteen-fold over the 1990s, while U.S.-based researchers declined.[24] In 1999, over a quarter of new drugs approved by the FDA were first tested abroad,[25] and by 2008 that figure had jumped to more than three quarters of new drugs.[26]

Pharmaceutical companies based in First World countries have sought to conduct their research in the Third World,[27] drawn by lower costs and a more permissive regulatory environment.[28] The most popular new locations for foreign studies are developing regions such as the former Soviet Union, Latin America, India, China, South East Asia, and Africa.[29] Between 1995 and 2005, U.S. pharmaceutical companies conducted nearly one-third of their clinical studies in poor and low-income countries, and by 2005, approximately 40% of all international clinical trials occurred in these developing regions.[30] One journalist explained, "rich countries

[23] *See* 21 C.F.R. § 314.106(b)(1) (1994).

[24] SHAH, *supra* note 5, at 7.

[25] Mary Pat Flaherty et al., *Testing Tidal Wave Hits Overseas*, WASH. POST (Dec. 18, 2000), http://www.washingtonpost.com/wp-dyn/content/article/2008/10/01/AR2008100101117.html; *see also* Yevgenia Shtilman, *Pharmaceutical Drug Testing in the Former Soviet Union*, 29 B.C. THIRD WORLD L.J. 425, 434 (2009).

[26] Gardiner Harris, *Concern Over Foreign Trials for Drugs Sold in U.S.*, N.Y. TIMES (June 21, 2010), http://www.nytimes.com/2010/06/22/health/research/22trial.html.

[27] This Article uses the terms "Third World," "developing world," and variations thereof, interchangeably. They refer to poor and low-income regions, such as Africa, India, Southeast Asia, as well as parts of China, Latin America, and the former Soviet Union, where an increasing amount of human subject research takes place.

[28] *See* Mary Pat Flaherty et al., *Testing Tidal Wave Hits Overseas*, WASH. POST (Dec. 18, 2000), http://www.washingtonpost.com/wp-dyn/content/article/2008/10/01/AR2008100101117.html; *see also* William Dubois, *New Drug Research, The Extraterritorial Application of FDA Regulations, and the Need for International Cooperation*, 36 VAND. J. TRANSNAT'L L. 161, 167-68 (2003).

[29] *See* SHAH, *supra* note 5, at 7; Shtilman, *supra* note 25, at 434; Office of Inspector General, Dep't of Health and Human Servs., *The Globalization of Clinical Trials: A Growing Challenge in Protecting Human Subjects* 8-11 (Sept. 2001), *available at* http://oig.hhs.gov/oei/reports/oei-01-00-00190.pdf. For instance, a survey of the clinical trials reported in leading medical journals in 1995 and 2005 found that the number of studies conducted in Africa, Eastern Europe, Russia, and the Middle East had approximately doubled, while trials in the United States decreased by more than 10% and in Western Europe by nearly 5%. *See* Seth W. Glickman et al., *Ethical and Scientific Implications of the Globalization of Clinical Research*, 8 NEW ENG. J. MED. 816, 818 (2009).

[30] *See* Volnei Garrafa et al., *Between the Needy and the Greedy: The Quest for a Just and Fair Ethics of Clinical Research*, 36 J. MED. ETHICS 500, 500-01 (2010).

have the drugs and hypotheses, while poor countries have vast numbers of patients."[31]

Yet the "outsourcing" of medical research to the Third World has made it more difficult to regulate the ethics of human subject research. There are no binding international treaties that regulate human experimentation,[32] and the international ethical guidelines, such as the Nuremberg Code, lack any sanctions or enforcement mechanisms.[33] Government regulators in the Third World are "generally ill-equipped to oversee, much less manage, the clinical trials being held within their borders."[34] Moreover, these poorer countries have "strong incentives to encourage leniency in national and local oversight of the research"[35] to attract drug companies and obtain the financial benefits of clinical studies.[36] The "resulting 'regulatory vacuum' makes it difficult to ensure the welfare of trial participants,"[37] and effectively permits inadvertent, or even intentional, abuse of human subjects.[38] A series of recent headline articles in the Washington Post revealed that, in several instances, pharmaceutical companies had conducted clinical trials in the Third World in which researchers forged consent forms, lied to subjects about the nature of the study, or failed to reveal the potential dangers of the experimental drugs.[39] Unfortunately, cases like these may not constitute isolated aberrations—a 1996 study found that nearly *half* of the clinical trials conducted in Chile that year suffered from "ethical problems," most commonly a failure to obtain the subjects' consent.[40] In addition, international variations in acceptable experimental protocols allow for studies in the

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[31] Mary Pat Flaherty & Doug Struck, *Life by Luck of the Draw*, WASH. POST (Dec. 22, 2000), http://www.washingtonpost.com/wp-dyn/content/article/2008/10/01/AR2008100101188.html.

[32] *See* Dominguez-Urban, *supra* note 21, at 273.

[33] *See id.* at 273-74.

[34] *See* Shtilman, *supra* note 25, at 436.

[35] *See id.* at 435.

[36] *See* Robert Gatter, *Conflicts of Interest in International Human Drug Research and the Insufficiency of International Protections*, 32 AM. J.L. & MED. 351, 353 (2006).

[37] *See* Shtilman, *supra* note 25, at 436.

[38] *See* Dominguez-Urban, *supra* note 21, at 270- 71.

[39] *See* Karen De Young et al., *Latin America Is Ripe for Trials, and Fraud*, WASH. POST. (Dec. 21, 2000), http://www.washingtonpost.com/ac2/wp-dyn/A31027-2000Dec20 (explaining that researchers forged consent forms to test the drug cariporide on subjects without their consent, leading to the deaths of several participants); John Pomfret & Deborah Nelson, *An Isolated Region's Genetic Mother Lode*, WASH. POST. (Dec. 20, 2000), http://www.washingtonpost.com/wp-dyn/content/article/2008/10/01/AR2008100101158.html (indicating that researchers falsely promised free healthcare to impoverished Chinese villagers to draw their blood for genetic study, without explaining the purpose of the experiment); Sharon LaFraniere et al., *The Dilemma: Submit or Suffer*, WASH. POST. (Dec. 19, 2000), http://www.washingtonpost.com/wp-dyn/content/article/2008/10/01/AR20081001011 50.html (reporting that researchers failed to inform study participants of the FDA's concerns about the drug Zeldox's effect on heart rhythms and its refusal to approve the drug pending more safety tests).

[40] *See* LaFraniere et al., *supra* note 39.

Third World that would not satisfy First World regulatory scrutiny.[41] Even in the absence of clear ethical violations, language barriers and cultural differences between First World scientists and Third World human subjects make it difficult for investigators to ensure that their patients legitimately consented to participating in research.[42]

One high profile case of allegedly unethical pharmaceutical research occurred in Kano, Nigeria in 1996, when the American drug company Pfizer, Inc. sponsored a study of the experimental drug Trovan on hundreds of children during a meningitis outbreak in Northern Nigeria.[43] After eleven children died and many more were injured,[44] a group of Nigerian children and their guardians sued Pfizer in an American court, claiming that the company had tested the drug on them without disclosing the experimental nature or dangers of the research.[45] The lawsuit ultimately led to the Second Circuit case of *Abdullahi v. Pfizer, Inc.*,[46] in which the court declared that the prohibition on nonconsensual medical research constituted a universally accepted norm of international law,[47] and held that violation of this norm—even when it occurred abroad—was sufficiently heinous to support the universal jurisdiction of an American court.[48] The Second Circuit concluded "the norm prohibiting nonconsensual medical experimentation on human subjects has become firmly embedded and has secured *universal acceptance* in the community of nations."[49] The *Abdullahi* decision offered a source of both hope and despair—half a century after the Nuremberg Trial first announced the principle of informed consent, and the requirement became a widely accepted tenant of international law, violations continued to occur in the Third World.

### *C. Proposal for a Critique of Informed Consent in Third World Research*

Concerns about the welfare of human subjects in developing countries have led activists, academics, and government officials in the United States to call for reinforcement of the informed consent requirement in Third World pharmaceutical research.[50] This paper offers a critical analysis of that approach. Although the

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[41] *See* Dubois, *supra* note 28, at 168. For instance, an American pharmaceutical company sponsored a study in Hungary of an anti-psychotic drug on mental patients confined to locked wards—an accepted local practice that United States regulators would not tolerate due to the possibility of coercing consent. *See* LaFraniere et al., *supra* note 39.

[42] *See id.*

[43] *See* Dubois, *supra* note 28, at 163-64.

[44] Abdullahi v. Pfizer, Inc., 562 F.3d 163, 169 (9th Cir. 2009).

[45] *See id.*

[46] *Id*.

[47] *See id.* at 183-84.

[48] *See id.* at 177, 187.

[49] *Id.* at 183-84 (emphasis added).

[50] *See, e.g.*, Food and Drug Administration, *NIH Sees More Ethical Problems with Foreign IRBs; Steps Up Training*, FDA WEEK (Mar. 17, 2006) (indicating that activist group Public Citizen condemns government decision to view foreign ethical standards as equivalent to U.S. requirements); Ruqaiijah Yearby, *Good Enough to Use for Research, But Not Good*

assurance of experimental subjects' voluntary participation in Third World clinical studies is certainly a laudable goal, a rights-based notion of autonomous consent ignores *the actual context in which that consent takes place*—a terrain defined by the absence of essential medical treatment, desperation for healthcare, and important cultural differences. These circumstances belie the notion of an inalienable and universal right to freely assent to medical experimentation. As an alternative, this paper proposes that advocates concerned about the interests of human subjects in developing countries address the *distributive consequences* of globalized pharmaceutical testing. This approach seeks to ensure that Third World citizens enjoy the benefits of the clinical trials conducted in their communities.

This Article discusses the history of informed consent, critical analyzes this principle, and suggests an alternative approach to informed consent. Part II explores the concept of informed consent, including its philosophical bases, its implementation through FDA regulations, and current proposals on how to protect the principle in drug testing conducted abroad. Part III performs a critical analysis of the principle of informed consent; first providing an empirical examination of the realities of Third World human subject research, and then questioning both the coherence of an abstract "right" to informed consent, as well as the possibility of truly autonomous "consent" to such research. In Part IV, this Article suggests an alternative approach based on the principle of distributive justice, in which pharmaceutical companies ensure that the communities that bear the risks of clinical studies also enjoy the medical benefits of such research. Finally, Part V provides a brief conclusion and reflects on the implications of this critique.

## II. THE PRINCIPLE OF INFORMED CONSENT: THEORY, POLICY, AND ADVOCACY

This section provides background on the principle of informed consent. Part A explores the theoretical bases of the informed consent requirement to reveal the philosophical assumptions on which it relies. Part B demonstrates that, in addition to the lack of international or local regulation of Third World clinical studies, the FDA applies a lower informed consent standard for foreign research. Finally, Part C recounts the proposals advocated by legal and medical scholars who seek to protect human subjects in the Third World by reinforcing the informed consent requirement.

### *A. The Theoretical Bases of Informed Consent*

The principle of informed consent in human subject research is not a self-evident axiom of medical ethics, but instead relies on several philosophical assumptions. Grounded in "notions of liberal individualism, as expressed by eighteenth and nineteenth century Western philosophers," the informed consent requirement draws predominantly on the moral principle of "personal autonomy."[51] Personal autonomy ideals hold that one's "personal self-governance" should be "free from control or

*Enough to Benefit from the Results of that Research*, 53 DEPAUL L. REV. 1127, 1150 (2004) (calling for the creation of a compulsory international standard of ethical protections for human subject research, to be drafted, implemented, and enforced through an international body); Office of Inspector General, *supra* note 29, at iii (recommending that the FDA encourage more rigorous monitoring of foreign research sites by sponsors to ensure human subject protections).

[51] Elysa Gordon, *Multiculturalism in Medical Decisionmaking: The Notion of Informed Waiver*, 23 FORDHAM URB. L.J. 1321, 1326-27 (1996).

interference by others."[52] This principle thus relies on two more fundamental assumptions: that all human beings have an individual right to self-governance and that all human beings have the ability to freely choose their own destinies.[53] The informed consent requirement similarly depends on these two theoretical bases.

The informed consent requirement draws on the notion of inalienable and universal individual rights. First, it functions in the same way that legal philosopher Ronald Dworkin defined a "political right"—as a kind of "trump" over any otherwise "decisive," collective, or utilitarian justification.[54] It protects the individual's privilege to consent to participation in a clinical study and ensures that it is predominant over any competing government, scientific, or societal interest in the medical research.[55] Thus, the Nuremberg Code mandates the principle of informed consent to "protect[] individual subjects first by protecting their rights."[56] Indeed, the Nuremberg Code refers to the voluntary participation of human subjects in scientific research as "absolutely essential."[57] Senator Jacob Javitz of New York, who sponsored the amendment that first mandated the informed consent requirement for research submitted to the FDA, similarly emphasized the importance of limiting the acceptable procedures of medical study to protect the individual right to informed consent:

> I am for experimentation. I feel deeply that some risks must be assumed in experimentation. But we must hold the balance between personal dignity and personal responsibility and the right of the individual to know how his life is being disposed of, at least with his consent, and the virtues of experimentation.[58]

Second, the informed consent principle operates in the same way that Dworkin defined a universal right: an argument that may be asserted "against any collective justification in any circumstances reasonably likely to be found in political society."[59] Indeed, the Nuremberg judges based their declaration on "a natural law theory, deriv[ed] from universal moral, ethical, and legal concepts."[60] Moreover, the International Covenant on Civil and Political Rights specifically articulates the informed consent requirement as one of the "inalienable rights of all members of the

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[52] *Id.* at 1325.

[53] *See id.* ("Autonomy acknowledges that all human beings have a capacity for moral dignity and that those who possess moral dignity are determiners of their own destinies.").

[54] RONALD DWORKIN, TAKING RIGHTS SERIOUSLY 364-65 (1978).

[55] *See* Gordon, *supra* note 51, at 1344.

[56] Annas, *supra* note 11, at 121.

[57] *The Nuremberg Code*, *supra* note 17.

[58] 108 CONG. REC. 17,397 (1962) (statement of Sen. Javits), *reprinted in* 22 A LEGISLATIVE HISTORY OF THE FEDERAL FOOD, DRUG & COSMETIC ACT AND ITS AMENDMENTS 325 (1979).

[59] DWORKIN, *supra* note 54, at 365.

[60] Annas, *supra* note 11, at 121.

human family . . . derive[d] from the inherent dignity of the human person."[61] The covenant also declares: "no one shall be subjected without his free consent to medical or scientific experimentation."[62] The Second Circuit's holding in *Abdullahi*, that Pfizer's sponsorship of nonconsensual medical research in Nigeria constituted a violation of human rights sufficient to invoke the jurisdiction of an American court,[63] further reflects this universal conception of the principle of informed consent. Informed consent draws on a theory of inalienable and universal individual rights that transcend both collective interests and cultural contexts.

The principle of informed consent also assumes an individual's ability to exercise freedom of choice. Absent a belief in a person's ability to freely decide to volunteer for medical research, informed consent would amount to a meaningless protection. Thus, the informed consent requirement "reflect[s] a belief that an individual has a right to be free from nonconsensual interference with his or her person, and a basic moral principle that it is wrong to force another to act against his or her will."[64] For instance, the Nuremberg Code emphasizes that a human subject must be "so situated as to be able to exercise free power of choice" and that he or she must be provided sufficient information about the study so "as to enable him to make an understanding and enlightened decision."[65] Similarly, Senator Javits invoked the importance of personal decision-making in human subject research:

> If . . . we cannot tell a mature adult who is going to be used for experimentation with a drug which has not yet been reasonably demonstrated to be safe and who is well able to come to the decision that he wants it himself . . . where is the dignity, the responsibility, and the freedom of the individual?[66]

In addition, the FDA has promulgated more stringent requirements for clinical studies that involve children who may be too young to legitimately choose to consent.[67] Finally, courts have held that a physician is not liable for violating the informed consent requirement if she fails to provide subjects with information that would not have affected their decision to participate.[68] In other words, informed consent calibrates the mandatory disclosure of information on the basis of its relevance to the subject's *choice* to join an experimental study. The notion that individuals are capable of making the autonomous decision to participate in scientific research, and that protection of this autonomy ensures an important freedom, provides the second philosophical basis for the informed consent

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[61] International Covenant on Civil and Political Rights, Preamble, 999 U.N.T.S. 171 (Mar. 23, 1976).

[62] *Id*. at art. 7.

[63] *See* Abdullahi, 562 F.3d at 177, 187.

[64] BARRY R. FURROW ET AL., HEALTH LAW 75 (6th ed. 2008).

[65] *The Nuremberg Code*, *supra* note 17.

[66] Statement of Sen. Javits, *supra* note 58, at 325.

[67] *See* 21 C.F.R. § 50.55 (2010).

[68] *See, e.g.*, Plumber v. Dep't of Health & Human Res., 634 So. 2d 1347, 1351 (La. Ct. App. 1994).

requirement.[69] The principle of informed consent seeks to protect the ideal of "personal autonomy" celebrated by Western liberal philosophy. It ultimately rests on the theoretical foundations of individual rights and freedom of choice.

### *B. The FDA's Informed Consent Policies for Foreign Research*

As previously discussed, there are no binding international treaties governing human subject research, and Third World governments are often either unable or unwilling to effectively police the studies that occur within their borders. Instead, First World countries that house the pharmaceutical companies and consume the tested drugs provide the principal source of consistent regulatory authority for Third World medical research.[70] The United States, home to the largest pharmaceutical market in the world,[71] offers an important example. A pharmaceutical manufacturer that wishes to sell a drug in the United States must first submit a new drug application (NDA) to the FDA.[72] According to the FD&C, the applicant must submit "substantial evidence" that the drug is safe and effective based on "adequate and well-controlled investigations, including clinical investigations."[73] The FDA requires that all medical research performed to market a drug in the United States satisfy the principle of informed consent.[74] Its regulations, however, prescribe differing standards and enforcement of this requirement depending on whether the clinical studies are conducted domestically or abroad.

To regulate clinical studies that are conducted within the United States, the FDA has promulgated an extensive set of guidelines known as the "investigational new drug process" (IND).[75] These regulations dictate, *inter alia*, the organization of the phases of clinical study, the experimental protocols used in the individual trials, the responsibilities of both the investigators and the sponsors involved in the research, and the format of the submitted data.[76] An "institutional review board" (IRB) must oversee and approve the research for compliance with FDA regulations.[77] The IND process specifically requires that investigators obtain the informed consent of every human subject who participates in their study,[78] and even prescribes the form and conditions in which investigators may obtain that consent. First, investigators may only seek an individual's consent "under circumstances that provide the prospective subject . . . sufficient opportunity to consider whether or not to participate and that

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[69] RUTH R. FADEN ET AL., A HISTORY AND THEORY OF INFORMED CONSENT 7-8 (1986).

[70] *See* Dominguez-Urban, *supra* note 21, at 270.

[71] *See id.* at 245.

[72] *See* 21 U.S.C. § 355(a) (2008).

[73] 21 U.S.C. § 355(d) (2008).

[74] *See* 21 C.F.R. §§ 312.60, 312.120(a)(1) (2010).

[75] *See* 21 C.F.R. § 312 (2010); HUTT, *supra* note 7, at 624.

[76] *See* 21 C.F.R. §§ 312.20-70 (2010). The FDA's power to mandate these guidelines comes from its ability to exempt researchers from the usual prohibition on the shipment of unapproved drugs to conduct clinical studies. *See* 21 U.S.C. § 355(i) (2008).

[77] 21 C.F.R. § 312.66 (2010).

[78] *See* 21 C.F.R. § 312.60 (2010).

minimize the possibility of coercion or undue influence."[79] Next, to inform the participants about the nature of the research, the investigators must give each potential subject, "in language understandable to [them],"[80] eight basic elements of information regarding the study[81] along with six additional elements when appropriate.[82] Finally, the investigators must document each subject's written consent in a signed form and provide each subject with a copy of his or her form.[83] Children receive additional informed consent protections.[84] The sponsors of clinical trials are responsible for monitoring the research and ensuring compliance with the IND regulations, including the informed consent requirements.[85] The FD&C defines violation of these informed consent standards as a "[p]rohibited act,"[86] against which the FDA may bring injunction proceedings[87] or criminal prosecutions.[88]

Clinical studies conducted outside of the United States may advance through one of two pathways for FDA acceptance. First, they may proceed through the IND process, which "bring[s] the investigator, regardless of the location of the research, under the federal regulations governing the conduct of research in the United States."[89] Second, investigators and sponsors may choose to conduct their foreign research independently.[90] In this alternative pathway, the FDA does not directly regulate the research, but requires as a condition for acceptance that the study be "conducted in accordance with good clinical practice," including "obtaining and documenting the freely given informed consent of the subject."[91] The phrase "good clinical practice" (GCP) comes from the human experimentation guidelines

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[79] 21 C.F.R. § 50.20 (2010).

[80] *Id.*

[81] 21 C.F.R. § 50.25(a) (2010). The eight basic elements are: (1) a statement that the study involves research, an explanation of its purposes, and a description of the procedures to be followed; (2) any reasonably foreseeable risks to the subject; (3) any reasonably foreseeable benefits to the subject; (4) appropriate alternative procedures that might be advantageous to the subject; (5) a description of the extent of the confidentiality of records identifying the subject; (6) an explanation of any compensation or medical treatments available if injury occurs; (7) an explanation of whom to contact for answers to questions about the research and research subjects' rights; and (8) a statement that participation is voluntary, that refusal to participate will involve no penalty, and that the subject may discontinue participation at any time without penalty. *See* 21 C.F.R. §§ 50.25(a)(1)-(8) (2010).

[82] *See* 21 C.F.R. § 50.25(b) (2010).

[83] 21 C.F.R. § 50.27(a) (2010).

[84] *See* 21 C.F.R. § 50.55 (2010).

[85] *See* 21 C.F.R. § 312.56 (2010).

[86] 21 U.S.C. § 331(e) (2008).

[87] 21 U.S.C. § 332 (2008).

[88] *See* 21 U.S.C. § 333 (2008).

[89] Erin Talati, *An Open Door to Ending Exploitation: Accountability for Violations of Informed Consent Under the Alien Tort Statute*, 155 U. PA. L. REV. 231, 240 (2006).

[90] *See* 21 C.F.R. § 312.120(a) (2010).

[91] 21 C.F.R. § 312.120(a)(1)(i) (2010).

promulgated by the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use in 1995, at which the United States, the European Union, and Japan attempted to harmonize their pharmaceutical development regulations.[92] The FDA further requires that an "independent ethics committee," similar to an IRB,[93] oversee and approve foreign research conducted outside of an IND.[94] Although the FDA will not accept a foreign study that fails to either fulfill the GCP requirements or document its subjects' informed consent, it will still "examine data from such a study."[95]

The FDA imposes a higher standard of informed consent, and provides greater enforcement of that requirement, for clinical trials performed domestically than for research conducted outside of the United States. First, the IND informed consent standards are more rigorous than the GCP requirements.[96] The IND provisions dictate the circumstances under which investigators may seek subjects' consent, the language they should use, and the elements of information they must provide.[97] Yet the GCP standard merely mandates that investigators inform subjects "of all aspects of the trial that are relevant to [their] decision to participate" and document their consent "by means of a written informed consent form."[98] These "extremely vague" requirements provide subjects with "significantly less assurance that actual informed consent will be obtained."[99]

Second, the FDA subjects research performed under an IND to more stringent enforcement of the informed consent requirements than foreign research conducted outside an IND. The FDA has the authority to directly enforce the IND informed consent standards through injunctions and criminal prosecutions.[100] It has previously sent warning letters threatening to bring such proceedings when investigators and

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[92] *See* International Conference on Harmonization: Draft Guidelines on Good Clinical Practice, 60 Fed. Reg. 42,948 (Aug. 17, 1995); Michelle D. Miller, *The Informed-Consent Policy of the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use*, 30 CORNELL INT'L L.J. 203, 233-34 (1997).

[93] *See* Human Subject Protection, Foreign Clinical Studies Not Conducted Under an Investigational New Drug Application, 73 Fed. Reg. 22,805 (Apr. 28, 2008) (to be codified at 21 C.F.R. pt. 312).

[94] 21 C.F.R. § 312.120(1)(a)(i) (2010).

[95] 21 C.F.R. § 312.120(a)(2)(2010).

[96] Although the IND regulations define their scope as including all clinical research conducted in support of an NDA, *see* 21 C.F.R. § 50.1(a) (2010), both the language of the IND informed consent provisions, *see* Shtilman, *supra* note 25, at 432 n.32., and the articulation of a separate GCP requirement for foreign trials conducted outside of an IND, *see* 21 C.F.R. § 312.120(a)(1)(i) (2010), suggest that the FDA intends separate informed consent standards depending on whether studies proceed within or outside of the IND process.

[97] *See* 21 C.F.R. § 50.25 (2010).

[98] *See* International Conference on Harmonization: Draft Guidelines on Good Clinical Practice, 60 Fed. Reg. 42,948 (Aug. 17,1995).

[99] Miller, *supra* note 92, at 235-36.

[100] *See* 21 U.S.C. §§ 331(e)-333 (2008).

sponsors under an IND failed to satisfy its informed consent requirements.[101] In contrast, the GCP informed consent standards for foreign trials conducted outside of an IND are only *a condition of acceptance* for the research[102]—investigators and sponsors suffer no penalties for violations other than rejection of the flawed study. Indeed, although it will not officially accept the study, the FDA "will examine data" from foreign research conducted outside of an IND that violates the GCP informed consent requirements.[103] Although the FDA requires adherence to the informed consent principle for all research submitted in support of an NDA, the fact that foreign researchers may choose whether to submit to the stricter IND rules or proceed according to the less rigorous GCP guidelines means that FDA regulations effectively provide less stringent application of the informed consent standard for medical research conducted outside of the United States.

### *C. The Advocacy for Informed Consent in Third World Research*

In response to the lack of regulation of Third World research and the resulting ethical violations in places like Kano, commentators in both the legal and medical communities have sought to protect human subjects by advocating for the reinforcement of the informed consent principle. Their suggestions comprise a wide variety of approaches, including international collaboration, national legislation, and private action.[104] The proposed reforms, however, can broadly be grouped into three main strategies that all seek to strengthen the informed consent standard in Third World clinical studies: improved standards, increased monitoring of medical research, and more rigorous enforcement of the requirement.[105]

Commentators have advocated several ways to strengthen the substance of the informed consent standard as applied in the developing world. At the most basic level, scholars have called for the FDA to apply a more rigorous informed consent requirement to research abroad and to give human rights groups a voice in the formulation of this standard.[106] Commentators have also proposed that international institutions or state governments articulate clearer and more binding informed consent requirements—for example, through a United Nations Covenant on Human Experimentation[107] or the promulgation of ethics guidelines by the Third World nations that host medical research.[108] Academics from the field of medicine have also suggested that the informed consent standard take account of cultural, social,

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[101] *See, e.g.*, Food and Drug Administration, *Avlon Industries 19-Jan-07*, U.S. FOOD AND DRUG ADMINISTRATION, (Jan. 19, 2007).

[102] *See* 21 C.F.R. § 312.120(a)(1) (2010).

[103] 21 C.F.R. § 312.120(a)(2) (2010).

[104] *See, e.g.*, JANET REHNQUIST, U.S. DEP'T OF HEALTH AND HUMAN SERVS., THE GLOBALIZATION OF CLINICAL TRIALS: A GROWING CHALLENGE IN PROTECTING HUMAN SUBJECTS (2001), *available at* http://oig.hhs.gov/oei/ reports/oei-01-00-00190.pdf.

[105] *Id*.

[106] *See* Miller, *supra* note 92, at 242.

[107] *See* Annas, *supra* note 11, at 136.

[108] *See* Remigius N. Nwabueze, *Ethical Review of Research Involving Human Subjects in Nigeria: Legal and Policy Issues*, 14 IND. INT'L & COMP. L. REV. 87, 111 (2003).

and linguistic differences between the First and Third Worlds by integrating local communities into the determination of the requirement's content.[109] In addition, scholars have proposed reform of the process for obtaining informed consent, advocating the use of alternative media, more thorough documentation, and the involvement of communication experts to ensure that participants fully understand the nature of the research.[110] Finally, legal commentators have proposed a theoretical reconceptualization of the standard, suggesting that property law may provide an alternative basis for the informed consent requirement that would better protect the bodily integrity of research subjects.[111] All these reforms seek to reinforce the principle of informed consent by improving the content of the legal standard that implements it.

Commentators have also argued for increased monitoring of clinical trials in the Third World. For example, the Office of Inspector General for the Department of Health and Human Services recommended that the FDA encourage pharmaceutical companies to perform more rigorous oversight of their foreign research sites' human subject protections.[112] Scholars have also suggested that international health organizations and other non-governmental groups use new communication and media technologies to provide greater surveillance of clinical research in the developing world.[113] Both legal and medical scholars have proposed strengthening the independence and capacity of the ethics committees and review boards in the Third World that provide local supervision for clinical research.[114] At the most extreme, advocates have called for the international centralization of the ethical oversight for medical research through the mandatory registration of clinical trials with the World Health Organization.[115] These proposals all seek to ensure adherence to the informed consent requirement by expanding oversight of drug testing in developing countries.

Finally, scholars have proposed more rigorous enforcement of the informed consent standard in the Third World through a variety of legal mechanisms. One scholar has hypothesized that the FDA might bring criminal prosecutions against

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[109] *See* Ezekiel J. Emanuel et al., *What Makes Clinical Research in Developing Countries Ethical? The Benchmarks of Ethical Research*, 189 J. INFECTIOUS DISEASES 930, 934 (2004).

[110] *See* Zulfiqar A. Bhutta, *Beyond Informed Consent*, 82 BULL. WORLD HEALTH ORG. 771, 775 (2004), *available at* http://www.who.int/bulletin/volumes/82/10/771.pdf.

[111] *See* Jay Dyckman, *The Myth of Informed Consent: An Analysis of the Doctrine of Informed Consent and Its (Mis)Application in HIV Experiments on Pregnant Women in Developing Countries*, 9 COLUM. J. GENDER & L. 91, 112-13 (1999).

[112] *See* Office of Inspector General, *supra* note 29, at iii.

[113] *See* Fazal Khan, *The Human Factor: Globalizing Ethical Standards in Drug Trials Through Market Exclusion*, 57 DEPAUL L. REV. 877, 910 (2008).

[114] *See* Samiran Nundy & Chandra M. Gulhati, *A New Colonialism? – Conducting Clinical Trials in India*, 352 NEW ENG. J. MED. 1633, 1635 (2005); Nwabueze, *supra* note 108, at 113-15.

[115] *See* Molly McGregor, *Uninformed Consent: The United Nations' Failure to Appropriately Police Clinical Trials in Developing Nations*, 31 SUFFOLK TRANSNAT'L L. REV. 103, 117 (2007).

pharmaceutical companies that sponsor unethical research.[116] Alternatively, some proposals would establish an international tribunal for human experimentation that would enforce a code of ethics mandatory for all clinical studies.[117] In a different vein, one commentator has suggested that the First World governments with the most lucrative pharmaceutical markets—the United States, the European Union, and Japan—should use the threat of market exclusion to deter drug companies from sponsoring unethical research.[118] Finally, several scholars have argued that the Alien Tort Statute, which grants U.S. district courts subject matter jurisdiction over torts arising from violations of international law,[119] could open U.S. domestic courts as a forum for private enforcement of the informed consent standard.[120] In general, all these proposals seek to increase enforcement to deter future violations of the informed consent requirement. Commentators concerned about the ethics of medical research in the Third World have advocated for a variety of reforms that would reinforce the principle of informed consent, primarily through development of the substance of the legal standard, improvement in the level of oversight for clinical trials in the developing world, and expansion of the mechanisms available to enforce the requirement.

## III. A CRITIQUE OF INFORMED CONSENT IN THIRD WORLD HUMAN SUBJECT RESEARCH

This section critically analyzes the principle of informed consent in Third World human subject research. Part A provides an empirical examination of the conditions in which Third World medical experiments occur, to demonstrate that the informed consent requirement operates in an environment defined by a lack of effective healthcare and profound cultural diversity. Part B then critiques the notion of an inalienable and universal "right" to informed consent, in light of human subjects' competing interest in accessing lifesaving medications and the uniquely Western values underlying the requirement. Part C critiques the notion that "informed consent" protects the free choice to submit to an experimental study, given that desperation for effective medical treatment drives so many subjects to participate.

### *A. A Contextualization of Third World Research*

The emphasis on reinforcing the principle of informed consent often fails to take account of the actual context in which consent is given. The political, economic, and

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[116] *See* Dubois, *supra* note 28, at 165.

[117] Sarah Bahir, *An International Legal System Regulating the Trade in the Pharmaceutical Sector and Services Provided by Human Subjects*, 6 ASPER REV. INT'L BUS. & TRADE L. 157, 170 (2006); *see also* Annas, *supra* note 11, at 137.

[118] *See* Khan, *supra* note 113, at 909.

[119] *See* 28 U.S.C. § 1350 (2008).

[120] *See, e.g.*, Samantha Evans, *The Globalization of Drug Testing: Enforcing Informed Consent Through the Alien Tort Claims Act*, 19 TEMP. INT'L & COMP. L.J. 477, 504 (2005); Erin Talati, *An Open Door to Ending Exploitation: Accountability for Violations of Informed Consent Under the Alien Tort Statute*, 155 U. PA. L. REV. 231, 277 (2006); Amy F. Wollensack, *Closing the Constant Garden: The Regulation and Responsibility of U.S. Pharmaceutical Companies Doing Research on Human Subjects in Developing Nations*, 6 WASH. U. GLOBAL STUD. L. REV. 747, 769 (2007).

social frameworks of many Third World countries play an important role in determining whether participants in medical experimentation actually enjoy the intended benefits of the informed consent requirement.[121] An examination of the circumstances in which human subjects in developing countries consent to participate in clinical studies reveals an environment defined by a lack of access to healthcare, desperation for medical treatment, and cultural unfamiliarity with Western science and bioethics.[122]

Reliable medical care is often unavailable in the Third World. In poor and low-income countries, "public health institutions have serious difficulties in providing adequate health care, something that creates obstacles with regard to the recruitment, training, and support of specialised [sic] healthcare professionals."[123] While the world's annual per capita expenditure on health is $639, and in the United States the number climbs to over $6,000, in sub-Saharan Africa the same figure plummets to $11, and for several countries in the region it is less than $4.[124] As a result, effective healthcare is available in developing countries "only for populations belonging to the highest social strata, and from which participation in clinical trials is rare."[125] Approximately half of the Third World does not have access "to even the most basic drugs,"[126] and 80% must instead rely on traditional healers.[127] Journalist Sonia Shah describes the widespread poverty and sickness at the University Teaching Hospital in Lusaka, Zambia, where foreign researchers recruited children with AIDS and infectious diarrhea for a trial of the drug nitazoxanide:

> [T]housands of parents straggled into Lusaka's clinics and hospital, clutching tiny bundles: their shrunken, malnourished babies and toddlers whose innards, it seemed, were seeping out . . . Outside, the rutted roads overflowing with water had turned into orange swamps . . . The toddlers whose parents agreed to enroll them in the trial in Lusaka were extremely ill. They'd been plagued with diarrhea for days. Most were severely underweight. Half were infected with HIV. The children were dying.[128]

The lack of Western medicine is actually one of the reasons pharmaceutical companies increasingly conduct their clinical studies in the Third World—it

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[121] *See, e.g.*, PATRICIA A. MARSHALL, WHO SPECIAL PROGRAMME FOR RESEARCH AND TRAINING IN TROPICAL DISEASES, ETHICAL CHALLENGES IN STUDY DESIGN, AND INFORMED CONSENT FOR HEALTH RESEARCH IN RESOURCE-POOR SETTINGS (2007).

[122] *Id*.

[123] Claudio Lorenzo et al., *Hidden Risks Associated with Clinical Trials in Developing Countries*, 36 J. MED. ETHICS 111, 113 (2010).

[124] *Compare Spending on Health: A Global Overview*, WORLD HEALTH ORG. (Mar. 2007), http://www.who.int/mediacentre/factsheets/fs319/en/index.html, *with* Gernard I. Msamanga & Wafaie W. Fawzi, *The Double Burden of HIV Infection and Tuberculosis in Sub-Saharan Africa*, 337 NEW ENG. J. MED. 849, 849 (1997).

[125] Lorenzo et al., *supra* note 123, at 113.

[126] *See* Solomon R. Benatar, *Distributive Justice and Clinical Trials in the Third World*, 22 THEORETICAL MED. BIOETHICS 169, 171 (2001).

[127] SHAH, *supra* note 5, at 100.

[128] *Id.* at 28.

provides a vast pool of "treatment-naïve"[129] human subjects who have not received other medicines. Thus, it allows researchers to more clearly identify the tested drug's effect.[130] One recruiter of experimental subjects explained simply, "South Africa is a great country. . . . There are lots of individuals [with AIDS] who are not treated."[131]

The lack of access to healthcare in the Third World creates desperation for medical treatment that often drives the sick and impoverished to participate in experimental research. The website for one pharmaceutical company boasts, "The vast majority of people [in the Third World] have only the most basic healthcare . . . [allowing] clinical trials [to] provide study participants with access to more sophisticated medicine."[132] In fact, numerous surveys of the participants in Third World clinical research have consistently revealed that the primary reason they join the trials is to obtain healthcare.[133] In a study of Ugandan parents who consented to allow their children to participate in a trial of malaria treatment, the authors concluded, "[m]any parents felt that they could not have refused to participate because their child was sick and they either did not know or did not believe that their child would receive treatment outside of the study."[134] One participant in a diabetes drug study in India explained, "[l]ook, I didn't have a stable job; insulin costs 1700 rupees a month. I have two daughters. And I weighed 49 kg."[135] Moreover, clinical trials in the Third World often involve disadvantaged and "socially vulnerable" subjects[136] who may be particularly desperate for treatment, such as drug addicts, sex workers, and pregnant mothers.[137] While research administrators have "expressed concern that thorough informed consent would be overshadowed by patient desperation for therapy," one human subject recruiter admitted to exploiting the situation:

> Say you need 1,000 patients in your trial. If you tried Western Europe, it would take you a long time to find untreated patients . . . [In a developing country], you might find those patients in half the time . . . [as] the healthcare systems aren't as sophisticated . . . [and] because of that, there is an increased interest in accessing drugs via clinical research, and therefore we can leverage that interest.[138]

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[129] *Id.* at 105.

[130] *See id.* at 104-05.

[131] *Id.* at 105.

[132] *Id.* at 8.

[133] *See, e.g.*, Paul S. Applebaum et al., *Voluntariness of Consent to Research: A Preliminary Empirical Investigation*, 30 IRB: ETHICS & HUM. RES. 10 (2009); Christine Pace et al., *Quality of Parental Consent in a Ugandan Malaria Study*, 95 AM. J. PUB. HEALTH 1184 (2005); David Wendler et al., *Why Patients Continue to Participate in Clinical Research*, 168 ARCHIVES INTERNAL MED. 1294 (2008).

[134] Pace et al., *supra* note 133, at 1184.

[135] SHAH, *supra* note 5, at 119.

[136] *See* Garrafa et al., *supra* note 30, at 501.

[137] *See* SHAH, *supra* note 5, at 85, 87, 141, 167.

[138] Sonia Shah, *Globalizing Clinical Research*, THE NATION 24 (July 1, 2002).

The U.S. Embassy in Beijing recently went so far as to "warn[] U.S. medical researchers against working in impoverished, rural areas of China," where "health care is poor and people are unable to protect their rights."[139] The lack of healthcare often serves as an important motivating factor for the subjects of clinical research in the Third World.

Despite their desire for First World medical treatment, the subjects of human research in the developing world often come from cultures unfamiliar with the basic concepts of Western science and bioethics. For instance, in some African languages, there is no word for "research" or "science," nor any concept of an "experiment" or a "placebo control."[140] "In traditional societies, the concepts of research, randomization, risks, side effects, and voluntary participation may be difficult for researchers to explain and potential participants to grasp."[141] More complicated scientific concepts are even more unfamiliar: "when language barriers exist and such concepts as germ theory or viral agents are alien, a description of an AIDS-related investigation . . . becomes difficult to relay to participants."[142]

European philosophical concepts may be similarly foreign to some Third World societies. Many Bantu languages lack a term corresponding to the English word "person," instead conceiving of personhood in terms of one's tribe, village, or social group.[143] Rather than define selfhood by the Western emphasis on the individual, in these cultures "it cannot be extricated from a dynamic system of social relationships, both of kinship and of community as defined by the village."[144] Political differences also render basic notions of Western bioethics strange to test subjects in the developing world. For instance:

> [In] nations governed for decades by dictators and despots, the Western concept of freedom of choice is weak or nonexistent . . . In countries wracked by recent wars or oppressed by secret police, test subjects are reluctant to sign their names to any document . . . Even in relatively peaceful, stable countries in Asia and Latin America, authoritarian cultural traditions can impede the process.[145]

Studies have confirmed that Third World research subjects frequently do not understand the concept of informed consent, even when investigators follow the proper procedures for obtaining it.[146] A survey of researchers working in the Third World who actually came from those regions revealed overwhelming concern with

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[139] Pomfret & Nelson, *supra* note 39 (internal quotation marks omitted).

[140] SHAH, *supra* note 5, at 151.

[141] Bhutta, *supra* note 110, at 774.

[142] Michele Barry, *Sounding Board: Ethical Considerations of Human Investigation in Developing Countries*, 319 NEW ENG. J. MED. 1083, 1084 (1988).

[143] *Id.* at 1083.

[144] *Id.*

[145] LaFraniere et al., *supra* note 39.

[146] *See, e.g.*, Bhutta, *supra* note 110, at 774.

the cultural appropriateness of U.S. ethical guidelines.[147] When human subjects in the Third World give their informed consent to participate in clinical studies, they do so in an environment defined by a lack of access to effective healthcare, a desperation for medical treatment, and a culture unfamiliar with the principles of Western science and bioethics.[148]

### *B. A Critique of the Right to Informed Consent in Third World Research*

These background conditions render the notion of a cognizable "right" to informed consent in Third World human subject research vulnerable to critical analysis. An allegedly inalienable and universal principle of informed consent cannot sustain itself in an environment defined by a lack of medical treatment and profound cultural diversity. First, given the absence of effective healthcare in much of the developing world, one must balance the informed consent standard against the right of human subjects to access lifesaving drugs through participation in clinical research—a contested question of policy, rather than an absolute ethical imperative. Second, the uniquely Western notions underlying the informed consent requirement render its enforcement in the Third World a kind of cultural imperialism, not a universal responsibility.

Although, as previously discussed, advocates of the informed consent requirement present it as an inalienable right that trumps all competing considerations, in the Third World the principle conflicts with an equally compelling right of access to essential medicine. Critical legal theorist Duncan Kennedy explains that the promotion of a particular right nearly always confronts a "*counterright* that can be asserted in the same tone of voice and that cancels out the first right."[149] In fact, several legal commentators have advanced the notion of a human right to access medical treatment.[150] One scholar declares:

> [T]he normative framework of human rights requires adequate progress to fulfill universal access to essential medications. At a minimum in this regard, international human rights law requires a clear plan to be made and deliberate steps to be taken toward the progressive realization of the right to health and *does not permit policies or acts, even under pressure from other actors, which would entail regression* in terms of availability or affordability of medications.[151]

Absolute insistence on the protection of the informed consent principle would seem to conflict with this obligation. Given that current informed consent procedures already require an "enormous effort" from investigators, who sometimes need as

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[147] *See* A.A. Hyder et al., *Ethical Review of Health Research: A Perspective From Developing Country Researchers*, 30 J. MED. ETHICS 68, 70 (2004).

[148] *See, e.g.*, Bhutta, *supra* note 110, at 774.

[149] Duncan Kennedy, *The Critique of Rights in Critical Legal Studies*, LEFT LEGALISM/LEFT CRITIQUE 178, 212 (Wendy Brown & Janet Halley, eds., 2002).

[150] *See* Noah Novogrodsky, *The Duty of Treatment: Human Rights and the HIV/AIDS Pandemic*, 12 YALE HUM. RTS. & DEV. L.J. 1, 17 (2009).

[151] Alicia Ely Yamin, *Not Just a Tragedy: Access to Medications as a Right Under International Law*, 21 B.U. INT'L L.J. 325, 329 (2003) (emphasis added).

much as 45 minutes to counsel each human subject,[152] many international health advocates have deliberately avoided demanding reinforcement of ethical research standards for fear of "imposing impossible demands and idealistic ethical standards on companies that can easily take their business elsewhere."[153] One bioethicist explained, "It takes half a second to look at how much more burdened the developing world is with ill health and disability. What we need, if anything, is more health research in the developing world, not less."[154] Indeed, a rights-based approach to Third World human subject research cannot easily reconcile the informed consent requirement with the demand for universal access to essential medical treatment.

The counterright of access to essential medical treatment renders the informed consent principle an indeterminate policy preference subject to debate, rather than an indisputable and overriding "trump." Kennedy writes:

> "[T]he inquiry into how to concretize the abstract right occurs in the presence of a countervailing right . . . This means that there are two opposing concretization projects going on.'"[155] One might believe passionately in *both* the abstract right to informed consent *and* the abstract right of access to essential medical treatment, but in the context of Third World human subject research, the practical implementation of one right inevitably leads to the derogation of the other. In such a situation, the informed consent principle loses its inalienable quality, its "absolute[] essential[ness]",[156] and instead "function[s] as no more than [an] interest."[157]

Resolution of the contest between the rights to informed consent and medical access will ultimately depend on one's personal ideology. Kennedy explains that "what determines the balance is not a chain of reasoning from a right or even from two rights, but a *third* procedure, one that in fact involves considering open-textured arguments from morality, social welfare, expectations, and institutional competence and administrability."[158] For instance, one could easily assert that any of the proposed informed consent reforms discussed previously would endanger the right of access to medical treatment in the Third World, and then make a convincing case against it on the basis of policy. African physicians, "desperate for a solution to the AIDS pandemic," made precisely this argument when objecting to "burdensome informed consent procedures in the face of widespread death."[159] Thus, an insistence on the principle of informed consent does not free the regulation of Third World

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[152] LaFraniere et al., *supra* note 39.

[153] Shah, *supra* note 138, at 28.

[154] *Id.*

[155] Kennedy, *supra* note 149, at 201.

[156] *The Nuremberg Code*, *supra* note 17.

[157] Kennedy, *supra* note 149, at 211.

[158] *Id.* at 196.

[159] Benjamin Mason Meier, *International Protection of Persons Undergoing Medical Experimentation: Protecting the Right of Informed Consent*, 20 BERKELEY J. INT'L L. 513, 544-45 (2002).

medical research from the realm of politics, nor does it provide a clear way forward for the implementation of human subject protections. Instead, it entangles advocates in difficult and subjective questions of how best to balance subjects' conflicting interests in both personal autonomy and access to essential medicines. Such a debate requires resort to "non-rights arguments"[160] that depend on the preferences of the observer. The suggestion that informed consent protections are self-evidently the desirable approach to Third World clinical research wanes when confronted with the competing claim of the participants' right to access medical treatment.

Cultural differences between the First and Third Worlds further reveal that the informed consent standard is a uniquely Western concept, rather than a universal right appropriate for all societies. Post-colonial legal scholar Makau Mutua has argued that the notions of "human rights and Western liberal democracy are virtually tautological," and that this "exclusivity and cultural specificity necessarily deny the concept [of human rights] universality."[161] He notes that "[t]here is virtual agreement that the early formulation and codification of human rights standards was dominated by Western cultural and political norms."[162] Indeed, the Nuremberg Code's pedigree is distinctly Western, as it was born from a criminal trial presided over by American judges, in which American lawyers prosecuted German scientists who committed crimes against European victims.[163] The Declaration of Helsinki has been criticized along similar lines.[164] In fact, the International Conference on Harmonization, which devised the GCP informed consent standards that the FDA applies to foreign research, did not include any developing countries.[165] Thus, although it aspires to universality, the informed consent requirement actually relies on a conception of autonomous individuality that may not be applicable to more communitarian, or even authoritarian, Third World societies. For instance, two Pakistani researchers who studied informed consent procedures in Pakistan and Swaziland found that:

> [R]esearchers were often forced to penetrate layer after layer of tribal hierarchy and corrupted bureaucracy in order to obtain informed consent. Sometimes they had to ask the village elders or the husbands of women participants first, or employ police escorts, or have tea and snacks, "regardless of the time it took." Plus, they had to struggle with the fact that some subjects don't have telephones, or permanent addresses, and may even be afraid to sign their names.[166]

The researchers concluded that their findings "demonstrate[d] the inadequacy and complexity of applying western-based concepts of informed consent to developing

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[160] *Id.* at 210.

[161] Makau Wu Mutua, *The Ideology of Human Rights*, 36 VA. J. INT'L L. 589, 592 (1996).

[162] *Id.* at 605.

[163] *See* Abdullahi, 562 F.3d at 177-78.

[164] *See* Dominguez-Urban, *supra* note 21, at 274.

[165] The sponsors of the Conference were the European Commission, the European Federation of Pharmaceutical Industry Associations, the Japanese Ministry of Health and Welfare, the Japanese Pharmaceutical Manufacturers Association, the U.S. FDA, and the Pharmaceutical Research and Manufacturers of America. *See* Miller, *supra* note 92, at 228.

[166] SHAH, *supra* note 5, at 151.

countries."[167] Far from a universal right, the informed consent requirement is a culturally contingent concept that is frequently alien to societies in the Third World.

When commentators nevertheless advocate for a universal informed consent standard regardless of local cultural context, they essentially espouse a form of cultural imperialism. Mutua believes that "the unrelenting universalist push [for human rights] seeks to destroy difference by creating the rationale for various forms of intervention and penetration of other cultures with the intent of transforming them into the liberal model."[168] He condemns this practice as "cultural imperialism."[169] Similarly, legal scholars have criticized enforcement of the informed consent doctrine in Third World medical research as a form of "ethical imperialism" which is not only ineffective, but may actually "undermine the nonindividualistic society's fabric."[170] In a culture where men consent on behalf of their wives and daughters,[171] or local leaders consent on behalf of community members,[172] an insistence on applying the informed consent requirement may itself violate the principle of autonomy.[173] Such a universalist approach would both "diminish[] an individual's right to decide how and by whom decisions of consequence to his or her life are made,"[174] and disrespect the integrity of the community that participates in the research.[175] African physicians have thus "bitterly opposed the informed consent standard, arguing that Westernized notions of informed consent merely impose a form of 'medical-ethical imperialism' on developing nations."[176] Instead, they prefer to allow local health experts, bioethicists, and affected groups to assess the risks and benefits of medical research.[177] Because the informed consent standard is culturally contingent, rather than universal, its reinforcement in Third World clinical trials would exacerbate a potentially destructive form of "ethical imperialism." The informed consent requirement does not protect an inalienable and universal right; instead, it reflects a contestable policy judgment premised on a set of uniquely European cultural values and balanced against Third World citizens' interests in obtaining healthcare through participation in clinical studies.

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[167] *Id.*

[168] Mutua, *supra* note 161, at 657.

[169] *Id.* at 656.

[170] Dominguez-Urban, *supra* note 21, at 280.

[171] *See* Esther Change, *Fitting a Square Peg into a Round Hole?: Imposing Informed Consent and Post-Trial Obligations on United States Sponsored Clinical Trials in Developing Countries*, 11 S. CAL. INTERDISC. L.J. 339, 346 (2002).

[172] *See* Dominguez-Urban, *supra* note 21, at 280.

[173] *See id.*

[174] Gordon, *supra* note 51, at 1323.

[175] *See* Dominguez-Urban, *supra* note 21, at 280.

[176] Meier, *supra* note 159, at 546.

[177] *See id.*

### *C. A Critique of the Possibility of Informed Consent in Third World Research*

The fact that a lack of healthcare frequently drives human subjects in the Third World to submit to medical research belies the notion that the informed consent requirement meaningfully protects their free choice to participate. In practice, the doctrine of informed consent does nothing to correct the radical power disparity between researchers with the authority to dispense lifesaving pharmaceuticals and their sick and impoverished patients. Given that participation in clinical trials is often the only way for human subjects to obtain essential treatment, the informed consent requirement merely masks the potentially compelled nature of all medical experimentation in the Third World.

The life or death interest that many Third World participants have in submitting to clinical research renders autonomy a meaningless concept. Feminist legal theorist Catharine MacKinnon discusses the criminal law of rape:

> The line between rape and intercourse commonly centers on some measure of the woman's "will." But from what should the law know woman's will? . . . [W]omen are socialized to passive receptivity; may have or perceive no alternative to acquiescence; may prefer it to the escalated risk of injury and the humiliation of a lost fight; submit to survive.[178]

Human subjects in the developing world, without other access to medical treatment, must similarly "consent to survive." The constraints of this reality undermine any attempt to identify a legitimately "free" exercise of a subject's "will" to submit to experimentation.[179] Thus, the "written informed consent form"[180] by which the FDA separates permissible medical study from nonconsensual research cannot fairly represent the "voluntariness" of a subject's decision to join a clinical study. The choice between life and death is not much of a choice at all. George J. Annas, head of the health law department at Boston University's School of Public Health, remarked:

> I'd argue you can't do studies ethically in a country where there is no basic health care . . . You can tell a person there that this is research, but they hear they have a chance to get care or else refuse their only good

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[178] Catharine A. Mackinnon, *Feminism, Marxism, Method, and the State: Toward a Feminist Jurisprudence*, THE CANON OF AMERICAN LEGAL THOUGHT 869, 880 (David Kennedy & William W. Fisher III eds., 2006).

[179] *But cf.* Ruth Gavison, *Feminism and the Public/Private Distinction*, 45 STAN. L. REV. 1, 16-17 (1992) ("[N]othing we decide is really 'free' in the sense that it is determined by our own wishes and preferences. We are constrained by various limits: opportunities, socialization, expectations, resources and perceptions. Many of these constraints are person-made and not inevitable. Similarly, nothing is voluntary and equal. The worker who *must* earn a living and can sell only his labor is not free to choose unemployment, even if the only available work is humiliating and exploitative. Consent becomes anything but the product of bargaining between free and equal adults.").

[180] International Conference on Harmonization: Draft Guidelines on Good Clinical Practice, 60 Fed. Reg. 42,949 (1995) (proposed Aug. 17, 1995).

> chance at care. How can you put them in that position and then say they are giving informed consent?[181]

In rape, Mackinnon suggests, "the issue is less whether there was force and more *whether consent is a meaningful concept*."[182] The same question could be asked of Third World human subject research. "The best evidence of voluntary, informed consent is when some subjects drop out or refuse to participate in a trial."[183] Yet in a survey of researchers working in developing countries, "45 percent reported that their low-literacy subjects *never* refused to participate."[184] One doctor who worked for Pfizer in Kano asked, "[g]iven [the study's subjects] poverty and lack of access to decent medical care, 'Honestly, did they have a choice?'"[185]

In the absence of meaningful autonomy, the informed consent requirement instead serves to conceal the often-compelled nature of participation in Third World medical study. Research inherently entails more risks than standard medical treatment, since subjects may receive an inert placebo or a potentially dangerous new drug. Thus, "only those who 'have absolutely no choice' can be expected to agree to the impersonal care doled out in a random trial . . . And these mostly poor patients who serve as subjects live in a world apart from the socially powerful doctors who experiment upon them."[186] In regard to rape law, Professor Dorothy Roberts argues: "the pervasive effect of male dominance makes it impossible to say definitively that some of women's sexual relations with men (called sex) are 'free' and others (called rape) are 'coerced.'"[187] Similarly, the desperate need for medicine in the Third World makes it impossible to discern where consensual experimentation ends and exploitation begins. The "inequality of knowledge, authority, and wealth between the researcher and the volunteer"[188] renders the informed consent principle more an ethical protection for pharmaceutical companies than a material one for human subjects. By marking off and condemning one form of clinical study—nonconsensual experimentation—the informed consent requirement justifies a much broader range of effectively compelled medical research on disempowered Third World patients.

The current FDA regulations of informed consent reflect this power imbalance on a global scale. MacKinnon explains: "The law of rape divides the world of women into spheres of consent according to how much say we are legally presumed to have over sexual access to us . . . Little girls may not consent; wives must . . . [D]ividing and protecting the most vulnerable becomes a device for not protecting

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[181] LaFraniere et al., *supra* note 39.

[182] Mackinnon, *supra* note 178, at 880 (emphasis added).

[183] SHAH, *supra* note 5, at 148.

[184] *Id.*

[185] Joe Stephens, *Where Profits and Lives Hang in Balance*, THE WASH. POST (Sept. 26, 2011), http://www.washingtonpost.com/wp-dyn/content/article/2007/07/02/AR2007070201255.html.

[186] SHAH, *supra* note 5, at 119.

[187] Dorothy E. Roberts, *Rape, Violence, and Women's Autonomy*, 69 CHI.-KENT L. REV. 359, 370 (1993).

[188] Dyckman, *supra* note 111, at 98.

everyone."[189] As previously discussed, the FDA similarly divides human subjects into "spheres of consent." American children receive the most protection, followed by American adults, followed by the rest of the world. Accordingly, fewer and fewer Americans volunteer for medical research.[190] Instead, the rest of the planet, especially the unregulated Third World, is presumed available for experimentation subject to baseline limitations.[191] The signature on the informed consent form effectively conceals the reality that the investigators who control lifesaving medical treatment wield enormous power over their subjects, who *must* submit to experimental research in order to survive.

The "informed" nature of the consent does not redeem it. In the law of rape, MacKinnon writes, "If the accused knows us, consent is inferred . . . Men believe that it is less awful to be raped by someone one is close to."[192] Yet "women feel as much, if not more, traumatized by being raped by someone we have known."[193] By analogy, the informed consent requirement recognizes as consensual a subject's participation in a study if she has "sufficient knowledge and comprehension of the elements of the subject matter involved."[194] Knowledge of the particular dangers of a study, however, does not necessarily indicate the voluntariness of a Third World subject's participation. Instead, the consent may well have been effectively compelled by personal circumstances and may sometimes just terrify the subject. For instance, one doctor recounted a study in Tanzania involving the administration of HIV tests on pregnant mothers, in which government health officials requested that the women not be told the purpose of the tests nor given the results.[195] She explains, "The host country's decision was based on the judgment that the results could provoke hysteria within the population about a disease with no cure and for which limited resources were available, even for palliative treatment."[196] Because the subjects of Third World clinical research are often driven to submit by medical necessity, rather than considered reflection on the risks and benefits of participation, the fact that their consent is "informed" does not deprive it of its compelled character.

Rather than define permissible medical research by the existence of a signed informed consent document, one might consider the perspectives of the participating human subjects. MacKinnon believes that:

> A feminist distinction between rape and intercourse . . . lies in the *meaning* of the act *from women's point of view* . . . What is wrong with rape is that it is an act of the subordination of women to men. Seen this

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189 MacKinnon, *supra* note 178, at 878-79.

190 *See* SHAH, *supra* note 5, at 4-5.

191 *Cf.* Dyckman, *supra* note 111, at 107 ("[The Nuremberg Code and Declaration of Helsinki] privilege societies rich enough to afford choice and autonomy. In this sense, the doctrine does not embody Western values, but presumes privileged status.").

192 MacKinnon, *supra* note 178, at 879.

193 *Id.*

194 *The Nuremberg Code*, *supra* note 17.

195 Barry, *supra* note 142, at 1084.

196 *Id.*

> way, the issue is not so much what rape "is" as the way its social conception is shaped to interpret particular encounters.[197]

Similarly, medical research could be understood as nonconsensual if it feels that way to the subjects themselves. In fact, one survey of women who enrolled in an AIDS study in South Africa found that nearly 90 percent reported feeling "compelled to take part, even though they all had signed an informed consent form."[198] The same survey revealed that 99 percent of the women "believed [that] the hospital would not allow them to quit the study once it began."[199] Despite the implementation of the informed consent requirement, the perspectives of the actual human subjects involved in Third World medical research reveal that they frequently experience the clinical studies as compulsory.[200] Because pharmaceutical trials often offer the only sources of essential healthcare in the Third World, and many human subjects choose to submit to experimentation for precisely this reason, the informed consent standard only serves to legitimize compelled medical research in the name of an illusory autonomy.

## IV. BEYOND INFORMED CONSENT: DISTRIBUTIVE JUSTICE IN THIRD WORLD HUMAN SUBJECT RESEARCH

Instead of a rights-based approach, advocates for human subjects' welfare might consider the distributive consequences of medical research in the Third World. Distributive justice in Third World medical research would address "the equitable distribution of the risks and benefits arising from [the use of] underprivileged test subjects in Western pharmaceutical research."[201] Although investigators conduct an increasing amount of clinical studies in developing countries, comparatively little of this research involves medicines to treat Third World maladies, or treatments that would be affordable to a Third World consumer. Reform of the clinical testing process based on the principle of distributive justice thus seeks to ensure that the communities that bear the risks of medical experimentation also enjoy the benefits of that research through access to affordable drugs for local illnesses.

The outcomes of the global economy for new drug research skew heavily against the Third World. Developing countries disproportionately endure the dangers of medical research in comparison to the benefits that such research yields for them.[202] Out of over 1500 new drugs developed worldwide between 1975 and 2004, only ten were intended to treat diseases primarily prevalent in low-income countries.[203] "This indicates that during the past 30 years, that is, the period in which the involvement of poor and low-income countries . . . has been the greatest, only slightly more than 1% of pharmacological innovations were directed at diseases that predominantly affect

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[197] MacKinnon, *supra* note 178, at 881 (second emphasis added).

[198] *See* LaFraniere et al., *supra* note 39.

[199] *Id.*

[200] *See id.*

[201] Shtilman, *supra* note 25, at 429.

[202] *See* Lorenzo et al., *supra* note 123.

[203] *Id.* at 111.

the populations in these countries."[204] Scholars refer to this discrepancy as the "10/90 gap"[205]—of the $56 billion annual global expenditure on medical research and development, 87% of the money targets the health needs of the world's richest 16%.[206] Thus, rather than focus on Third World health problems such as malaria or multidrug-resistant tuberculosis, "[t]he diseases that are of most interest [in international clinical trials] are mainly the degenerative diseases—arthritis, obesity, heart disease—the diseases of people in the developed world."[207]

Even when Third World medical studies address diseases of local concern—such as HIV or parasites—they often produce treatments that are too expensive for the subjects' communities to afford. For example, one study conducted in Thailand led to the development of a treatment to prevent the transmission of HIV from infected mothers to their infants.[208] Yet the drug ultimately cost $50—far beyond the reach of most Thai women, and thus, "useless for the community in which the test was performed."[209] Similarly, a trial in Zambia of the drug nitazoxinade, used to treat parasitic disease, yielded little long-run benefit for the community.[210] The treatment was uniquely tailored to First World concerns and never licensed for use in Zambia—"if [the pharmaceutical company's] hunt for experimental bodies had ended in Zambia, their market clearly began elsewhere. The children of Zambia shouldered the burden for nitazoxanide's development, but they are hardly beneficiaries of the drug's advantages."[211] The fact that Third World nations often cannot afford the drugs tested in their communities becomes especially poignant when one considers that, after the desire to obtain medical treatment, the most frequently reported reason that human subjects in the developing world volunteer for clinical research is to "contribut[e] to finding better treatments for . . . people in *the participant's country*."[212] Even in the absence of any rights-based injustices, the entire economy of globalized pharmaceutical research produces an inequitable distribution of risks and benefits, as Third World subjects disproportionately bear the burdens of medical research for the sake of First World consumers.

A distributive justice approach to human subject research reform would seek to correct this imbalance by ensuring that the communities that undertake the risks of medical research also share in the benefits. The International Ethical Guidelines for

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[204] *Id.*

[205] Garrafa et al., *supra* note 30, at 501.

[206] Benatar, *supra* note 126, at 170. This figure implies that "the needs of 90% of the world's population have to be met from the remaining 10% of research funding." Garrafa et al., *supra* note 30, at 501.

[207] Sonia Shah, *Globalizing Clinical Research: Big Pharma Tries Out First World Drugs on Unsuspecting Third World Patients*, THE NATION MAGAZINE (Sept. 28, 2011), http://www.thirdworldtraveler.com/Health/Globalizing_ DrugResearch.html.

[208] *See* D.R. Cooley, *Distributive Justice and Clinical Trials in the Third World*, 22 THEORETICAL MED. BIOETHICS 151, 152 (2001).

[209] *Id.*

[210] *See* SHAH, *supra* note 5, at 33-35.

[211] *Id.* at 35.

[212] Wendler et al., *supra* note 133, at 1296 (emphasis added).

Biomedical Research Involving Human Subjects, promulgated in 2002 by the Council for International Organizations of Medical Sciences in collaboration with the World Health Organization,[213] endorses such a policy. Guideline 10 states that sponsors and investigators who undertake research in a community with limited resources must make every effort to ensure that "the research is responsive to the health needs and the priorities of the . . . community" and that "any intervention or product developed, or knowledge generated, will be made reasonably available for the benefit of that . . . community."[214] Unfortunately, this language is fairly vague and the principle has not been followed in most cases.[215] Nevertheless, scholars of bioethics have begun to suggest specific policies to ensure more equitable outcomes from Third World medical experimentation. These reforms include dissemination of the results of clinical studies to participating communities, maintenance of a favorable risk-benefit ratio for the regions where studies are conducted, post-trial provision of medical treatment to human subjects if the experimental treatment proves beneficial, and collaborative partnerships between First World investigators and Third World research institutions.[216] These policies would begin to correct the distributive injustices of the globalized economy for medical research. In the long run, they could even increase access to essential healthcare in the Third World and reduce the role that desperation for medical treatment plays in many subjects' decision to submit to experimental study, potentially providing a route toward redeeming the informed consent requirement.

## V. CONCLUSION: TOWARD A "KANO CODE"

The actual context of medical experimentation in the developing world undermines both the inalienability and universality of such a right and the possibility of true human subject autonomy. Advocates for the informed consent standard present it as an absolute ethical imperative that trumps all competing considerations and transcends cultural contexts. They claim that the requirement protects freedom of choice by ensuring that a subject's participation in experimental research is voluntary. The lack of healthcare in much of the Third World, however, implicates subjects' competing "right" to access essential medical treatment, which potentially conflicts with any straightforward reinforcement of the often-burdensome informed consent standard. Moreover, the cultural differences between some First and Third World countries suggest that the notion of informed consent may reflect uniquely Western values, rather than a universal principle. The fact that many subjects volunteer solely to obtain lifesaving medical care demonstrates that the informed consent standard does not meaningfully protect autonomy, but instead conceals the often compelled nature of participation in Third World clinical research. Thus, as an alternative to a rights-based approach to the new drug testing process, the benefits of

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[213] *International Ethical Guidelines for Biomedical Research Involving Human Subjects*, COUNCIL FOR INT'L ORGS. OF MEDICAL SCIENCES 17-18, http://www.cioms.ch/publications/layout_guide2002.pdf (last visited Jan. 2, 2012).

[214] *Id.* at 51.

[215] *See* Cooley, *supra* note 208, at 151-52.

[216] *See* Emanuel et al., *supra* note 109, at 932-34; Zhiyong Zong, *Should Post-Trial Provision of Beneficial Experimental Interventions Be Mandatory in Developing Countries?*, 34 J. MED. ETHICS 188, 190 (2007).

medical research to the Third World human subjects, who bear the cost, should be more equitably allocated to advance the principle of distributive justice.

In light of this critique, the incident at Kano takes on a new significance. The Nigerian plaintiffs sued Pfizer for allegedly violating their right to informed consent. Yet, even if Pfizer *had* correctly followed the informed consent procedures, how many sick and untreated patients would *actually* have turned down the offer of free medicine? What material difference would informed consent have made in the lives of the Nigerian children who had few other alternatives but to accept Pfizer's experimental treatment? In fact, the informed consent standard loses much of its meaning long before most Third World medical trials ever even begin; especially since pharmaceutical companies commission studies to obtain FDA approval to market new drugs *in the United States*, and simply choose developing nations as testing sites because the countries have large numbers of untreated sick people on whom to test the drugs.[217] Third World subjects endure the risks of experimentation for the benefit of consumers in the United States. *This* inequality embodies the true injustice of Third World medical research.

One way the pharmaceutical industry might choose to correct this power imbalance would be through the formation of a "multi-stakeholder initiative" (MSI).[218] An MSI is a form of "civil regulation"[219] that facilitates dialogue between the various stakeholders engaged in a particular economic sector, such as corporations, non-governmental organizations, governments, academics, labor representatives, and affected communities. These parties then collaborate on developing and implementing a set of human rights standards for the relevant industry.[220] Prominent MSIs include "The Fair Labor Association," which addresses working conditions in factories worldwide,[221] "The Kimberly Process," which attempts to halt the flow of conflict diamonds from Africa,[222] "Fairtrade

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[217] *See* Stephens, *supra* note 185. For instance, Pfizer defended its Trovan research in Nigeria as "philanthropic," on the ground that it sponsored the trials only to gain approval for the use of the drug in meningitis epidemics, which occur mainly in the developing world. *See id.* However, Dr. George McCracken, a meningitis specialist who co-authored the guidelines for meningitis research, described that argument as "a little bit disingenuous. They do gain from it. They gained knowledge about how the drug works. It's not 100 percent altruistic." *Id.* In fact, once the FDA approved Trovan for any purpose, American pediatricians would be free to prescribe it for a broad range of infections, including sinusitis, bronchitis, gonorrhea, and pneumonia. *See id.*

[218] *See* Dara O'Rourke, *Multi-stakeholder Regulation: Privatizing or Socializing Global Labor Standards*, 34 WORLD DEV. 899, 899 (2006).

[219] Peter Utting, *Regulating Business Via Multistakeholder Initiatives: A Preliminary Assessment*, http://www.unsys tem.org/ngls/Section%20II.pdf (last visited Jan. 2, 2012).

[220] *See generally* O'Rourke, *supra* note 218 (discussing non-governmental regulation initiatives in the United States and Europe, their models of regulation, codes of conduct, and criteria for evaluating effectiveness); Utting, *supra* note 219 (discussing the emergence of multistakeholder initiatives, their purpose and roles, and makes a prediction towards their effectiveness).

[221] *See* FAIR LABOR ASS'N, http://www.fairlabor.org/ (last visited Sept. 20, 2011).

[222] *See* KIMBERLY PROCESS, http://www.kimberleyprocess.com/home/index_en.html (last visited Sept. 20, 2011).

International," which promotes trade justice,[223] and the "Extractive Industries Transparency Initiative," which attempts to improve transparency and accountability in the extractives sector.[224] An MSI for international medical research would bring together private pharmaceutical companies, global health organizations, Third World research institutions, human subjects, and local communities to collaboratively develop a set of voluntary research standards for more equitably distributing the risks and benefits of medical experimentation. Companies that followed these standards would be certified as compliant and allowed to advertise their products as such.[225] Because human subjects and their communities would play an active role in the process, the new research standards developed by an international drug testing MSI would begin to resolve the power disparity that often undermines the informed consent principle. First, the affected communities' own preferences would decide the policy balance between expanded access to medical treatment and increased regulatory oversight of clinical studies. Second, the new research guidelines would reflect the values of the society in which the research took place, rather than an imposed Western worldview. Finally, the human subjects would help craft their own ethical protections—allowing them the opportunity to select how the research itself would proceed, rather than the false choice of whether to accept lifesaving treatment at all.[226] A medical research MSI would empower Third World communities to develop a "Kano Code," a Nuremberg Code for the globalized pharmaceutical industry.

Over half a century ago, the International Military Tribunal in Nuremberg promulgated the informed consent requirement in response to the human rights atrocities that occurred during World War II. Today, an MSI-developed "Kano Code" must address the new distributive injustices that accompany the international market for clinical drug testing. A "Kano Code" would mandate that foreign clinical studies more equally allocate both their risks *and their benefits*, on the basis of specific directives derived from the interests of the affected communities and the distributive reforms discussed earlier. A Kano Code would ensure that, although the suffering children of Kano may not have had much choice as to whether to participate in Pfizer's study, the children and their communities would at least share in the knowledge and new treatments developed as a result of their participation. So far, advocates for the informed consent standard have distinguished ethical experimentation by the evidence of a "Yes," nearly any "Yes" offered by a human subject. Yet, as Nietzsche wrote, many patients in the Third World have a "hidden Yes" inside them, fueled by a desperation for essential healthcare and stronger than all "Nos" or "Maybes" that the dangers of medical research might otherwise

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[223] *See* FAIRTRADE INT'L, http://www.fairtrade.net/about_us.0.html (last visited Sept. 20, 2011).

[224] *See* EXTRACTIVE INDUSTRIES TRANSPARENCY INSTITUTE, http://eiti.org/ (last visited Sept. 20, 2011).

[225] *See* O'Rourke, *supra* note 218, at 899.

[226] Alternatively, host countries in the developing world might negotiate bilateral agreements with the sponsors of medical research, conditioning permission to conduct local trials on the promise to share more of the benefits of the research. Garrafa et al., *supra* note 30, at 501.

warrant.[227] In light of the increasing use of human subjects from the Third World, an equitable process for new drug testing demands a reach beyond the principle of informed consent, beyond "Yeses," "Nos," and "Maybes," beyond Nuremberg, and toward a more just economy of international medical research.

[227] NIETZSCHE, *supra* note 1, at 340.