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Introduction

On October 1, 2010, news broke of a study in which U.S. doctors intentionally infected Guatemalans with gonorrhea, cancroid, and syphilis to study new methods of prevention.[1] For the past sixty years, the events of the study were buried in files and forgotten.[2] By chance, Professor Susan Reverby of Wellesley College discovered the unpublished notes and presented the first discussion of the study in her article, "*Normal Exposure*" *and Inoculation Syphilis: A PHS* "*Tuskegee*" *Doctor in Guatemala, 1946–48*.[3]

As is now known, from 1946–48, the Venereal Disease Research Laboratory of the U.S. Public Health Service (PHS), the Pan American Sanitary Bureau (PASB), and the Guatemalan government spearheaded a study[4] that intentionally infected and tested Guatemalan prisoners, asylum inmates, soldiers, and orphaned children.[5] The research team, led by Dr. John C. Cutler, exposed Guatemalans to syphilis "through the use of infectious prostitutes or directly through [an] inoculum made from tissue of human and animal syphilitic gummas and chancres,"[6] and then treated the

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1. U.S. DEP'T. OF HEALTH AND HUMAN SERVS., FACT SHEET ON THE 1946-1948 U.S. PUBLIC HEALTH SERVICE SEXUALLY TRANSMITTED DISEASES (STD) INOCULATION STUDY 1 (2010) [hereinafter FACT SHEET], *available at* http://www.hhs.gov/1946inoculationstudy/1946_std_inoculations_factsheet-eng.pdf (stating the purpose of the study was "to look for new ways to prevent STDs, including gonorrhea, cancroid, and syphilis").

2. *See* Susan M. Reverby, *"Normal Exposure" and Inoculation Syphilis: A PHS "Tuskegee" Doctor in Guatemala, 1946–48*, 23 J. POL'Y HIST. 6, 20 ("The extraordinary efforts [Dr. Cutler] had made to produce disease and understand various kinds of prophylaxis were buried in the files.").

3. *See* The CNN Wire Staff, *U.S. Apologizes for Infecting Guatemalans with STDs in the 1940s*, CNN, Oct. 1, 2010, http://www.cnn.com/2010/WORLD/americas/10/01/us.guatemala.apology/index.html (last visited Apr. 2, 2012) (reporting the origins of the Guatemala study and the revelation of the study due to Professor Reverby's efforts) (on file with the Washington and Lee Journal of Civil Rights and Social Justice).

4. *See* CTR. FOR DISEASE CONTROL AND PREVENTION, Report on Findings from the U.S. Public Health Service Sexually Transmitted Disease Inoculation Study of 1946–1948, Based on Review of Archived Papers of John Cutler, MD, at the University of Pittsburgh 4 (2010), http://www.hhs.gov/1946inoculationstudy/cdc_rept-std_inoc_study.html (last visited Apr. 2, 2012) (stating the parties involved in the research study) (on file with the Washington and Lee Journal of Civil Rights and Social Justice).

5. *See* Reverby, *supra* note 2, at 12 (stating the researchers chose, as subjects, "the usual quartet of the available and contained: prisoners in a national penitentiary, inmates in Guatemala's only mental hospital, children in the national orphanage, and soldiers in a barracks in the capital").

6. *Id*. at 9.

Guatemalans with penicillin.[7] Although the researchers acknowledged they could not use such methods in the United States,[8] they experimented in secrecy and did not seek consent from human subjects.[9]

Shortly following news of the Guatemala study, the Centers for Disease Control and Prevention (CDC) responded: "Such abuses could not occur today in research funded or conducted by the U.S. government. A series of safeguards established over the past [forty] years provide protection for human participants, whether in the United States or overseas, in medical research from these types of abuses."[10] In January, 2011, President Obama asked the Presidential Commission for the Study of Bioethical Issues (PCSBI) to reexamine the current state of domestic and international ethics to ensure nothing similar to the Guatemala study happens again.[11] Not only is the PCSBI conducting a thorough examination of whether existing standards and practices are adequate for international clinical trials, but it is also conducting a retrospective examination of the Guatemala study and its context.[12] As a result, the United States' current protections for human subjects are unlikely to continue as the PCSBI focuses on improving such protections and creating a global standard.

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7. *See id*. ("After learning what they could from each exposure that caused actual infection (and not all did), they used penicillin, expecting, if not always, curing the infections.") (citations omitted).

8. *See id*. at 18–19 (stating that "[e]veryone involved with these studies seemed to know they were treading on complicated ethical grounds" and that some of those involved acknowledged such experiments could not be done in the United States).

9. *See id*. at 19 (discussing the lack of informed consent given by the research subjects and how the researchers suppressed information due to concern "about the possibility of having anything said about [the] program that would adversely affect its continuation") (quotations omitted).

10. FACT SHEET, *supra* note 1, at 1.

11. *See* Memorandum on Review of Human Subjects Protection, 2010 DAILY COMP. PRES. DOC. 1015 (Nov. 24, 2010), http://origin.www.gpo.gov/fdsys/pkg/DCPD-201001015/pdf/DCPD-201001015.pdf (asking the Commission "to convene a panel to conduct, beginning in January 2011, a thorough review of human subjects protection to determine if federal regulations and international standards adequately guard the health and well-being of participants in scientific studies supported by the Federal Government").

12. *See* Amy Gutmann, Commissioner Chair of the Presidential Commission for the Study of Bioethical Issues, *Opening Remarks and Executive Director's Report*, THE PRESIDENTIAL COMMISSION FOR THE STUDY OF BIOETHICAL ISSUES (Mar. 1, 2011), http://www.tvworldwide.com/events/bioethics/110228/default.cfm?id=13284&type=flv&test=0&live=0 (last visited Apr. 2, 2012) (discussing the adequacy of standards and practices for international clinical trials) (on file with the Washington and Lee Journal of Civil Rights and Social Justice).

Through the PCSBI, the ethics of using human subjects has come to the foreground of the U.S. government's attention. Even in recent history, safeguards codified in U.S. federal regulations and found in other international sources have been both inadequate and not rigorously enforced.[13] In response to both contemporary experiments involving human subjects and the interest of the PCSBI in improving human protection standards, this Note addresses whether modern legal standards adequately compel researchers to obtain informed consent and contrasts the Guatemala study with modern human subject studies. In Part I, the details of the Guatemala study, the ethical and legal standards of the time, and the medical researchers' compliance with those standards are examined. Part II analyzes modern informed consent, draws parallels between the Guatemala study and modern research methods, and discusses flaws in modern informed consent standards and practices. Finally, Part III advocates for improving U.S. protections by enacting the Research Participants Protection Modernization Act of 2011.

I. The Guatemala Study

The U.S. government responded to news of the Guatemala study with a statement expressing regret, outrage, and a commitment to high ethical standards.[14] Nevertheless, the U.S. public expressed fear that the study could reignite minorities' suspicion of medical research,[15] concerns that

13. *See infra* Part II.D (discussing modern informed consent, lack of compliance, and private pharmaceutical companies' continued exploitation of human subjects despite FDA regulations and international guidelines); *see also* John Daniels, *U.S. Funded AIDS Research in Haiti: Does Geography Dictate How Closely the United States Government Scrutinizes Human Research Testing?*, 11 Alb. L.J. Sci. & Tech. 203, 203 (2000) (discussing that U.S. regulated research studies often are not reviewed adequately enough to ensure researchers are complying with ethical standards, such as informed consent).

14. *See* Hillary Rodham Clinton, U.S. Sec'y of State, and Kathleen Sebelius, U.S. Sec'y of Health and Human Services, Joint Statement by Secretaries Clinton and Sebelius on a 1948–1948 Study (Oct. 1, 2010), *available at* http://www.state.gov/secretary/rm/2010/10/148464.htm (last visited Apr. 2, 2012) (apologizing for the Guatemala study and expressing regret) (on file with the Washington and Lee Journal of Civil Rights and Social Justice); *see also* the White House, Office of the Press Secretary, Read-out of the President's Call with Guatemalan President Colom (Oct. 1, 2010), *available at* http://www.whitehouse.gov/the-press-office/2010/10/01/read-out-presidents-call-with-guatemalan-president-colom (last visited Apr. 2, 2012) (summarizing the private telephone conversation between President Obama and President Colom in which President Obama communicated regret) (on file with the Washington and Lee Journal of Civil Rights and Social Justice).

15. *See* Arthur Caplan, *Horrific Medical Tests of Past Raise Concerns for Today: As*

using human subjects in prisons or poor communities warrants caution,[16] and worries that the United States still engages in egregious research with human participants.[17] These misgivings demonstrate that the Guatemala study provides a helpful reference point against which to compare current studies and ethics.

A. Inception

The Guatemala study was established to test the effectiveness of treating syphilis with penicillin and to discover the mechanism that transmitted syphilis.[18] Gonorrhea and cancroid studies also occurred.[19] The United States received the brunt of public attention,[20] but it did not control

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More Research Moves Outside U.S., Are We Still Exploiting the Poor?, MSN TODAY HEALTH, Oct. 1, 2010, http://today.msnbc.msn.com/id/39463624/ns/today-today_health (last visited Apr. 2, 2012) (stating that "[t]rust in medical research remains tenuous because of what was done to great-grandparents and friends" of participants in the Tuskegee study) (on file with the Washington and Lee Journal of Civil Rights and Social Justice).

16. *See* Amy Goodman, *From Tuskegee to Guatemala, via Nuremburg*, THE CAPITAL TIMES, Oct. 7, 2010, http://host.madison.com/ct/news/opinion/column/article_9d6531a7-db5d-5854-a858-4ddfcea25a16.html (last visited Apr. 2, 2012) (stating that "efforts are being made to loosen restrictions" that protect subjects from abusive practices such as those in the Guatemala study, so "[w]e need to ask what 'informed consent' means inside a prison, or in a poor community when money is used as an incentive to 'volunteer'") (on file with the Washington and Lee Journal of Civil Rights and Social Justice).

17. *See* Richard S. Saver, *Medical Research Regulation After More Than Twenty-Five Years: Old Problems, New Challenges, and Regulatory Imbalance*, 19 ANN. HEALTH L. 223, 227 (2010) ("Opinion polls suggest the public's confidence in the research [oversight] system has been eroding, a trend, no doubt fueled by intense media coverage of subject deaths at leading academic medical centers, regardless of how anomalous such episodes may be."); *see also* Stephen Soldz, *Guatemalan Research Horrors and U.S. Hipocracy: CIA Unethical Research Ignored*, ZNET, Oct. 4, 2010, http://www.zcommunications.org/guatemalan-research-horrors-and-us-hypocrisy-by-stephen-soldz (last visited Apr. 2, 2012) ("According to top US officials, abusing people in the name of research without their permission is awful, truly awful . . . . However, US officials have so far been totally silent about horrific, unethical research conducted by US government researchers [as part of the CIA] within the last decade.") (on file with the Washington and Lee Journal of Civil Rights and Social Justice).

18. *See* CTR. FOR DISEASE CONTROL AND PREVENTION, *supra* note 4 at 4 (stating that "the primary purpose of the studies was to develop human models of transmission of *Treponema pallidum*—the bacteria that causes syphilis—by sexual transmission and . . . inoculation").

19. *See id*. at 2–3 (describing that in addition to syphilis the researchers also studied gonorrhea and chancroid).

20. *See supra* notes 15–17 and accompanying text (discussing the American public's reaction to news of the Guatemala study).

the research directly.[21] Responsibility was channeled through the Pan American Sanitary Bureau (PASB).[22] The PASB enlisted the aid of Guatemala and the United States and officially sponsored the Guatemala study as part of its commitment to "maintaining and improving the health of all the people of the [twenty-one] American publics and also to preventing the occurrence and spread of transmissible diseases in international commerce."[23] However, even though it was a separate entity from the PASB, the U.S. Public Health Service (PHS) exerted substantial control of the study behind the scenes.[24]

Conveniently for the United States and the PASB, an ideal testing site was created by the interest of a leader in Guatemala's health industry, influence from the United States, and Guatemala's demographics. The selection of Guatemala for the research site was based largely on the suggestion of Dr. Juan Funes, chief of the Venereal Disease Control Division of the Guatemalan Sanidad Publica.[25] Like other Latin American countries that enlisted the aid of the PHS,[26] Guatemala was seeking to build a health infrastructure, and Dr. Funes' familiarity with the PHS facilitated the relationship.[27] The United States wielded enormous economic[28] and political[29] pressure during this time, which likely encouraged the

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21. *See* CTR. FOR DISEASE CONTROL AND PREVENTION, *supra* note 4, at 1 (explaining that the PHS and the PASB "collaborated with several government agencies in Guatemala on U.S. National Institutes of Health-funded studies involving deliberate exposure of human subjects with bacteria that cause sexually transmitted diseases").

22. *See id*. at 5 (stating that the PASB received a grant from the United States to conduct the Guatemala study with the aid of U.S. personnel and Guatemalan cooperation).

23. Bolivar J. Lloyd, *The Pan American Sanitary Bureau*, 20 AM. J. PUB. HEALTH & NATION'S HEALTH 925 (1930), *available at* http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1556056/pdf/amjphnation00625-0021.pdf.

24. *See* Reverby, *supra* note 2, at 11 (stating that "one historian has argued the Pan American Sanitary Bureau 'functioned until the late 1930s…as a virtual branch of the [PHS]'") (citing MARCOS CUETO, MISSIONARIES OF SCIENCE: THE ROCKEFELLER FOUNDATION AND LATIN AMERICA xiii (Bloomington 1994)).

25. *See* CTR. FOR DISEASE CONTROL AND PREVENTION, *supra* note 4, at 5 (stating that Dr. Funes proposed that the United States should conduct the research in Guatemala).

26. *See* Reverby, *supra* note 2, at 11 (discussing the PHS's involvement in developing public health infrastructure in Latin America).

27. *See* Reverby, *supra* note 2, at 9 ("The PHS training of Dr. Juan Funes, Guatemala's leading venereal disease public health official, made the forging of close cooperation easier and the building of a public health infrastructure important.").

28. *See id*. ("The United Fruit Company [, a U.S. company,] owned and controlled much of Guatemala, the quintessential 'banana republic,' in the first half of the twentieth century.").

29. *See id*. ("Between 1944 and the U.S.-led CIA coup of the elected government in

Guatemalan government's collaboration. Moreover, Guatemala was an attractive site because syphilis was not yet prevalent among Guatemalans, supplying a fresh demographic of subjects.[30] Contraction of the diseases could be authentic also because Guatemalan law permitted prostitutes to visit male prisoners.[31]

Given the benefits of testing in Guatemala, the PASB received funding from the PHS.[32] When the PASB allocated responsibilities, it decided the U.S. Venereal Disease Research Laboratory would head the research and provide medical personnel while the Guatemalan government would facilitate training and afford cooperation with government entities.[33] Although deception and secrecy later characterized this study,[34] the scientific community initially regarded the study favorably, and even the U.S. Surgeon General was "keenly interested."[35]

B. Testing Procedures

Respected scientists had high expectations for the Guatemala study because the U.S. researchers examined "syphilization" (human response to fresh infection) and methods of prevention after sexual exposure.[36] Though animal experimentation had provided insight, the researchers wanted to study syphilization via "normal exposure."[37] Normal exposure entailed

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1954, efforts were made at labor protection laws, land reform, and democratic elections.").

30. *See id*. at 11 ("Unlike Alabama, where the PHS expected to find a large number of subjects with the late latent stage of the disease already, Guatemala offered subjects who did not yet have syphilis.").

31. *See* CTR. FOR DISEASE CONTROL AND PREVENTION, *supra* note 4, at 5–6 (stating that "prostitution was legalized to the extent that prostitutes were allowed to pay regular visits to men in penal institutions") (citations omitted).

32. *See id*. (stating that "[a] research grant was made by the USPHS Division of Research Grants," the unit in charge of United States National Institute of Health extramural funding, to the PASB).

33. *See* CTR. FOR DISEASE CONTROL AND PREVENTION, *supra* note 4, at 6 (describing the responsibilities that the VRDL and the Guatemalan government assumed).

34. *See* Reverby, *supra* note 2, at 16 (stating that "[d]eception was central" to the Guatemala study).

35. *See* CTR. FOR DISEASE CONTROL AND PREVENTION, *supra* note 4, at 6 (listing several eminent scientific researchers interested in the study before the study commenced).

36. *See id*. at 12 ("Cutler and Funes had two goals. One was to use what was called 'syphilization' to test the human response to 'fresh infective material to enhance body response to disease . . . [to understand] superinfection and reinfection.' The second goal was to find ways to prevent the disease immediately after exposure.") (citations omitted).

37. *See id*. ("Animal experimentation, especially with rabbits, was long a mainstay in twentieth-century syphilis research, but it could not answer these pressing research

male prisoners receiving visits by prostitutes who were infected, either naturally or artificially.[38] The researchers encountered a problem, however. Even if promised medication, the inmates resisted testing because they believed the frequent samples left them weakened.[39] What is more, the research did not progress as planned because either many men did not contract syphilis[40] or tested positive before normal exposure.[41] Consequently, the group of uninfected subjects grew too small to provide an adequate sample, and the researchers had to abandon testing prisoners.[42]

After fruitless results with prison inmates and inconclusive blood tests on naturally infected children,[43] the researchers turned to patients in the National Mental Health Hospital to determine whether penicillin could be a prophylaxis, not just a cure.[44] Though consent was given, it came from the hospital, not individual patients.[45] The hospital bartered consent for items such as anticonvulsant drugs and cutlery,[46] and qualifying patients[47] were

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questions. The PHS researchers wanted to do a study where they knew there would be a good deal of what they politely called 'normal exposure' to the disease in humans.").

38. *See id*. (stating that men were infected by "prostitutes who tested positive for either syphilis or gonorrhea" or by "uninfected prostitutes [who] had inoculums of the diseases placed on their cervixes"). Interestingly, regardless of which prostitute was employed, U.S. taxpayers paid the prostitutes via the PHS grant. *Id*.

39. *See* Reverby, *supra* note 2, at 13 ("'[T]he inmates were for the most part uneducated and superstitious. Most of them believed they were being weakened' by the frequent blood withdrawals. Even though penicillin and iron pills were promised, 'in their minds there was no connection between the loss of a large tube of blood and possible benefits of a small pill.'").

40. *See id*. ("Not enough of the sexually well-serviced men . . . even when plied with alcohol, seemed to be getting syphilis.") (citations omitted).

41. *See id*. ("The next problem the researchers ran into regarded the blood tests: too many positives even before more 'normal exposure' occurred.").

42. *See id*. ("Since [the researchers] needed men who either had never had the disease or had already been cured of the disease for their studies, they discovered their pool was too small for statistical significance to be possible.").

43. *See* Reverby, *supra* note 2, at 13. Due to the difficulties encountered in prisons, the researchers studied the effectiveness of the blood tests on children between the ages of six and sixteen in the National Orphanage. *Id*. Notably, the researchers did not infect children with syphilis. *Id*. at 13–14. However, the researchers had difficulty ascertaining why eighty-nine children who had no clinical signs of syphilis yielded positive test results, so the researchers abandoned testing this particular population.

44. *See* CTR. FOR DISEASE CONTROL AND PREVENTION, *supra* note 4, at 8–9 (discussing the switch to studies asylum inmates rather than prisoners) (citations omitted).

45. *See* Reverby, *supra* note 2, at 14 ("As in Tuskegee and throughout the global South in these years, the cooperation was sought with the institution, not with the subject-inmates or their families.").

46. *See id*. at 14 (stating the researchers found "the best way to gain that cooperation was by offering supplies . . . [such as] anti-convulsant drugs . . . a refrigerator for

bribed to participate with cigarettes.[48] In order to expose a male patient to the inoculum, a doctor abraded the subject's penis and dripped "syphilitic emulsion" onto a cotton dressing for "at least an hour, sometimes two."[49] Due to cultural beliefs about men viewing women's bodies,[50] women received the inoculum on their forearms, faces, or mouths.[51]

In all the experiments, the records indicate that the human subjects gave no consent.[52] The U.S. Venereal Research Disease Laboratory became uncomfortable with using asylum patients as subjects.[53] So, when the study became too expensive, "the project in Guatemala became difficult to justify."[54] As a result, the United States' direct involvement concluded when the study was terminated in 1948. Two local physicians and the PASB continued to observe patients as late as 1953.[55] Questionable ethics

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biologicals, a motion picture projector that supplied the sole recreation for the inmates, metal cups, plates and forks to supplement the completely inadequate supply available") (citations omitted).

47. *See* CTR. FOR DISEASE CONTROL AND PREVENTION, *supra* note 4, at 10 (stating subjects were selected "based on baseline serologic findings and a history of syphilis, perceived cooperativity, and the likelihood that the subject would not be released" before the study concluded).

48. *See* Reverby, *supra* note 2, at 14 ("Individual subjects were offered cigarettes: an entire packet for inoculation, blood draws, or spinal taps, and a single cigarette for 'clinical observation.'") (citations omitted).

49. *Id*. at 15 ("[A] doctor held the subject's penis, pulled back the foreskin, abraded the penis slightly just short of drawing blood by scraping the skin with a hypodermic needle, introduced a cotton pledget (or small dressing), and dripped drops of the syphilitic emulsion onto the pad and through it to the roughed skin on the man's penis for at least an hour, sometimes two.").

50. *See id*. at 15 (stating that there were "local prejudices against male viewing of the body, even by physicians" (quotations omitted)).

51. *See id*. (stating that "the inoculum was inserted after needles were used to abrade the women's forearms, face or mouth").

52. *See* Reverby, *supra* note 2, at 21 (stating that the researchers "were morally capable of infecting people with syphilis, for their faith in their cause allowed them to infect people with this dreadful disease without their consent or even knowledge— at least when those people lacked power and white skin").

53. *See id*. at 19 (stating that U.S. authorities "seemed less concerned with the prostitute transmission studies taking place in the prison, but seemed more squeamish about the politics and morality of the inoculation studies taking place in the mental hospital") (citations omitted).

54. Reverby, *supra* note 2, at 17.

55. *See* CTR. FOR DISEASE CONTROL AND PREVENTION, *supra* note 4, at 22 ("Although syphilis serologic results and follow-up clinical observations were recorded on some subjects until 1953, there is no record of what activities occurred after patient follow-up was taken over by PASB and the two local physicians, nor whether further human inoculation studies were performed . . . .").

continued, however, because "while the majority of exposed and infected subjects appear[ed] to have eventually been prescribed doses of penicillin, treatment was routinely delayed for several months after exposure and a substantial number of subjects were never treated."[56]

C. Informed Consent

Though it may not be obvious from the behavior in the Guatemala study, both the American public and the medical profession were well-aware of unethical experiments.[57] Criticism was voiced in the United States as early as 1833, when U.S. surgeon William Beaumont announced that doctors ought to secure "free consent" from patients before procedures.[58] In fact, surgeons and hospital administrators sought written consent from patients in the late nineteenth and twentieth centuries.[59]

Despite early advocacy for patient rights, attitudes shifted with the onset of World Wars I and II when scientific research became "one essential key to our security as a nation, to our better health, to more jobs, to high standard of living, and to our cultural progress."[60] The medical profession itself did not advocate for patient rights but successfully "undertook great efforts . . . to block legal initiatives aimed at the restriction of experiments on humans."[61] The U.S. government intervened only when

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56. *Id*. at 21.

57. *See* WOLFGANG WEYERS, THE ABUSE OF MAN: AN ILLUSTRATED HISTORY OF DUBIOUS MEDICAL EXPERIMENTATION 174 (Ardor Scribendi, Ltd. 2003) ("[P]rofound respect for the rights of individuals inherent in the Constitution of the United States of America [initially] lowered the threshold for tolerance for unconscionable treatment of patients.").

58. *See id*. ("Nowhere, however, was criticism of human experimentation as vociferous as in the United States . . . As early as 1833, an American surgeon, William Beaumont, called for the procurement of 'free consent' of patients prior to having any medical experiment performed on them.") (citing THE NAZI DOCTORS AND THE NUREMBERG CODE: HUMAN RIGHTS IN HUMAN EXPERIMENTATION 121–44 (George J. Annas & Michael A. Grodin eds., New York, Oxford University Press 1992)).

59. *See id*. at 178 ("In the late nineteenth and early twentieth centuries, the growing number of lawsuits concerning unauthorized surgical procedures prompted surgeons and hospital administrators to introduce forms for written consent.").

60. *Id*. (citing FADEN RR ET AL., FINAL REPORT OF THE ADVISORY COMMITTEE ON HUMAN RADIATION EXPERIMENTS 10 (1995)).

61. WEYERS, *supra* note 57, at 214; *see also* U.S. DEP'T. OF HEALTH AND HUMAN SERVS., INFORMATION ON PROTECTION OF HUMAN SUBJECTS IN RESEARCH FUNDED OR REGULATED BY U.S. GOVERNMENT: HOW TODAY'S RULES PROHIBIT ETHICAL ABUSES IN HUMAN SUBJECTS RESEARCH 1 (2010) [hereinafter INFORMATION ON PROTECTION], *available at* http://www.hhs.gov/1946inoculationstudy/information_on_protection_of_human_subjects_in_research.pdf ("There was tremendous growth in research around World War II. Human subjects research entered what some scholars have described as an 'unashamedly

it sensed "serious adverse reactions from the public"[62] and greatly enlarged its spending on medical research during this period.[63] As a result, when the Guatemala study occurred in the late 1940s, the U.S. government both broadly funded and routinely ignored active human experimentation.

In light of the flexible approach to ethics adopted by medical researchers and the financial endorsement by the U.S. government, one could speculate that the researchers knew their actions could be deemed morally unethical, but they were unsure of legal standards.[64] According to the Department of Health and Human Services, no specific codes, laws, or regulations governed the ethics of human experimentation during that time period.[65] While no binding law oversaw experimentation in an international setting, U.S. law did control research conducted in the United States. Consequently, it was likely that the U.S. research team in Guatemala was aware of legal and ethical standards.

1. U.S. Legislation & Ethical Codes

At the time of the Guatemala study, the United States had no legislation that required medical researchers to obtain informed consent.[66] The American public, however, had expressed interest in regulating animal and human research.[67] Between 1900 and 1924, state legislatures discussed

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utilitarian phase.'").

62. *Id*. (stating that consent was only sought when "researchers and administrators of the Committee of Medical Research sensed the possibility of serious adverse reaction from the public").

63. *See id*. at 174 ("In 1945, the U.S. government spent approximately $700,000 on medical research. Ten years later, the total had climbed to $36 million . . . .").

64. *See* Reverby, *supra* note 2, at 19 ("Malaria specialist G. Robert Coatney, who had done prison malaria studies, visited the project in February 1947. In reporting to Cutler after he returned to the States, he explained that he had brought Surgeon General Thomas Parran up to date and that with a merry twinkle [that] came into his eye . . . [he] said, 'You know, we couldn't do such an experiment in this country.'") (quotations omitted) (citations omitted).

65. *See* INFORMATION ON PROTECTION, *supra* note 61, at 1 ("Prior to World War II there were no specific codes of ethics, laws, or regulations governing the conduct of human subjects research.").

66. *See* Jennifer J. Couture, Note, *The Changes in Informed Consent in Experimental Procedures: The Evolution of a Concept*, 1 J. OF HEALTH & BIOMED. L. 125, 134 (2004) (stating that since the turn of the century, the FDA had regulations in place to protect the public from harmful experimental or untested treatments; however, these regulations largely focused on protecting consumers from misbranded or adulterated food, drugs, and cosmetics).

67. *See* WEYERS, *supra* note 57, at 195–202 (discussing legislation regulating animal vivisection and other legislation opposing experimentation on humans supported by public

bills that restricted experimentation on humans and animals, though none passed successfully.[68] The first federal bill regarding human experimentation, Senate Bill 3424, was introduced by Senator Gallinger of New Hampshire in 1900.[69] The bill proposed regulating experiments in the District of Columbia by requiring prior disclosure of research methods, mandating written consent from human subjects,[70] and prohibiting experimentation upon vulnerable people.[71] Both the medical profession and Congress rejected the bill.[72] Indeed, the president of the American Medical Association (AMA) considered Senate Bill 3424 unnecessary because experiments using human subjects were "rare."[73] Remarkably, human subject research, including vivisection (experimental surgery on a living organism), occurred across the country at this time.[74]

No legislation governed human subject research, and the effect of William Beaumont's ethics code and others proposed at this time were "practically nil."[75] The AMA, however, had addressed the issue of ethics

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groups).

68. *See id*. at 202 (discussing that proposed legislation in Illinois, Pennsylvania, and other state legislatures were considering regulating human and animal experimentation) (citations omitted).

69. *See id*. at 201 ("Senator Gallinger introduced a proposal for the regulation of experiments on humans in the District of Columbia.").

70. *See id*. (stating that "Senate Bill 3424 required prior disclosure of 'the objects and methods of the proposed experiment' to Commissioners of the District, who could then issue a specific license for performance of the experiment" that had to include the witnessed and notarized written permission of test subjects) (citing S.E. LEDERER, SUBJECTED TO SCIENCE: HUMAN EXPERIMENTATION IN AMERICA BEFORE THE SECOND WORLD WAR 143–46 (1997)).

71. *See id*. (stating that a subject had to be at least twenty years old and "in full and complete possession of all his or her reasoning faculties" and experiments involving children, "women during and for one year after pregnancy," and "any aged, infirm, epileptic, insane, or feeble-minded person were prohibited") (citing S.E. LEDERER, SUBJECTED TO SCIENCE: HUMAN EXPERIMENTATION IN AMERICA BEFORE THE SECOND WORLD WAR 143–46 (1997)).

72. *See id*. at 202 ("The proposed legislation was rejected out of hand, and harshly, by the medical profession . . . [And] Gallinger's bill was defeated [by Congress], as was a new version of it that he introduced in 1902.").

73. *See id*. (stating that the medical profession and Congress rejected the bill because "experiments in humans were so rare that a special act of Congress was not needed to control them").

74. *See id*. at 195–210 (describing experiments such as human and animal vivisection or exposing healthy children to diseases that inspired the public to call for regulation) (citations omitted).

75. *See* WEYERS, *supra* note 57, at 43–44 ("[Beaumont's proposal] and other ethical codes for experiments on humans were proposed in the early 1830s, a time when systematic medical experiments had just begun. The impact of those proposals, however, were practically nil.").

generally.[76] In 1847, nearly a hundred years before the Guatemala study, the AMA issued The Principles of Medical Ethics[77] to outline physicians' obligations.[78] Physicians were to treat patients with "attention and humanity."[79] But, it also warned physicians "to avoid all things which have a tendency to discourage the patient and to depress his spirits" because physicians ought to be "a minister of hope and comfort."[80] These conflicting messages suggest that informed consent may not have been a priority if it interfered with medical results or good spirits.[81] However, after the Nuremberg trials, when human experimentation received more international outrage, the AMA issued a clearer statement:[82]

> In order to conform to the ethics of the American Medical Association, three requirements must be satisfied: (1) the voluntary consent of the person on whom the experiment is to be performed; (2) the danger of each experiment must be previously investigated by animal experimentation; and (3) the experiment must be performed under proper medical protection and management.[83]

Despite this step towards more protective guidelines, the AMA's principles still lacked specific provisions dealing with consent that was not only voluntary, but also informed and protecting of vulnerable people.[84] As

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76. *See* American Medical Association House of Delegates, *Minutes of New Orleans Session: Principles of Medical Ethics*, 1903 J. AM. MED. ASS'N 1379, 1379 (stating the ethical principles physicians owed).

77. *See* American Medical Association, *History of AMA Ethics: Ethics Timeline: 1847 to 1940*, http://www.ama-assn.org/ama/pub/physician-resources/medical-ethics/code-medical-ethics/history-ama-ethics/ethics-timeline-1847-1940.page (last visited Apr. 2, 2012) (stating that in 1847 the "AMA Code of Medical Ethics [was] written and published") (on file with the Washington and Lee Journal of Civil Rights and Social Justice).

78. *See* American Medical Association House of Delegates, *supra* note 76, at 1379 (stating that physicians have duties towards their patients, to each other and the profession at large, and the public, and each obligation has an article enumerating the duties).

79. *See id*. at 1379–80 (stating the ethical code to which the AMA recommended medical officials adhere).

80. *Id*. at 1379.

81. *See* Douglas Andrew Grimm, *Informed Consent for All! No Exceptions*, 37 N.M.L. REV. 39, 39 (2007) (stating that physicians were cautioned not to disclose all medical truths to patients and "the American Medical Association's first code of ethics warned the physician 'to avoid all things which have a tendency to discourage the patient and to depress his spirits'").

82. *See* WEYERS, *supra* note 57, at 351–52 (stating that the AMA was induced "to issue guidelines for experiments on human beings" at the same time as the *Nuremberg Code* was drafted).

83. *Id*. at 631 (emphasis added).

84. *See id*. at 352 ("Compared with earlier regulations . . . the AMA principles were

a result, even ethics codes that self-regulated the medical profession did not truly protect human subjects.

2. U.S. Case Law

Though statutory law was scarce and ethics codes were ineffective, a small body of case law emerged in the years before the Guatemala study.[85] In 1914, while sitting on the New York Court of Appeals, Justice Benjamin Cardozo decided *Schloendorff v. Society of N.Y. Hospital*.[86] The decision has "probably [had] the most impact on the doctrine of informed consent."[87] In *Schloendorff,* a woman consented to exploratory surgery and explicitly withheld consent to surgical removals; the surgeon removed a tumor anyway.[88] Justice Cardozo found that even though the surgery benefited the patient, "[e]very human being of adult years and sound mind has a right to determine what shall be done with his own body; and a surgeon who performs an operation without his patient's consent, commits an assault, for which he is liable in damages."[89] Consequently*, Schloendorff* established that a patient has the right to actively participate in making medical choices.[90] After *Schloendorff*, the patient's right to give or withhold consent to medical procedures (particularly surgical operations) was celebrated, and courts throughout the United States followed Cardozo's principles.[91]

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somewhat primitive, lacking provisions for informed consent and the protection of particularly vulnerable populations.").

85. *See* Peter M. Murray, *History of Informed Consent*, 10 IOWA ORTHOPAEDIC J. 104, 105 (1990) (describing the history of American case law that has shaped modern informed consent).

86. Schloendorff v. Soc'y of N.Y. Hosp., 211 N.Y. 125, 129–30 (1914), *overruled by* Bing v. Thunig, 2 N.Y.2d 656 (1957) (determining that "[e]very human being of adult years and sound mind has a right to determine what shall be done with his own body; and a surgeon who performs an operation without his patient's consent, commits an assault, for which he is liable in damages").

87. Murray, *supra* note 85, at 105.

88. *See* WEYERS, *supra* note 57, at 178 ("[A] woman consented to an exploratory abdominal operation but insisted that no surgical removal be performed. After her surgeon removed a fibroid tumor discovered during the course of the operation, she brought suit against the hospital.").

89. *Schloendorff*, 211 N.Y. at 129–30.

90. *See id*. at 130 (stating that the principle that a patient has a right to give consent "is true except in cases of emergency where the patient is unconscious and where it is necessary to operate before consent can be obtained").

91. *See, e.g.*, Birnbaum v. Siegler, 76 N.Y.S.2d 173, 174 (N.Y. App. Div. 1948) ("Performance of an operation without valid consent previously obtained constitutes an

After *Schloendorff*, a patient may have had the right to consent to surgical procedures, but the standards were still very different for individuals in mental institutions. Medical researchers often used these populations, who were unable to give legal consent, because researchers knew that abuse of "those who lacked advocacy . . . would likely go unnoticed."[92] Affirming this attitude, the Supreme Court decided *Buck v. Bell*.[93] The Court famously upheld a Virginia law that permitted sexual sterilization of intellectually disabled persons without the person's consent.[94] Instead of supporting individual patient consent, the Supreme Court endorsed the principle that the State's consent (via a mental institution superintendent) was sufficient.[95]

Although the Supreme Court established in *Buck v. Bell* that consent to medical procedures need not be sought from asylum patients,[96] the Court implicitly abandoned this doctrine sixteen years later. In *Skinner v. Oklahoma*,[97] the Court invalidated a statute that forced sterilization of

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assault on the patient, for which the surgeon would be liable.") (citing Schloendorff v. Soc'y of N.Y. Hosp., 211 N.Y. 125, 130 (1914), *overruled by* Bing v. Thunig, 2 N.Y.2d 656 (1957)); *see also* Bonner v. Moran, 126 F.2d 121, 122 (D.C. Cir. 1941) (adopting the rule that "surgical operation is a technical battery, regardless of its results, and is excusable only when there is express or implied consent by the patient; or, stated somewhat differently, the surgeon is liable in damages if the operation is unauthorized") (citing *Schloendorff*, 211 N.Y. at 130); *see also* Donald v. Swann, 137 So. 178, 180 (Ala. Ct. App. 1931) (adopting the "general rule . . . supported by unquestioned authority" that "every human being of adult years and sound mind has a right to determine what shall be done with his own body" so any operation performed without consent and over the patient's protests is an assault and battery) (citing *Schloendorff*, 211 N.Y. at 130).

92. *See* WEYERS, *supra* note 57, at 174 ("[T]he evidence of intolerance of Americans in regard to experiments on humans led scientists to utilize the most vulnerable populations [such as prisoners, orphans, and mental patients].").

93. Buck v. Bell, 274 U.S. 200, 207 (1927) (finding that "[i]t is better for all the world, if instead of waiting to execute degenerate offspring for crime, or to let them starve for their imbecility, society can prevent those who are manifestly unfit from continuing their kind" and "the principle that sustains compulsory vaccination is broad enough to cover cutting the Fallopian tubes") (citing Jacobson v. Massachusetts, 197 U.S. 11 (1905)).

94. *See id*. at 205–07 (finding that a Virginia law that allowed sterilization for the health of the patient and the betterment of society was constitutionally sound).

95. *See id*. at 205 (stating that the statute permitted a superintendent, who is "of opinion that it is for the best interests of the patients and of society that an inmate under his care should be sexually sterilized . . . may have the operation performed upon any patient afflicted with hereditary forms of insanity, imbecility, [etc.]").

96. *See supra* notes 93–98 and accompanying text (explaining that the Supreme Court upheld a law that allowed superintendents of mental institutions to substitute their consent for that of the patients).

97. Skinner v. Oklahoma, 316 U.S. 535, 538 (1942) (finding that an Oklahoma statute that permitted sexual sterilization of recidivist criminals who committed crimes of moral

recurring criminals.[98] The Court found that the statute contravened the Equal Protection Clause of the Fourteenth Amendment[99] because sexual sterilization caused "irreparable injury."[100] Although the Court did not directly address a prisoner's right to grant or withhold consent, the emphasis the Court placed on the irreversibility of the injury diminishes the notion that the State's consent may be substituted for a patient's consent.[101] Hence, *Schloendorff* suggested that doctors must seek consent from their patients or face liability, but whether the government may consent instead of an asylum patient or criminal remained less clear.[102]

3. Guatemalan & International Standards

While the United States had limited legal authority pertaining to human subject research, Guatemala and international law had fewer sources. Due to the influence by the military and U.S. economic power, Guatemala was known for its "relative freedoms" immediately post-World War II.[103]

Until 1944, just before the Guatemala study, General Ubico administered law without challenge and governed Guatemala with military rule[104] (militarization of Guatemalan society was interrupted from 1944–54

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turpitude ran afoul of the Equal Protection Clause of the Fourteenth Amendment).

98. *See id*. at 536–37 (stating that a "habitual criminal" was "a person who, having been convicted two or more times for crimes 'amounting to felonies involving moral turpitude'" and "[m]achinery is provided for the institution by the Attorney General of a proceeding against such a person in the Oklahoma courts for a judgment that such person shall be rendered sexually sterile").

99. *See* U.S. CONST. amend. XIV, § 1 ("No state shall . . . deny to any person within its jurisdiction the equal protection of the laws.").

100. *See Skinner*, 316 U.S. at 541 ("[The statute] runs afoul of the equal protection clause, though we give Oklahoma that large deference which the rule of the foregoing cases requires . . . marriage and procreation are fundamental to the very existence and survival of the race . . . any experiment which the State conducts is to his irreparable injury.").

101. *See id*. ("Any experiment which the State conducts is to his irreparable injury. He is forever deprived of a basic liberty.").

102. *See supra* notes 86–94 and accompanying text (discussing *Schloendorff* and the essentialness of informed consent to experimental medical procedures).

103. Reverby, *supra* note 2, at 11 ("When the PHS looked to Guatemala for its research in the immediate post-World War II years, it came into the country during the period known for its relative freedoms.").

104. *See* HILDE HEY, GROSS HUMAN RIGHTS VIOLATIONS: A SEARCH FOR CAUSES: A STUDY OF GUATEMALA AND COSTA RICA 28 (The Hague 1995) ("General Ubico ruled Guatemala for fourteen years, between 1931 and 1944; he advanced military rule without being challenged.").

due to a coup led by the CIA).[105] General Ubico also advanced the interests of the United Fruit Company,[106] a U.S. entity that "owned and controlled much of Guatemala" at that time.[107] As a result, the Guatemalan military continued to rigidly secure internal law and order during the Guatemalan study,[108] but the U.S. economic influence also likely incentivized cooperation.[109] Moreover, with the cooperation of Guatemala's Ministry of Health, the National Army of the Revolution, the National Mental Health Hospital, and the Ministry of Justice, no real regulation was imposed on the study.[110] Instead, the Guatemalan government demanded medical services as the price of cooperation.[111]

Bolstered by Guatemala's endorsement, the Pan American Sanitary Bureau orchestrated the Guatemala study.[112] The PASB enacted The Pan American Sanitary Bureau Code in 1924,[113] onto which Guatemala signed in 1924 and the U.S. Senate ratified in 1925.[114] The purpose of the code

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105. *See* Reverby, *supra* note 2, at 11 (stating that the CIA led a coup of the elected government in 1954).

106. *See* HEY, *supra* note 104, at 28 (stating that General "Ubico enhanced the interests of foreign companies, particularly the United Fruit Company").

107. Reverby, *supra* note 2, at 11.

108. *See* HEY, *supra* note 104, at 28 (discussing the militarization of Guatemalan government).

109. *See* United Fruit Historical Society, *Chronology*, http://www.unitedfruit.org/chron.htm (last visited Apr. 2, 2012) (describing the United Fruit Company's history, its extensive influence, and the freedoms the Guatemalan government allowed the company) (on file with the Washington and Lee Journal of Civil Rights and Social Justice).

110. *See* Reverby, *supra* note 2, at 9 ("[T]he PHS cooperated with officials at the Guatemala's Ministry of Health, the National Army of the Revolution, the National Mental Health Hospital and Ministry of Justice on what was benignly called 'a series of experimental studies on syphilis in man.'").

111. *See id*. at 17 ("[The Guatemalan officials] asked Cutler to test and treat men in army barracks, to do surveys of disease in the lowlands, and to provide more penicillin for the country as part of the price for cooperation. He traded off drugs for malaria at the orphanage for the right to continue blood testing.").

112. *See* CTR. FOR DISEASE CONTROL AND PREVENTION, *supra* note 4, at 5 (stating that the PASB received a grant from the United States to conduct the Guatemala study with the aid of U.S. personnel and Guatemalan cooperation).

113. *See* Seventh Pan American Sanitary Conference, *The Pan American Sanitary Code: International Sanitary Convention Signed at Habana, Cuba, November 14, 1924*, 40 PUB. HEALTH REP. 483, 484–85 (1925), *available at* http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1975980/pdf/pubhealthreporig02451-0001.pdf (stating that "[t]he Presidents of Argentine, Brazil, Chile, Colombia, Costa Rica, Cuba, Dominican Republic, Guatemala, Haiti, Honduras, Mexico, Salvador, Panama, Paraguay, Peru, United States of America, Uruguay, and Venezuela" entered into a sanitary convention to promote and protect the health of their nations).

114. *See id*. at 483 ("In executive session on February 23, 1925, the Senate of the

was to "better promot[e] and protect[] the public health."[115] The code focused on preventing the spread of infectious diseases by mandating each country to report outbreaks of diseases and take precautionary measures at borders, ports, or airports.[116] Significantly, despite extensive regulation of travel, the code mentions no premium on the value of human life or dignity, an attitude shared by the Guatemala study's research team.[117]

In addition to oversight imposed by the PASB, the World Health Organization (WHO), a specialized agency of the United Nations, ratified a constitution in 1946 onto which both the United States and Guatemala signed.[118] Guatemala and the United States dedicated themselves to the objective of "attainment by all peoples of the highest possible level of health"[119] and "developing an informed public opinion among all peoples on matters of health."[120] However, the WHO did not have its First World Health Assembly until 1948.[121] Prior to the Assembly, the Interim Commission endeavored to take over the fight against venereal diseases and to integrate regional health organizations such as the PASB.[122] As a result, the WHO did not have much influence during the time of the Guatemala study, and the PASB's goals, with its minimal concern for individuals, remained the dominant attitude.[123]

United States ratified the international sanitary convention of the American Republics . . . .").

115. *Id*. at 484.

116. *See id*. at 489–97 (discussing the sanitary codes and documentation needed for people traveling and transporting goods between countries).

117. *See generally id*. at 483–98.

118. *See* Constitution of the World Health Organization (New York, July 22, 1946) 14 U.N.T.S. 185, *entered into force* Apr. 7, 1948, *available at* http://whqlibdoc.who.int/hist/official_records/constitution.pdf (showing the signatures of the delegates of Guatemala and the United States).

119. *Id*. at Chapter I: Objective, Art. 1.

120. *Id*. at Chapter II: Functions, Art. 2(r).

121. *See* YVES BEIGBEDER, THE WORLD HEALTH ORGANIZATION, 12–13 (Martinus Nijhoff Publishers 1998) (stating that the First World Health Assembly met in June 1948 when it adopted most of the policies of the Interim Commission).

122. *See id*. at 12 (stating that objectives of the Interim Commission were to take over "the activities of former health organizations," which included fighting against venereal diseases and integrating regional health organizations).

123. *See supra* note 36–59 and accompanying text (discussing the PASB's lack of concern for human life and dignity).

4. Compliance of the Researchers

The medical researchers in Guatemala did not seek consent from the study participants and tried to conceal their actions.[124] However, given the notoriety of human experimentation, the U.S. researchers were likely aware of the issue.[125] When one evaluates the researchers' choices against U.S., Guatemalan, and international standards, a confusing picture emerges.

Both the U.S. medical profession and the American public altered their opinions repeatedly on the matter of human experimentation during the first half of the twentieth century—advocating against experimentation, denying that experimentation occurred, and finally turning a blind eye.[126] Early ethical code proposals were largely ignored,[127] and when one considers the events of the Guatemala study and the legality of those actions, it is important to note that while the AMA's advisory statement may have tugged at the moral heartstrings of physicians, it was not binding.[128] The medical profession favored medical progress rather than informed consent.[129] Still, the researchers in Guatemala tried to conceal their actions[130] because they realized the profession would not publicly approve of the methods used.[131]

Like the medical profession, U.S. case law sent a conflicting message. Under *Schloendorff*, a doctor ought to seek informed consent,[132] and

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124. *See* Reverby, *supra* note 2, at 16–18 (discussing the deceptions that characterized the research).

125. *See id.* at 18–20 (discussing the concerns that Cutler and other U.S. researchers had about the ethics of the study).

126. *See supra* notes 60–63 and accompanying text (discussing early activism against medical experimentation without consent and the changes in attitude with the advent of World Wars I and II).

127. *See supra* note 65 and accompanying text (stating that the effect of ethical codes during this time were "practically nil").

128. *See* American Medical Association House of Delegates, *supra* note 76, at 1379 (stating that the AMA ethical code was only "suggested and advisory").

129. *See supra* notes 60–61 and accompanying text (discussing the attitude of the medical profession post-World Wars I and II).

130. *See id*. (noting that the researchers tried to experiment in secrecy, and Cutler's supervisor warned, "I hope you will not hesitate to stop the experimental work in the event of there being an undue amount of interest in that phase of the study").

131. *See* Reverby, *supra* note 2, at 20 ("Cutler, too, acknowledged that other syphilogists thought human experimentation on penicillin as a prevention for syphilis that required inoculation with the disease 'could not be ethically carried out.'").

132. *See supra* notes 89–94 and accompanying text (discussing that *Schloendorff* established the importance of informed consent in medical procedures).

Skinner suggested that criminals may claim similar protections.[133] However, because *Buck v. Bell* was not overruled, it remained unclear whether asylum patients have comparable rights.[134] Moreover, no U.S. legislation or case law defined what was appropriate internationally.[135] In addition to the cacophony of U.S. messages, the Guatemalan government prioritized providing services to its people rather than protection of individual rights.[136] International organizations did not clarify ethics either. The United States and Guatemala had voluntarily signed onto the WHO constitution, which valued developing an informed public opinion.[137] Yet, the United States and Guatemala supported the methods employed at the Guatemala study; thus, the Guatemala researchers did not comply with a guideline to which their governing country had voluntarily agreed.

The researchers did not fulfill the spirit of U.S. law or other standards because researchers did not prioritize the health and safety of patients by seeking consent.[138] Instead, the researchers pursued medical science's gain in a developing country with vulnerable people. Although the researchers may not have been legally bound to seek informed consent, it is more accurate to characterize them as intentionally avoiding the law. They deliberately deceived the participants[139] and knew their practices would not be received well in U.S. medical circles.[140] In addition, they sought a testing site in Guatemala, far from the United States' jurisdiction. However, if one considers the combination of confusing legal standards and the regularity of experimenting on human subjects at that time, the context

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133. *See supra* note 91 and accompanying text (suggesting that the Supreme Court implied that consent to medical procedures, specifically sexual sterilization, must be given by the individual rather than the State).

134. *See supra* note 91 and accompanying text (stating that the Supreme Court found that the State may substitute its consent to a medical procedure, specifically sexual sterilization, for that of an intellectually disabled person).

135. *See supra* notes 66–87 and accompanying text (discussing the lack of U.S. legislation and case law that applied in the international context).

136. *See supra* note 111 and accompanying text (stating that the Guatemalan government cooperated so that its people received other medical services).

137. *See supra* notes 119–26 and accompanying text (discussing the WHO's goals of providing the public with an informed opinion).

138. *See supra* notes 66–87 and accompanying text (discussing the consent requirements found in U.S. case law and implied in the AMA's Code).

139. *See* Reverby, *supra* note 2, at 16 ("Deception was central [to the researchers of the study].").

140. *See id*. at 18 ("Everyone involved with these studies [in Guatemala] seemed to know they were treading on complicated ethical grounds.").

of the research renders the researchers' actions more explicable, not more sympathetic.

II. Modern Informed Consent

The director of the National Institutes for Health, Dr. Francis Collins, characterized the Guatemala study as "a dark chapter in the history of medicine."[141] This dark chapter includes a litany of twentieth century U.S. studies such as STD studies at Tuskegee,[142] studies that abused prisoners[143] or patients of mental institutions,[144] and studies that exploited the poor.[145]

Unlike the 1940s, there are now a host of modern ethics standards for conducting research on human subjects outside the United States.[146] The landscape of informed consent has changed significantly, both domestically and internationally. The CDC asserted human subjects are protected by federal regulations that require Institutional Review Boards (IRBs) to monitor research continuously,[147] mandate that researchers fully explain the risks of participation and thereafter acquire informed consent, [148] and protect vulnerable populations.[149] The CDC did not mention the

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141. The CNN Wire Staff, *supra* note 3.

142. *See generally* SUSAN REVERBY, EXAMINING TUSKEGEE: THE INFAMOUS SYPHILIS STUDY AND ITS LEGACY (Waldo E. Martin Jr. & Patricia Sullivan eds., The University of North Carolina Press) (2010) (exploring the events of the Tuskegee syphilis experiment and the implications afterwards for medicine and "American life").

143. *See* Allen M. Horblum, *They Were Cheap and Available: Prisoners as Research Subjects in Twentieth Century America*, 315 BRIT. MED. J. 1437, 1437–41 (1997) (describing the history of using prisoners and the shift in the medical community from viewing prisoners as "raw material for medical experiments" at the beginning of the century to ending the practice in the 1970s).

144. *See generally* WEYERS, *supra* note 57.

145. *See id*.

146. *See, e.g.*, UNIVERSITY OF SOUTH FLORIDA HUMAN RESEARCH PROTECTION PROGRAM, POLICY NO. 304: TRANSNATIONAL HUMAN SUBJECTS RESEARCH (2010), *available at* http://www.research.usf.edu/dric/hrpp/irbpolicies/Policy%20304%20Transnational%20Human%20Subjects%20Research.pdf (establishing guidelines for use when USF or a USF affiliate conducts human subject research outside the United States).

147. *See* INFORMATION ON PROTECTION, *supra* note 61, at 2 ("Human subject research is reviewed and approved by an IRB . . . .").

148. *See id*. ("Dr. Cutler and his colleagues used deception to infect vulnerable captive individuals in Guatemala. This is prohibited today. Researchers must fully explain the risks associated with their study to all research participants. Participants must indicate their informed consent.").

149. *See id*. ("Current Federal regulations provide additional protections and special requirements for research involving children and prisoners and instruct IRBs to be cognizant

effectiveness of international sources in protecting human subjects, but these sources are still influential and aided in shaping U.S. regulations.[150] Ultimately, though there is a concerted effort to regulate human subject research, exact legal requirements remain confusing, just as informed consent regulations did at the time of the Guatemala study.

A. The Belmont Report

The Belmont Report was created in 1979 and was one of the first U.S. efforts to address the ethics of human experimentation.[151] Its basic principles intend to "assist in resolving ethical problems" that arise when researchers use human subjects.[152] The Report values three principles: respect, beneficence, and justice.[153] Respect represents a dual moral obligation that recognizes not only the right of each individual to exercise autonomy, but also that a person with diminished capacity (and therefore diminished autonomy) deserves protection.[154] Beneficence obliges researchers firstly, to do no harm, and secondly, to maximize benefits and

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of the special problems of research involving vulnerable populations . . . Studies seeking to enroll vulnerable subjects must provide additional safeguards to protect the rights and welfare of these subjects.").

150. *See* Joan M. Doherty, *Form Over Substance: The Inadequacy of Informed Consent and Ethical Review for Thai Injection Drug Users Enrolled in HIV Vaccine Trials*, 15 PAC. RIM L. & POL'Y J. 101, 112 (2006) ("Nonetheless, the Nuremberg Code and Declaration of Helsinki . . . have all influenced the creation of law and policy in the United States.") (citations omitted).

151. *See* National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, *The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research Summary* (1979), *available at* http://www.fda.gov/ohrms/dockets/ac/05/briefing/2005-4178b_09_02_Belmont%20Report.pdf ("[The Belmont Report] is the outgrowth of an intensive four-day period of discussions that were held in February 1976 at the Smithsonian Institution's Belmont Conference Center supplemented by the monthly deliberations of the Commission that were held over a period of nearly four years.").

152. *See id*. (stating that the Belmont Report "is a statement of basic ethical principles and guidelines that should assist in resolving the ethical problems that surround the conduct of research with human subjects").

153. *See id*. at Part B ("Three basic principles, among those generally accepted in our cultural tradition, are particularly relevant to the ethics of research involving human subjects: the principles of respect of persons, beneficence and justice.").

154. *See id*. at Part B.1 ("Respect for persons incorporates at least two ethical convictions: first, that individuals should be treated as autonomous agents, and second, that persons with diminished autonomy are entitled to protection.").

minimize risks.[155] The last concept of justice denotes a concern with distribution of fairness,[156] which can be conceptualized as equality.[157]

In applying the principles of respect, beneficence, and justice, informed consent emerges as a necessity.[158] Informed consent gives subjects the "opportunity to choose what shall or shall not happen to them."[159] This opportunity to choose is provided when the elements of information, comprehension, and voluntariness are satisfied.[160] Information demands sufficient disclosure,[161] which includes answering a subject's direct inquiries honestly and never withholding information about risks.[162] To ensure comprehension, researchers must "adapt the presentation of the information to the subject's capacities,"[163] and as risks to the subject increase, so does the obligation to certify comprehension.[164] Lastly, consent must be given voluntarily, without coercion or undue influence.[165]

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155. *See id*. at Part B.2 (defining beneficence as an obligation; as a result, "[t]wo general rules have been formulated as complementary expressions of beneficent actions in this sense: (1) do not harm and (2) maximize possible benefits and minimize possible harms").

156. *See id*. at Part B.3 (stating that justice is choosing "[w]ho ought to receive the benefits of research and bear its burdens" and "[a]n injustice occurs when some benefit to which a person is entitled is denied without good reason or when some burden is imposed unduly").

157. *See id*. ("Another way of conceiving the principle of justice is that equals ought to be treated equally.").

158. *See id*. at Part C.1 ("Applications of the general principles to the conduct of research leads to consideration of the following requirements: informed consent, risk/benefit assessment, and the selection of subjects of research.").

159. *Id*.

160. *See id*. (stating that the opportunity for choice "is provided when adequate standards for informed consent are satisfied" and "there is widespread agreement that the consent process can be analyzed as containing three elements: information, comprehension, and voluntariness").

161. *See id*. (stating that disclosure is "intended to assure that subjects are given sufficient information" and "[e]ven when some direct benefit to them is anticipated, the subjects should understand clearly the range of risk and the voluntary nature of participation").

162. *See id*. ("Information about risks should never be withheld for the purpose of eliciting the cooperation of subjects, and truthful answers should always be given to direct questions about the research.").

163. *See id.* ("Because the subject's ability to understand is a function of intelligence, rationality, maturity, and language, it is necessary to adapt the presentation of the information to the subject's capacities.").

164. *See id*. ("While there is always an obligation to ascertain that the information about risk to subjects is complete and adequately comprehended, when the risks are more serious, that obligation increases.").

165. *See id*. ("An agreement to participate in research constitutes a valid consent only if

B. The DHHS & the FDA's Current Regulations

Building on the Belmont Report's ethical foundation,[166] the central improvement to U.S. legal standards since the Guatemala study is federal regulation. The Department of Health and Human Services (DHHS) and the Food and Drug Administration (FDA) regulate all experiments involving human subjects in a dovetailing fashion so that at times they govern jointly and at other times independently.[167]

The DHHS binds fifteen U.S. agencies[168] and broadly oversees all human experiments that are "conducted, supported or otherwise subject to regulation by any federal department or agency."[169] Because the DHHS's authority stems from the Spending Clause,[170] its regulation is limited to instances where U.S. funds are involved.[171] DHHS regulations are known

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voluntarily given. This element of informed consent requires conditions free of coercion and undue influence.").

166. *See* Doherty, *supra* note 153, at 114 ("By promoting the concepts of respect for persons, beneficence, and justice, the Belmont Report provides the ethical foundation for the current federal laws governing research on human subjects in the United States.").

167. See Couture, *supra* note 66, at 134 ("The two agencies work in an interlocking system in which one or both govern all human experiments.") (citing Sharona Hoffman, *Regulating Clinical Research: Informed Consent, Privacy and IRBs*, 31 CAP. U. L. REV. 71, 76 (2003)).

168. *See* Yevengia Shtilman, *Pharmaceutical Drug Testing in the Former Soviet Union: Contract Research Organizations as Broker-Dealers in an Emerging Testing Ground for America's Big Pharma*, 29 B.C. THIRD WORLD L.J. 425, 438 (2009) ("Perhaps the most important regulation pertaining to human trials conducted both within and outside the United States to date is the DHHS policy for the protection of human subjects, referred to as the Common Rule because it binds fifteen agencies in addition to DHHS.") (citing Markus Schott, *Medical Research on Humans: Regulation in Switzerland, the European Union and the United States*, 60 FOOD & DRUG L.J. 45, 65 (2005)).

169. *See* Protection of Human Subjects, 45 C.F.R. § 46.101(a) (2010); *see also* Sharona Hoffman, *Regulating Clinical Research: Informed Consent, Privacy, and IRBs*, 31 CAP. U. L. REV. 71, 75–76 (2003) ("Clinical trials that involve treatments other than drugs and devices, such as surgery or bone marrow transplants, are not regulated by the FDA and are subject to DHHS regulation only if they are 'conducted, supported or otherwise subject to regulation by any federal department or agency.'").

170. *See* Robert Charrow, *Protection of Human Subjects: Is Expansive Regulation Counter-Productive?*, 101 NW. U. L. REV. 707, 713 (2007) ("The Common Rule [of the DHHS] is a child of the Spending Clause—the constitutional provision that authorizes the federal government to spend money and, by implication, to impose conditions on the receipt of that money.") (citing U.S. CONST. art. I, § 8, cl. 1; South Dakota v. Dole, 483 U.S. 203, 212 (1987)).

171. *See* Doherty, *supra* note 150, at 114–15 ("[R]esearch that is entirely funded by private sources (rather than government sources) lacks the requisite federal nexus for the Common Rule [of the DHHS] to apply.") (citing 45 C.F.R. § 46.101(a)).

as the "Common Rule," and they require informed consent and Institutional Review Boards for all government-funded research.[172] The FDA is an agency under the DHHS,[173] but it derives its authority from the Commerce Clause.[174] The FDA's scope is also limited to regulating clinical trials that develop new drugs and devices.[175] The FDA regulates private companies that "research on populations outside of the United States . . . if the company ultimately intends to seek FDA approval for use of the product in the United States."[176] The FDA has protections similar to the Common Rule, but did not elect to incorporate it.[177] Instead, the FDA requires compliance with additional protocols.[178] As a result, the Common Rule governs research funded by the U.S. government, but private entities are regulated only if they seek FDA approval.[179] Nevertheless, no matter which agency governs, both require informed consent and IRBs.[180]

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172. *See* 45 C.F.R. §§ 46.101–.505 (2010) (outlining various regulations for federally funded medical research involving human subjects); *see also* Gail Javitt, *Why Not Take All of Me? Reflections on the Immortal Life of Henrietta Lacks and the Status of Participants in Research Using Human Specimens*, 11 MINN. J.L. SCI. & TECH. 713, 713 (2010) ("The 'Common Rule,' as the federal human subject protection regulations are known as, sets forth requirements for the protection of all human subjects of federally funded research.") (citing 45 C.F.R. §§ 46.101–.505 (2009)).

173. *See* Couture, *supra* note 66, at 134 ("Although the FDA is an agency under the Department of Health and Human Services, it has taken the frontal role of regulating human experimentation, specifically in the areas of pharmaceuticals, biologies and medical devices.") (citing Sharona Hoffman, *Regulating Clinical Research: Informed Consent, Privacy and IRBs,* 31 CAP. U. L. REV. 71, 76 (2003)).

174. *See* Charrow, *supra* note 170, at 713 ("[T]he FDA derives its jurisdiction from the Commerce Clause.") (citing U.S. CONST. art. I, § 8, cl. 3).

175. *See* Enforcement Policy, 21 C.F.R. § 7.3(f) (2010) (defining the "products" under FDA jurisdiction as "including any food, drug, and device intended for human or animal use, any cosmetic and biologic intended for human use").

176. Doherty, *supra* note 150, at 115.

177. *See id*. ("The FDA did not sign on to the Common Rule, and therefore has a separate basis for regulating research on human subjects.") (citations omitted).

178. *See id*. (stating that a sponsor of a drug or vaccine "must file an investigational new drug application ('IND') with the FDA[, and i]f IND approval is secured by an investigator, then the study may begin, subject to strict compliance with the protocols accepted by the FDA") (citing DALE E. HAMMERSCHMIDT, UNDERSTANDING THE FDA'S IND PROCESS, IN INSTITUTIONAL REVIEW BOARD: MANAGEMENT AND FUNCTION 323, 325 (Robert J. Amdur & Elizabeth A. Bankert eds., 2002)).

179. *See id*. ("[T]he federal system of protections applies only to research funded by a federal agency that is subject to the Common Rule, and to private entities that will ultimately seek FDA review and approval.") (citing INSTITUTE OF MEDICINE, RESPONSIBLE RESEARCH: A SYSTEMS APPROACH TO PROTECTING RESEARCH PARTICIPANTS 138 (2003)).

180. *See supra* note 172 and accompanying text (discussing that both the Common Rule and the FDA require informed consent and IRBs).

The informed consent requirements of the Common Rule and the FDA are "virtually identical."[181] At a minimum, researchers must disclose the purpose of the research, its procedures; any "reasonably foreseeable" risks and discomforts; reasonable benefits of participation; any alternative and beneficial procedures; the confidentiality of the records kept; compensation and availability of medical treatment for injury; contact information for questions or in case of injury; and a statement that participation is voluntary and at-will.[182] Even if a participant signs a document indicating consent, the document is merely a record of informed consent; not informed consent itself.[183] Researchers must ensure that when presenting information and receiving a signature, the participant gives bona fide consent.[184]

The Common Rule and the FDA also require Institutional Review Boards.[185] The purpose of an IRB is to protect the rights and welfare of human subjects,[186] so IRBs have specific approval criteria for a proposed clinical trial as well as standards the trial must maintain.[187] Before an IRB may approve a clinical trial, the IRB follows the Belmont Report's requirements by ensuring that "(1) informed consent is obtained from subjects and documented (respect for persons, or autonomy),[188] (2) the risks

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181. *See* Doherty, *supra* note 150, at 116 ("The general requirements for informed consent are virtually identical in the Common Rule and the FDA regulations.") (citations omitted).

182. *See* 45 C.F.R. § 46.116(a) (2010) (listing the Common Rule's elements of informed consent); *see also* 21 C.F.R. § 50.25 (2010) (listing the FDA's elements of informed consent).

183. *See* Doherty, *supra* note 150, at 116–17 ("A document with a signature is not consent, but is merely a record of what was supposed to have been communicated between researchers and prospective participants.") (citations omitted).

184. *See id.* at 116 ("It is important for investigators to understand the difference between 'the presentation of the information, and even the signing of the consent document, and bona fide consent.'") (quoting ROBIN L. PENSLAR, THE IRB'S ROLE IN EDITING THE CONSENT DOCUMENT, IN INSTITUTIONAL REVIEW BOARD: MANAGEMENT AND FUNCTION 233 (Robert J. Amdur & Elizabeth A. Bankert eds., 2002)).

185. *See id*. (stating one of the primary protections required by the Common Rule and the FDA regulations is "prior review of proposed research by an independent ethical review committee") (citing Ezekiel J. Emanuel et al., *Oversight of Human Participants Research: Identifying Problems to Evaluate Reform Proposals*, 141 ANNALS OF INTERNAL MED. 282, 282 (2004)).

186. *See* Institutional Review Boards, 21 C.F.R. § 56.102(g) (2010) (stating the primary purpose of an IRB's "review is to assure the protection of the rights and welfare of the human subjects").

187. *See* Hoffman, *supra* note 169, at 77–78 (describing the details of IRB requirements).

188. Doherty *supra* note 150, at 117 (citing 45 C.F.R. §§ 46.111(a)(4) & (5) (2005); 21 C.F.R. §§ 56.111(a)(4) & (5) (2005)).

to subjects are minimized and are reasonable in relation to benefits (beneficence),[189] and (3) the selection of subjects is equitable (justice)."[190] Moreover, the proposed clinical trial must be sensitive to vulnerable populations such as children, prisoners, pregnant women, mentally disabled persons, and economically or educationally disadvantaged persons.[191] Even with these requirements, IRBs have a great deal of discretion and may require disclosure of additional information if "the information would meaningfully add to the protection of the rights and welfare of subjects."[192]

Despite the protections of informed consent and IRBs, the Common Rule contains loopholes and the FDA's oversight may be inapplicable. Research in foreign countries may substitute compliance with foreign procedures for the Common Rule if the "procedures . . . afford protections that are at least equivalent" to the Common Rule, which opens the possibility for relaxed oversight.[193] Also, because research must have a federal nexus for the Common Rule to apply,[194] the DHHS cannot regulate privately funded research.[195] Fortunately, the FDA is not so restricted and can regulate private clinical trials that develop new drugs and devices to be marketed in the United States.[196] In fact, the FDA does not "permit reliance

189. *Id.* (citing 45 C.F.R. §§ 46.111(a)(1) & (2) (2005); 21 C.F.R. §§ 56.111(a)(1) & (2) (2005)).

190. *Id.* (citing 45 C.F.R. § 46.111(a)(3) (2005); 21 C.F.R. § 56.111(a)(3) (2005)).

191. *See* 45 C.F.R. § 46.111(b) (2010) (requiring the inclusion of additional safeguards in studies to protect the rights and welfare of vulnerable subjects from the effects of coercion and undue influence); *see also* 21 C.F.R. § 56.111(b) (2010) (stating that additional safeguards are included in the study when some or all of the subjects are likely to be vulnerable to coercion or undue influence).

192. 45 C.F.R. § 46.109(b) (2010); 21 C.F.R. § 56.109 (2010).

193. *See* 45 C.F.R. § 46.101(h) (2010) ("[I]f a department or agency head determines that the procedures prescribed by the institution afford protections that are at least equivalent to those provided in this policy, the department or agency head may approve the substitution of the foreign procedures in lieu of [this policy's] procedural requirements . . . .").

194. *See* 45 C.F.R. § 46.101(a) (stating that the DHHS's authority "applies to all research involving human subjects conducted, supported or otherwise subject to regulation by any federal department or agency which takes appropriate administrative action to make the policy applicable to such research"); *see also* Doherty, *supra* note 150, at 115 ("[R]esearch that is entirely funded by private sources (rather than government sources) lacks the requisite federal nexus for the Common Rule [of the DHHS] to apply.") (citing 45 C.F.R. § 46.101(a)).

195. *See* Doherty, *supra* note 150, at 115 ("In the case of privately-funded research by pharmaceutical companies, the federal government would need an additional basis [other than the Common Rule] for regulating.").

196. *See* 21 C.F.R. § 7.3(f) (2010) (stating that the FDA has jurisdiction over articles, "including any food, drug, and device intended for human or animal use, any cosmetic and biologic intended for human use").

on a host country's ethics guidelines."[197] The FDA may only regulate a private actor that intends to market the drug in the United States.[198] Consequently, private companies that engage in clinical research overseas but opt not to market their product in the United States are subject to no federal oversight. Without federal oversight, participants could be exposed to abusive practices.

Unfortunately, federal protections have been labeled an "elaborate ritual" both because participants do not actually understand risks and benefits[199] and because frequently "the informed consent process serves only to insulate the researcher from subsequent malpractice claims and fails to provide the subject with the prospective benefit intended by the doctrine."[200] Moreover, IRBs have been criticized for not protecting human subjects effectively due to conflicts of interest[201] (despite federal prohibitions),[202] for valuing success of the experiment over ethics,[203] and

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197. Remigius N. Nwabueze, *Ethical Review of Research Involving Human Test Subjects in Nigeria: Legal and Policy Issues*, 14 IND. INT'L & COMP. L. REV. 87, 110 (2003).

198. *See* Doherty, *supra* note 150, at 115 ("[T]he federal system of protections applies only to research funded by a federal agency that is subject to the Common Rule, and to private entities that will ultimately seek FDA review and approval.") (citing INSTITUTE OF MEDICINE, RESPONSIBLE RESEARCH: A SYSTEMS APPROACH TO PROTECTING RESEARCH PARTICIPANTS 138 (2003)).

199. *See* Grimm, *supra* note 81, at 46 ("[T]he informed consent process for research has been characterized as an 'elaborate ritual' that does not result in true informed consent because of a lack of understanding regarding the risks and benefits of participation.") (citing Sandra J. Carnahan, *Promoting Medical Research Without Sacrificing Patient Autonomy: Legal and Ethical Issues Raised by the Waiver of Informed Consent for Emergency Research*, 52 OKLA. L. REV. 565, 575 (1999)).

200. *Id*. (citing Sandra J. Carnahan, *Promoting Medical Research Without Sacrificing Patient Autonomy: Legal and Ethical Issues Raised by the Waiver of Informed Consent for Emergency Research*, 52 OKLA. L. REV. 565, 575 (1999)).

201. *See id*. at 62–63 ("Some argue that an inherent conflict of interest exists because IRB members are potentially reluctant to pass judgment on their own colleagues' research due to the fact that they could find themselves applying to an IRB in the future for permission to conduct research.") (citing Sandra J. Carnahan, *Promoting Medical Research Without Sacrificing Patient Autonomy: Legal and Ethical Issues Raised by the Waiver of Informed Consent for Emergency Research*, 52 OKLA. L. REV. 565, 586–87 (1999)).

202. *See* Protection of Human Subjects, 45 C.F.R § 46.107(e) (2010) ("No IRB may have a member participate in [an] initial or continuing review of any project in which the member has a conflicting interest."); *see also* Grimm, *supra* note 81, at 63 (stating the conflict of interest problem "persists despite the fact that the federal regulations prohibit members with conflicts of interest from participating within the IRB") (citations omitted).

203. *See* Grimm, *supra* note 81, at 63 ("IRBs can also experience difficulty in remaining true to their mission. In *Grimes v. Kennedy Krieger Institute, Inc.*, a Maryland appellate court stated that IRBs can place a premium on the success of experiments, often to the detriment of the ethicality of experiments.") (citing Grimes v. Kennedy Krieger Inst.,

for inadequate review.[204] As a result, even though the Belmont Report's principles are reflected in U.S. regulation, ethics glitches persist.[205]

C. International Guidelines

Since the Guatemala study, not only have domestic regulations developed, but international guidelines have also blossomed. Modern informed consent typically requires that the human subject (or legally authorized representative) voluntarily consent to participate after being informed in a manner he or she understands.[206] The two leading guidelines are the Nuremberg Code and the Declaration of Helsinki, but other international guidelines that address informed consent and continue to influence the United States include the International Covenant on Civil and Political Rights and the World Health Organization's Guidelines for Good Clinical Practice.

One of the first international guidelines was the Nuremberg Code, which was created in 1947 in response to Nazi medical experimentation.[207] The Code finds voluntary informed consent "absolutely essential."[208] Additionally, an experiment should avoid unnecessary pain and injury to participants,[209] and subjects must have "sufficient knowledge and comprehension of the elements of the subjects matter involved . . . to make

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Inc., 782 A.2d 807, 817 (Md. 2001)).

204. *See id*. at 63–64 (stating a report presented to the Government Reform and Oversight Committee of the U.S. House of Representatives in 1998 "concluded that IRBs conducted only minimal ongoing review of research, . . . that too much was reviewed at too great a speed, that insufficient resources were allocated," and that "little training was provided") (citations omitted).

205. *See supra* notes 188-92 and accompanying text (discussing how the Belmont Report's principles are reflected in U.S. federal regulations).

206. *See, e.g*., Doherty, *supra* note 150, at 110 ("Informed consent provides a process for ensuring and documenting that a research participant (or his or her legally authorized representative) has acted according to his or her informed, considered, and freely made judgment.") (citations omitted).

207. *See* 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, 165 (2006) ("In response to the Doctors Trial (1946-1947), the Nuremberg Code was designed to safeguard the rights of subjects in medical research.") (citations omitted).

208. *See* NUREMBERG CODE (1947), *available at* http://www.fhi.org/training/en/RETC2/Resources/nuremburg_code.pdf ("The voluntary consent of the human subject is absolutely essential.").

209. *See id*. ("The experiment should be so conducted as to avoid all unnecessary physical and mental suffering and injury.").

an understanding and enlightened decision" to participate.[210] The Code has never been adopted or ratified by the United States,[211] and it may have lost current application as more expansive ethics guidelines have formed.[212] Still, "courts in the United States have allowed the Code to be introduced as evidence of ethical principles existing in customary international law."[213]

Because it was initially believed that the Nuremberg Code applied only to war crimes, not physicians,[214] organizations created other ethical guidelines.[215] In 1964 the World Medical Association adopted the Declaration of Helsinki, and it is now the most renowned set of guidelines for human research.[216] From 1978 to 2008 it was referenced in FDA regulations as a general ethical guideline.[217] Unlike the Nuremberg Code, the Declaration does not mandate informed consent.[218] It requires researchers, however, to inform subjects of anticipated benefits, risks, and

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210. *Id*.

211. *See* Shtilman, *supra* note 168, at 448 ("The United States has neither ratified nor adopted the *Nuremberg Code*.") (citing Grimes v. Kennedy Krieger Inst., Inc., 782 A.2d 807, 850 (Md. 2001); Ammend v. Bioport, Inc., 322 F. Supp. 2d 848, 872 (W.D. Mich. 2004)).

212. *See* Bahir, *supra* note 207, at 165 ("The *Nuremberg Code* has historical significance; but, its current application has . . . waned as more expansive ethical codes have risen.").

213. Shtilman, *supra* note 168, at 449 (citations omitted).

214. *See* Doherty, *supra* note 150, at 111 ("For many years after the creation of the *Nuremberg Code*, most physicians believed that the Code primarily applied to war crimes, and not to the medical establishment.") (citing Joanne Roman, *U.S. Medical Research in the Developing World: Ignoring Nuremberg*, 11 CORNELL J.L. & PUB. POL'Y 441, 451 (2002)).

215. *See id.* ("Subsequent documents developed by international organizations provided guidelines for ethics in research, and were intended to apply to multinational and intranational research.").

216. *See* Bahir, *supra* note 207, at 165 ("The Declaration of Helsinki, adopted in 1964 by the World Medical Association, is the most recognized set of guidelines in the area of biomedical research.").

217. *See* Adam H. Laughton, Note, *Somewhere to Run, Somewhere to Hide?: International Regulation of Human Subject Experimentation*, 18 DUKE J. COMP. & INT'L L. 181, 196 (2007) ("The Declaration was signed by the United States in 1975 and incorporated by the FDA into their regulations for overseas clinical research that same year. In spite of having been adopted into FDA regulations, the Declaration is a general statement of ethics, not a collection of legally binding principles.") (citations omitted).

218. *See* DECLARATION OF HELSINKI Part B.13 (2000), *available at* http://ohsr.od.nih.gov/guidelines/helsinki.html (last visited Apr. 2, 2012) ("After ensuring that the subject has understood the information, the physician should then obtain the subject's freely-given informed consent, preferably in writing. If the consent cannot be obtained in writing, the non-written consent must be formally documented and witnessed.") (on file with the Washington and Lee Journal of Civil Rights and Social Justice).

potential discomfort,[219] and vulnerable populations are afforded special protections.[220] The Declaration, like U.S. federal regulations,[221] suggests ethical review committees,[222] whereas the Nuremberg Code places ethical responsibility directly with researchers.[223] The Declaration is not legally binding on the United States,[224] although its "principles have been followed in other international, regional, and national guidelines and regulations."[225]

Despite the influential value of the other guidelines, the only legally binding treaty on the United States is the *International Covenant on Civil and Political Rights* (ICCPR).[226] Article 7 of the ICCPR states, "[n]o one shall be subject to torture or to cruel, inhuman or degrading treatment or punishment. In particular, no one shall be subjected without his free

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219. *See id*. ("In any research on human beings, each potential subject must be adequately informed of the aims, methods, sources of funding, any possible conflicts of interest, institutional affiliations of the researcher, the anticipated benefits and potential risks of the study and the discomfort it may entail.").

220. *See id*. at Part A.8 ("Some research populations are vulnerable and need special protection. The particular needs of the economically and medically disadvantaged must be recognized.").

221. *See* Shtilman, *supra* note 168, at 448 ("U.S. federal regulations depart from the Code's emphasis on the researcher's authority in that they place responsibility with research institutions and IRBs rather than with the researchers themselves.") (citing Adam H. Laughton, Note, *Somewhere to Run, Somewhere to Hide?: International Regulation of Human Subject Experimentation*, 18 DUKE J. COMP. & INT'L L. 181, 194 (2007)).

222. *See* DECLARATION OF HELSINKI, *supra* note 218, at Part B.4 (stating that independent ethical review committees have "the right to monitor ongoing trials," and should provide guidance and approval on ethical issues, and "be in conformity with the laws and regulations of the country in which the research experiment is performed").

223. *See* Shtilman, *supra* note 168, at 447 ("Unlike the FDA regulations and the Declaration of Helsinki, the Nuremberg Code places the responsibility of ensuring ethical medical experimentation directly in the hands of researchers.") (citing James Cekola, *Outsourcing Drug Investigations to India: A Comment on U.S., Indian and International Regulation of Clinical Trials in Cross-Border Pharmaceutical Research*, 28 NW. J. INT'L L. & BUS. 125, 144 (2007)).

224. *See* Daniels, *supra* note 13, at 213–14 (stating the *Declaration of Helsinki* is "accepted by the international medical community as providing for the highest standards of medical ethics in human experimentation, although in most countries, [including the United States], [it] lacks the force of law") (citing Barry R. Bloom, *The Highest Attainable Standard: Ethical Issues in AIDS Vaccines*, 279 SCI. 186, 186 (1998)).

225. *See* Bahir, *supra* note 207, at 166 (citations omitted).

226. *See* Kristen Farrell, *Human Experimentation in Developing Countries: Improving International Practices by Identifying Vulnerable Populations and Allocating Fair Benefits*, 9 J. HEALTH CARE L. & POL'Y 136, 143 (2006) ("The ICCPR is the only legally binding international treaty concerning human experimentation.") (citing Finnuala Kelleher, Note, *The Pharmaceutical Industry's Responsibility for Protecting Human Subjects of Clinical Trials in Developing Nations*, 38 COLUM. J.L. & SOC. PROBS. 67, 73 (2004)).

consent to medical or scientific experimentation."[227] Unfortunately, the ICCPR is self-enforcing and applies only to state actors; aside from establishing informed consent as a principle of law, it merely imparts abstract rights.[228]

More practically, as part of "an effort to harmonize the Code of Federal Regulations with other international standards for human clinical trials,"[229] the WHO issued the *Guidelines for Good Clinical Practice* (GCP) in 1995 with the goal of setting globally applicable standards for trial of private pharmaceutical products.[230] The GCP adopt the ethical principles delineated in the Declaration of Helsinki,[231] but further emphasize the application of ethics—a priority previous codes lacked.[232] Moreover, member countries are encouraged to enact national regulations.[233] If no national regulations exist, countries are encouraged to adopt the GCP.[234] In fact, the FDA permits the GCP to be a substitute for FDA regulations in certain circumstances.[235]

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227. International Covenant on Civil and Political Rights, part III, art. 6(1), Dec. 16, 1966, 999 U.N.T.S. 171 and 1057 U.N.T.S. 407, *entered into force* 23 Mar. 1976 [the provisions of article 41 (Human Rights Committee) entered into force 28 Mar. 1979], *available at* http://www2.ohchr.org/english/law/ccpr.htm#art4 (last visited Apr. 2, 2012) (on file with the Washington and Lee Journal of Civil Rights and Social Justice).

228. *See* Finnuala Kelleher, Note, *The Pharmaceutical Industry's Responsibility for Protecting Human Subjects of Clinical Trials in Developing Nations*, 38 COLUM. J.L. & SOC. PROBS. 67, 73 (2004) ("[W]hile the ICCPR confers absolute rights, it applies only to state actors and is not self-enforcing. It established informed consent as a principle of international law, but did little more.").

229. Shtilman, *supra* note 168, at 438.

230. *See* World Health Organization, *Guidelines for Good Clinical Practice (GCP) for Trials on Pharmaceutical Products* introduction (1995), *available at* http://apps.who.int/medicinedocs/pdf/whozip13e/whozip13e.pdf (last visited Apr. 2, 2012) ("The purpose of these WHO Guidelines for Good Clinical Practice (GCP) for trials on pharmaceutical products is to set globally applicable standards for the conduct of such biomedical research on human subjects.").

231. *See id*. at art. 1.2 ("All research involving human subjects should be conducted in accordance with the ethical principles contained in the current version of the Declaration of Helsinki.").

232. *See* Bahir, *supra* note 207, at 167 ("The WHO guidelines emphasize the implementation of the ethical principles, which was lacking in previous guidelines.").

233. *See* World Health Organization, *supra* note 230, at art. 1.5 ("Countries in which clinical trials are performed should have regulations governing the way in which these studies can be conducted.").

234. *See id*. ("In countries where regulations do not exist or require supplementation, relevant government officials may designate, in part or in whole, these Guidelines as the basis on which clinical trials will be conducted.").

235. *See* Investigational New Drug Application, 21 C.F.R. § 312.120 (2010) (stating that FDA will accept a "well-designed and well-conducted foreign clinical study not

The GCP is fashioned after the Declaration of Helsinki,[236] so a researcher only "should" seek informed consent.[237] Like the Declaration of Helsinki and U.S. federal regulations, the GCP suggests a prospective independent ethics committee[238] that conducts prospective[239] and ongoing review.[240] Still, the GCP protects vulnerable groups[241] and enumerates information[242] that should be provided "in a language and at a level of complexity understandable to the subject."[243]

III. Parallels with the Guatemala Study: Compliance & Exploitation

Despite domestic regulations and international ethics created since the Guatemala study, U.S. researchers often do not comply with these regulations and codes. The problem is that since the 1990s there has been a boom of "international health care research, especially in clinical drug and vaccine trials funded by sponsors in wealthy countries and conducted in

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conducted under an IND" if it meets the conditions of GCP and "the FDA is able to validate the data from the study through an onsite inspection if the agency deems it necessary").

236. *See* World Health Organization, *supra* note 230, at art. 1.2 (1995), *available at* http://apps.who.int/medicinedocs/pdf/whozip13e/whozip13e.pdf (last visited Apr. 2, 2012) ("All research involving human subjects should be conducted in accordance with the ethical principles contained in the current version of the Declaration of Helsinki.").

237. *See id*. at art. 3.3 ("The principles of informed consent in the current revisions of the Declaration of Helsinki and the International Ethical Guidelines for Biomedical Research Involving Human Subjects *should* be implemented in each clinical trial.") (emphasis added).

238. *See id*. at art. 3.2 ("The ethics committee should be constituted and operated so that its tasks can be executed free from bias and from any influence of those who are conducting the trial.").

239. *See id*. ("Subjects must not be entered into the trial until the relevant ethics committee(s) has issued its favourable opinion on the procedures.").

240. *See id*. (stating the committee "has an ongoing responsibility for the ethical conduct of research" so it must be "informed of subsequent amendments to protocol[,] any serious adverse events that occur during the trial, or other information likely to affect the safety of the subjects or conduct of the trial").

241. *See id*. at art. 3.3(e), (f) (discussing the necessity of specially protecting children, adults who are unable to give consent, "patients with incurable diseases, people in nursing homes, prisoners or detainees, the unemployed or people on a very low income, patients in emergency departments, some ethnic and racial minority groups, the homeless, nomads and refugees").

242. World Health Organization, *supra* note 230, at art. 3.3(d) (stating subject consent is acceptable only if one explains "the aim of the study; the expected benefits for the subjects and/or others; the possibility of allocation to a reference treatment or placebo; the risks and inconveniences—e.g. invasive procedures; and, where appropriate, an explanation of alternative, recognized medical therapy").

243. *Id*. at art. 3.3(a).

developing nations."[244] This boom results in susceptibility for a Guatemala-like study recurring because the protections for human subjects are not enforced sufficiently. It is important to recognize parallels between the Guatemala study and modern practices in order to understand that modern informed consent issues echo ethical issues in the Guatemala study.

Dubious medical experiments that are similar to the Guatemala study and funded by U.S. grants continue to occur both overseas and within the United States.[245] For example, the United States, via the Centers for Disease Control and Prevention and the National Institutes of Health, has funded AIDS research in locations such as Haiti,[246] Thailand, the Dominican Republic, and several African countries.[247] Yet, reports have shown that researchers either ignored ethical standards[248] or facially complied with standards but did not seek actual informed consent.[249] In fact, the revision of the Declaration of Helsinki in 2000 was due partly to the United States' lack of compliance with its own legal standards.[250]

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244. Farrell, *supra* note 226, at 136; *see also* Abdullahi v. Pfizer, Inc., 562 F.3d 163, 186 n.16 (2d Cir. N.Y. 2009) ("In the United States, for example, the number of foreign clinical investigators conducting drug research under an IND increased sixteen-fold in the 1990s.") (citations omitted).

245. *See, e.g.,* WEYERS, *supra* note 57, at 594–99 (discussing experiments within the United States that occurred during the 1990s that resulted in death to participants due to noncompliance with the FDA's regulations).

246. *See, e.g.*, Daniels, *supra* note 13, at 203–24 (discussing the ethics of a study conducted by Cornell University in Haiti that was largely funded by the United States, the violations of international law, and the lack of redress for the victims in U.S. courts).

247. *See, e.g.*, 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, 92 (1999) ("Since 1997, the Centers for Disease Control (CDC) and the National Institutes of Health (NIH) have paid for and conducted experiments on pregnant women infected with HIV in Thailand, the Dominican Republic, and several African nations.").

248. *See* Benjamin M. Meier, *International Protection of Persons Undergoing Medical Experimentation: Protecting the Right of Informed Consent*, 20 BERKELEY J. INT'L L. 513, 516 (2002) ("Although U.S. government agencies were conducting the testing [at the African AZT trials], these experiments took place without regard for U.S. medical research standards, which require . . . that patients be fully informed of all possible treatment options and that they receive, at a minimum, the prevailing standard of care.") (citations omitted).

249. *See* Dyckman, *supra* note 247, at 94 (discussing "the problematic nature of structuring a test regimen on the condition of the freely obtained consent of individuals who are not similarly situated to the researchers in terms of power or resources").

250. *See* ADRIANA PETRYNA, WHEN EXPERIMENTS TRAVEL: CLINICAL TRIALS AND THE GLOBAL SEARCH FOR HUMAN SUBJECTS 33–35 (2009) (stating the debate over the ethics of the clinical trials in Africa that used "AZT treatment to halt perinatal transmission of HIV" prompted the revision of the *Declaration of Helsinki*).

In addition to research funded by the United States, research conducted by American pharmaceutical companies also contains risk of noncompliance with ethics. The opportunity for risk is actually greater because the pharmaceutical industry pilots healthcare research that was once primarily conducted by the U.S. government.[251] This phenomenon is due largely to the fact that Americans have become increasingly reluctant to participate in drug trials,[252] so private companies are "gravitating to developing countries because of lower costs, the prevalence of diseases, and seemingly limitless numbers of impoverished patients."[253] The lack of adequate protections in the context of privately funded research has been evident in studies conducted in "broken, impoverished countries" such as Russia, India, South Africa as well as other Eastern European, Latin American, Asian, and African countries.[254]

One recent case, *Abdullahi v. Pfizer, Inc.*,[255] illustrates problems with private companies using vulnerable populations for human subjects;[256] its circumstances are strikingly similar to those of the Guatemala study in both its methods and in its approach to informed consent. In 1996, Pfizer, one of the world's largest pharmaceutical companies,[257] was seeking FDA

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251. *See* Christine D. Galbraith, *Dying to Know: A Demand for Genuine Public Access to Clinical Trial Results Data*, 78 MISS. L.J. 705, 708 (2009) ("The pharmaceutical industry now substantially overshadows the federal government as the single greatest source of financial support for conducting clinical trials.") (citing Shankar Vedantam, *Drugmakers Prefer Silence on Test Data,* WASH. POST, July 6, 2004, at A1).

252. *See* Shtilman, *supra* note 171, at 425 ("Pharmaceutical manufacturers have found Americans increasingly hesitant to participate in drug experiments because of skepticism about their safety.") (citing SONIA SHAH, THE BODY HUNTERS: TESTING NEW DRUGS ON THE WORLD'S POOREST PATIENTS 4–5 (2006)).

253. Farrell, *supra* note 226, at 136 (citing Finnuala Kelleher, Note, *The Pharmaceutical Industry's Responsibility for Protecting Human Subjects of Clinical Trials in Developing Nations,* 38 COLUM. J.L. & SOC. PROBS. 67, 67 (2004)).

254. *See* SONIA SHAH, THE BODY HUNTERS: TESTING NEW DRUGS ON THE WORLD'S POOREST PATIENTS 7 (2006) ("The most popular destinations [for drug companies angling for FDA approval] are not Western Europe and Japan, but rather the broken, impoverished countries of Eastern Europe and Latin America. Russia, India, South Africa, and other Asian and African countries have proven equally fruitful.") (citations omitted).

255. Abdullahi v. Pfizer, Inc., 562 F.3d 163, 187 (2d Cir. N.Y. 2009) (holding that the appellants had "pled facts sufficient to state a cause of action under the ATS for a violation of the norm of customary international law prohibiting medical experimentation on human subjects without their consent").

256. *See* Farrell, *supra* note 226, at 137 ("*Abdullahi v. Pfizer, Inc.* illustrates the problems that arise when vulnerable populations suffer as a result of their participation in clinical research studies.").

257. *See id*. (stating that Pfizer is "the world's largest pharmaceutical company") (citing *PFIZER INC.: World's Largest, Research-based, Pharmaceutical Company*

approval for its antibiotic Trovafloxacin Mesylate, marketed as "Trovan."[258] In Kano, Nigeria, three American and four Nigerian physicians (in conjunction with the Nigerian government) conducted clinical trials with children who were patients at Nigeria's Infectious Disease Hospital.[259] Trovan had never been tested on children in that form and previous animal tests had serious side effects.[260] The children were given no follow-up care, and eleven children died with many others left blind, paralyzed, deaf, or brain-damaged.[261]

Nigerian children brought suit in U.S. federal courts under the Alien Tort Statute (ATS) alleging that Pfizer, working in partnership with the Nigerian government, violated a customary international norm that prohibited involuntary medical experimentation when it tested Trovan without obtaining consent from the children or explaining the risks.[262] Despite FDA regulations, no Institutional Review Board had approved the trial.[263] Although the district court dismissed the action for lack of subject matter jurisdiction under the ATS, the Second Circuit decided that the district court reached that conclusion incorrectly[264] and remanded the case

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Created, BIOTECH WEEK, May 14, 2003, at 94).

258. *See Abdullahi*, 562 F.3d at 169 (stating that the Plaintiff's alleged that Pfizer "sought to gain the approval of the U.S. Food and Drug Administration for the use on children of its new antibiotic, Trovafloxacin Mesylate, marketed as 'Trovan'").

259. *See id*. at 169 (contending that Pfizer "dispatched three of its American physicians to work with four Nigerian doctors to experiment with Trovan on children who were patients in Nigeria's Infectious Disease Hospital in Kano, Nigeria"). "Working in concert with Nigerian government officials, the team allegedly recruited two hundred sick children who sought treatment . . . ." *Id.*

260. *See id*. ("Appellants contend that Pfizer knew that Trovan had never previously been tested on children in the form being used and that animal tests showed that Trovan had life-threatening side effects, including joint disease, abnormal cartilage growth, liver damage, and a degenerative bone condition.").

261. *See* Abdullahi v. Pfizer, Inc., 562 F.3d 163, 169 (2d Cir. N.Y. 2009) ("Pfizer allegedly concluded the experiment and left without administering follow-up care."). "According to the appellants, the tests caused the deaths of eleven children, five of whom had taken Trovan and six of whom had taken the lowered dose of Ceftriaxone, and left many others blind, deaf, paralyzed, or brain-damaged." *Id*.

262. *See id*. at 168 (stating the plaintiffs alleged Pfizer "violated a customary international law norm prohibiting involuntary medical experimentation on humans when it tested an experimental antibiotic on children in Nigeria, including themselves, without their consent or knowledge").

263. *See id*. at 170 ("The appellants allege that, in an effort to rapidly secure FDA approval, Pfizer hastily assembled its test protocol at its research headquarters. . . . Appellants [also] allege, however, . . . that at the time the letter was purportedly written, the IDH had no ethics committee.").

264. *See id*. at 169 (stating "that the district court incorrectly determined that the

because it found that informed consent is a norm of international law.[265] The court stated that "[t]he administration of drug trials without informed consent on the scale alleged in the complaints poses a real threat to international peace and security."[266]

Abdullahi takes place in recent times, but it illustrates similar problems as those present in the Guatemala study. Both studies experimented on vulnerable populations, both contained deficiencies in informed consent procedures to develop a new drug as quickly as possible, and both involved U.S. and foreign doctors and governments that condoned such actions. The Guatemala study was secret and was never litigated, but the Nigerian children (or their families) have the possibility of recourse under the ATS.[267] It remains to be seen what the final result will be of *Abdullahi* on remand, but if nothing else, it demonstrates a contemporary example of the limitations of current informed consent standards and shows the applicability of lessons that may be learned from the Guatemala study.

Another problem with private companies using human subjects in developing countries is that these companies view data generated by clinical trial as their property, an attitude supported by the FDA and courts.[268] Consequently, trials that reach publication often reflect only positive results, communicating a skewed success rate to the public.[269] Because positive studies are typically the ones published, past studies do not inform future studies, so harmful studies may be repeated.[270]

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prohibition in customary international law against nonconsensual human medical experimentation cannot be enforced through the ATS").

265. *See* Abdullahi v. Pfizer, Inc., 562 F.3d 163, 169 (2d Cir. N.Y. 2009) ("[T]he incorporation of this [informed consent] norm into the laws of this country and this host of others is a powerful indication of the international acceptance of this norm as a binding legal obligation . . . .").

266. *Id*. at 185.

267. *See supra* notes 262–67 and accompanying text (discussing the Second Circuit's recognition that the Nigerian children may have a cause of action under the ATS).

268. *See* Galbraith, *supra* note 251, at 708 ("[Private pharmaceutical] companies have taken the position that if they are funding the research, the data produced should consequently be deemed their property, protectable through patent, trade secret, and contract law. Additionally, the FDA has generally supported this view, and the courts by and large have similarly agreed.").

269. *See id*. ("[O]nly a small fraction of trial outcomes are eventually published in medical journals or in some other peer-reviewed format. Moreover, research has shown that most of the pieces ultimately published tend to be about trials that demonstrate the treatment under investigation was in fact superior . . . .").

270. *See id*. (stating that practically, "future studies are generally not informed by previous research").

Obviously, repeating harmful trials places human subjects unnecessarily at risk.[271] The FDA approval process requires human clinical trials,[272] but Americans are reluctant to participate.[273] Consequently, drug companies are incentivized to conduct trials overseas. The problem lies in that governments of developing countries frequently choose not to regulate clinical trials because they want their citizens to gain access to health care, even through risky clinical participation.[274] These attitudes about preferring health care treatment, even if risky, are disturbingly similar to the Guatemalan government's attitude when it traded cooperation for medical surveys and supplies.[275]

The lack of consistent Institutional Review Board review, a requirement under U.S. law and present in nearly all international standards, leads to a greater opportunity for abuses to occur because there is no persistent check on ethical practices.[276] This problem is exacerbated in private pharmaceutical trials because such private actors are not required to report clinical trials if they choose not to seek FDA approval.[277] Private companies, therefore, have greater opportunity to ignore ethical review.[278] Though there are now extensive international guidelines, too many overlapping and nonbinding guidelines have created an overly complicated system. During the Guatemala study, legal forces often were not binding.[279]

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271. *See id*. ("[W]hen clinical investigators replicate trials that have previously been shown to be ineffective or even harmful, human subjects are placed at considerable risk.").

272. *See* Shtilman, *supra* note 168, at 425 (stating the FDA approves new drugs "on the basis of their efficacy and safety as determined by the results of time-consuming and expensive three-phase human clinical trials") (citations omitted).

273. *See id*. ("Pharmaceutical manufacturers have found Americans increasingly hesitant to participate in drug experiments because of skepticism about their safety.") (citing SONIA SHAH, THE BODY HUNTERS: TESTING NEW DRUGS ON THE WORLD'S POOREST PATIENTS 4–5 (2006)).

274. *See id*. ("[D]espite potential safety risks, government entities in underdeveloped nations are often reluctant to regulate their citizens' participation in experimental drug trials because these trials are often perceived as the only method of obtaining otherwise unaffordable medical treatment.").

275. *See supra* note 46 and accompanying text (discussing the Guatemalan government's trade for the use of human subjects).

276. *See supra* notes 184–92 and accompanying text (discussing the role of IRBs).

277. *See supra* note 195 and accompanying text (discussing that a loophole in the federal regulations is that a private company may not be regulated if it does not seek FDA approval).

278. *See supra* notes 190–205 and accompanying text (explaining loopholes in the federal regulations).

279. *See supra* note 65 and accompanying text (discussing that no laws were binding on the Guatemala study's researchers in the 1940s).

Likewise, current domestic and international regulations present similar problems because, though regulations exist, either guidelines are not binding or loopholes prevent adequate protection.[280]

Clinical studies conducted in developing nations are often the best source of available healthcare, so perhaps the failure to seek informed consent and IRB review is the lesser of two evils.[281] It is true that "potentially exploitative clinical research also serves a valuable purpose because it develops life-saving and life-improving medications."[282] Nevertheless, sidestepping ethics by touting the importance of providing health care over protections for human subjects reflects the same attitude that the Guatemalan government displayed in a study that employed extraordinarily invasive and painful procedures.[283] The U.S. government denounced the Guatemala study as employing practices that should never be repeated,[284] and these practices included avoidance of ethical responsibility.[285] Likewise, if the Guatemala study is truly not to be repeated, avoidance of ethical obligations should not be tolerated today. However, with such loose regulations governing human subject research today, can it truly be said that a study similar to the Guatemala study cannot recur?

IV. Learning from the Guatemala Study: Improving Informed Consent Standards through the Research Participants Protection Modernization Act of 2011

The United States' current regulatory scheme as well as the inclusion of international guidelines has created a complex system that governs informed consent standards. Both U.S. legal standards and international guidelines have tried to improve informed consent protections for human

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280. *See supra* notes 190–205 and accompanying text (explaining loopholes in the federal regulations).

281. *See* Farrell, *supra* note 226, at 136 ("Moreover, this research [by private pharmaceutical companies] may be the best source of health care available to certain vulnerable populations.").

282. *Id*.

283. *See supra* notes 36–59 and accompanying text (discussing the procedures used in the Guatemala study).

284. *See* Memorandum *supra* note 11 and accompanying text (stating President Obama's charge to the Presidential Commission for the Study of Bioethical Issues).

285. *See supra* notes 123–43 and accompanying text (analyzing how the researchers of the Guatemala study avoided ethical responsibility).

subjects through devices such as Institutional Review Boards.[286] However, the enforcement of laws and principles is what actually protects human subjects, not the existence of the law or principle.

The Alien Tort Statute provides an opportunity for human subjects to receive redress for violations of informed consent,[287] but the ATS does not prevent violations of informed consent. Realistically, human subjects who are victims of questionable research practices often do not have the financial resources to bring lawsuits in the United States. Pervasively, the problem is that the main enforcer of ethical obligations—IRBs—are overworked and "too weak and ineffective" to actually protect human subjects.[288] Without adequate oversight, the informed consent system and other protections for human subjects is a façade for exploitation that creates the risk of repeating the Guatemala study. Even with the ATS, more is needed for reasonable protection. What is needed is U.S. federal legislation with some teeth in it.

There is a piece of legislation that would fortify informed consent standards and protect human subjects: the Research Participants Protection Modernization Act of 2011 (RPPMA). Colorado Representative Diana DeGette—who sponsored similar bills in 2002,[289] 2003,[290] 2006,[291] and 2009[292]—introduced RPPMA on July 22, 2011.[293] Though Congress has not yet enacted the RPPMA into law, Congress should enact it because it

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286. *See* Doherty, *supra* note 150, at 130 ("Mechanisms such as informed consent and prospective review by IRBs have evolved to protect human subjects of clinical research.") (citing Alice K. Page, *Ethical Issues in International Biomedical Research: An Overview*, 37 J. HEALTH L. 629, 652–53 (2004)).

287. *See* Alien Tort Statute, 28 U.S.C. § 1350 (2011) ("The district courts shall have original jurisdiction of any civil action by an alien for a tort only, committed in violation of the law of nations or a treaty of the United States.").

288. *See* Saver, *supra* note 17, at 225 ("Legitimate concerns have been raised about IRBs' increasing workloads, limited resources, insufficient expertise, and lack of independence, suggesting that the IRB review system is simply too weak and ineffective to protect subjects.").

289. *See* Human Research Subject Protections Act of 2002, H.R. 4697, 107th Cong. (2002).

290. *See* Protection for Participants in Research Act, H.R. 3594, 108th Cong. (2003).

291. *See* The Protection for Participants in Research Act of 2006, H.R. 5578, 109th Cong. (2006).

292. *See* Protection for Participants in Research Act of 2009, H.R. 1715, 111th Cong. (2009).

293. *See* Research Participants Protection Modernization Act of 2011, H.R. 2625, 112th Cong. (2011) (detailing when DeGette introduced the RPPMA to the House of Representatives).

contains three principles that would improve the current regulatory structure. Firstly, the RPPMA requires review of existing regulations with the goal of harmonizing the Common Rule and FDA regulations and extending the Common Rule to all research.[294] The RPPMA also provides financial incentives to IRBs and investigators to comply with federal regulations. And, finally, the RPPMA grants the Department of Health and Human Services' Office for Human Research Protections (OHRP) enhanced enforcement authority.[295]

The Research Participants Protection Modernization Act of 2011 intends "[t]o amend the Public Health Service Act with respect to human subject research to improve protections for human subjects and, where appropriate because of the type of research involved, to reduce regulatory burdens."[296] To meet this goal, the RPPMA directs the Secretary of Health and Human Services to review and harmonize the Common Rule of the Department of Health and Human Services and FDA regulations.[297] In particular, the Secretary is instructed to determine whether thirteen matters should be modified:

1. How to address potential financial conflicts of interest;[298]
2. Whether the list of exemptions from the Common Rule should be expanded to include new categories;[299]

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294. *See id*. at § 491(A)(a)(1) ("[A]ll human subject research shall be conducted in accordance with the Common Rule, and as applicable to the human subjects involved in such research, with the vulnerable-populations rules.").

295. *See id*. at § 491(B) (discussing increased enforcement abilities of the OHRP).

296. *See id*.

297. *See id*. at § 491A(c)(2)(C)(i) ("The Secretary shall, with respect to the HHS Human Subject Regulations, consider the matters specified in clause (iii) and make a determination of whether any of the provisions of such Rule or any guidance associated with such Rule should be modified accordingly."); *see also* Press Release, House Representative Diana DeGette, DeGette Introduces Research Participants Protection Act (July 22, 2011), *available at* http://degette.house.gov/index.php?option=com_content&view=article&id=1096:degette-introduces-research-participants-protection-act&catid=89:health (last visited Apr. 2, 2012) ("The Research Participants Protection Act instructs the Secretary of Health and Human Services to review and harmonize federal policy on protecting research participants . . . .") (on file with the Washington and Lee Journal of Civil Rights and Social Justice).

298. *See* H.R. 2625, at § 491A(c)(2)(C)(iii)(I) ("How requirements regarding the definition and management of potential financial conflict of interest, including both investigator and institutional conflicts of interest, should be strengthened and enforced to protect human subjects more effectively.").

299. *See id*. at § 491A(c)(2)(C)(iii)(II) ("Whether the list of exemptions from applicability of the HHS Human Subject Regulations . . . should be expanded to include new categories.").

3. "Whether and under what circumstances research that studies human tissue or other clinical specimens should not be considered a clinical investigation;"[300]
4. Whether the list of categories eligible for expedited review under the Common Rule should be expanded;[301]
5. "Whether institutional review boards include sufficient numbers of minority individuals as board members when reviewing proposals designed to include human subjects who are minority individuals;"[302]
6. Whether the number of IRB members who are nonscientific members and unaffiliated with the institution should be increased;[303]
7. "Whether institutional review boards include sufficient numbers of individuals with appropriate scientific expertise;"[304]
8. "How to enhance the protection of people with diminished decision-making capacity;"[305]
9. How to reduce regulatory burdens for IRBs in multistate research while protecting human subjects;[306]
10. How to modify "the requirements for managing and reporting adverse events and unanticipated problems" both to increase consistency between the DHHS and the FDA, and to reduce regulatory burden;[307]
11. How informed consent requirements should be modified to reduce regulatory burdens while protecting human subjects,

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300. *Id*. at § 491A(c)(2)(C)(iii)(III).

301. *See id*. at § 491A(c)(2)(C)(iii)(IV) ("Whether the list of categories of research that are eligible for expedited review under the HHS Human Subject Regulations . . . should be expanded to include new categories of research eligible for expedited review.").

302. *Id*. at § 491A(c)(2)(C)(iii)(V).

303. *See* Research Participants Protection Modernization Act of 2011, H.R. 2625, 112th Cong. § 491A(c)(2)(C)(iii)(VI) (2011) ("Whether the requirements for the number of members of an institutional review board who are individuals whose primary expertise is in nonscientific areas, and the number of members of an institutional review board who are individuals who are not affiliated with the institution served by the board, should be increased.").

304. *Id*. at § 491A(c)(2)(C)(iii)(VII).

305. *Id*. at § 491A(c)(2)(C)(iii)(VIII).

306. *See id*. at § 491A(c)(2)(C)(iii)(IX) ("How the requirements for institutional review board review in multisite research should be modified to reduce regulatory burden while protecting human subjects, including use of a lead institutional review board.").

307. *Id*. at § 491A(c)(2)(C)(iii)(X).

"including clarification of the circumstances in which informed consent does not need to be in writing;"[308]

12. How research under FDA regulations should comply with the *Guidelines for Good Clinical Practice* and how to further educate investigators in compliance; and[309]
13. "Such additional matters as the Secretary determines to be appropriate."[310]

Inquiring into and potentially modifying these thirteen areas—including the catchall of "such additional matters"—means informed consent standards will receive scrutiny that is long overdue. Moreover, the Secretary is required to publish determinations in the Federal Register, which means that the public would have an opportunity to comment on the findings.[311] Although the DHHS' Common Rule and FDA regulations are substantially similar,[312] inconsistencies exist, and these inconsistencies create confusion because there are two sets of rules. The RPPMA seeks to harmonize the two sets of regulations, which would bring about efficiency and effectiveness in the law as well as simplify the process for researchers. Moreover, if Congress would extend the Common Rule to research conducted by private companies, as suggested by RPPMA, it would strengthen the protections for human subjects and settle confusion about the Common Rule's applicability to private companies.

In addition to subjecting these thirteen areas to further scrutiny and potentially modifying them, the RPPMA would further benefit informed consent standards by amending the rules for IRBs. Investigators for research will be required to notify IRBs of any significant financial interest and whether the research has been submitted to another IRB and that IRB's findings.[313] Significantly, investigators will also be required to disclose

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308. *See* Research Participants Protection Modernization Act of 2011, H.R. 2625, 112th Cong. § 491A(c)(2)(C)(iii)(XI) (2011) ("How the requirements for approval and oversight of human subjects research that poses no more than minimal risk to participants . . . should be modified to reduce regulatory burden . . . while protecting research participants, including clarification of the circumstances in which informed consent does not need to be writing.").

309. *See id*. at § 491A(c)(2)(C)(iii)(XII) ("Whether research . . . should comply with the guideline published by the Food and Drug Administration . . . entitled 'Good Clinical Practice: Consolidated Guideline,' and how investigators can be educated effectively regarding compliance with this guideline.").

310. *Id*. at § 491A(c)(2)(C)(iii)(XIII).

311. *See id*. at § 491A(c)(2)(C)(ii) ("The Secretary shall publish the determination required by clause (i) in the Federal Register.").

312. *See supra* note 179 and accompanying text (stating that the Common Rule and the FDA regulations are "virtually identical").

313. *See* Research Participants Protection Modernization Act of 2011, H.R. 2625, 112th

whether they have been "disqualified or restricted by any Federal, State, or local entity in their ability to conduct human subject research."[314] These disclosures must be submitted when the research is proposed, or as soon as the circumstances arise.[315] In addition to encouraging transparency, requiring these disclosures would aid in eliminating the concern that harmful studies are repeated merely because the product is not pursued for FDA marketing, thereby solving another current problem with human subject research.[316]

As for financial incentives, the RPPMA encourages compliance by allowing institutions to recover costs from complying with human subject protections as direct costs from government sponsors of the research.[317] The RPPMA also addresses the issue of educating IRBs and investigators by restricting the Secretary of Health and Human Services from awarding a grant, cooperative agreement, or contract for human subject research "unless the public entity or private academic institution . . . maintains or contracts for a program to educate investigators and board members on the protection of human subjects in research."[318] Removing funding for studies that do not educate the researchers or IRBs provides a practical reason for researchers to focus more on informed consent procedures as well as a method to reeducate parties involved in human subject research about the importance and goals of informed consent procedures.

Finally, the RPPMA provides the Office for Human Research Protections with more enforcement abilities. The Director of OHRP would have authority to establish criteria for assuring compliance with human subject protections; would direct activities at the federal level to protect human subjects; would "carry out educational and quality improvement programs for human subject protections for principal investigators,

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Cong § 491(A)(d)(1)(A)(i),(iii) (2011) (describing the requirements for an investigator submitting research to an IRB).

314. *Id*. at § 491(A)(d)(1)(A)(ii).

315. *See id*. at § 491(A)(d)(1)(B) ("A notification required by subparagraph (A) shall be submitted to the institution served by the board—(i) at the time of submitting the proposal for human subject research to the board; or (ii) in the case of circumstances arising after such submission, immediately.").

316. *See supra* notes 269–81 and accompanying text (discussing the problems of harmful studies repeating).

317. *See* H.R. 2625, at § 491(A)(d)(3) ("Institutions may recover costs associated with compliance for human subject protections under this part from government sponsors of research as direct costs.").

318. Research Participants Protection Modernization Act of 2011, H.R. 2625, 112th Cong. § 491(A)(e) (2011).

members of institutional review boards, and other appropriate persons;" would advise entities about how to comply with human subject protections; would make grants for recruiting and training minority individuals to serve on IRBs; and would "consult with experts in biomedical, behavioral, and social sciences research."[319] Currently, the Office for Human Research Protections calls for the Division of Compliance Oversight (DCO) to evaluate noncompliance with DHHS regulations and then the OHRP decides what, if any, regulatory action is needed.[320] By enacting the RPPMA, the FDA and DHHS would continue to include IRBs within their regulatory structures, but would be able to increase oversight and accountability through the OHRP, because the OHRP would have more robust authority to ensure continual compliance with U.S. regulations.

Interestingly, the same day that the Representative DeGette proposed the Research Participants Protection Modernization Act of 2011, the DHHS and the FDA issued an announcement of proposed rulemaking that would address several of the issues recommended in RPPMA.[321] The DHHS' proposal to improve protections for human subjects focuses on seven areas, many of which mirror the RPPMA's goals. The proposed improvements are as follows:

1. Revising the existing risk-based framework to more accurately calibrate the level of review to the level of risk.
2. Using a single Institutional Review Board review for all domestic sites of multi-site studies.
3. Updating the forms and processes used for informed consent.
4. Establishing mandatory data security and information protection standards for all studies involving identifiable or potentially identifiable data.

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319. *Id*. at § 491(B)(b) (describing the duties of the Director).

320. *See* Office for Human Research Protection, *Compliance Oversight*, http://www.hhs.gov/ohrp/compliance/ (last visited Apr. 2, 2012) ("OHRP asks the institution involved to investigate the allegations and to provide OHRP with a written report of its investigation. The Office then determines what, if any, regulatory action needs to be taken to protect human research subjects.") (on file with the Washington and Lee Journal of Civil Rights and Social Justice).

321. *See* Press Release, Department of Health and Human Services Press Office, HHS Announces Proposal to Improve Rules Protecting Human Research Subjects, (Jul. 22, 2011), http://www.hhs.gov/news/press/2011pres/07/20110722a.html (last visited Apr. 2, 2012) (announcing a proposal to improve rules aimed at enhancing oversight and protecting human research subjects) (on file with the Washington and Lee Journal of Civil Rights and Social Justice).

5. Implementing a systematic approach to the collection and analysis of data on unanticipated problems and adverse events across all trials to harmonize the complicated array of definitions and reporting requirements, and to make the collection of data more efficient.
6. Extending federal regulatory protections to apply to all research conducted at U.S. institutions receiving funding from the Common Rule agencies.
7. Providing uniform guidance on federal regulations.[322]

The goal of the new proposal is to better uphold the ethical principles behind the Common Rule, and public comment is being sought until October 26, 2011.[323] Though the proposed rule is a step in the right direction, the rule addresses the 2001 findings of the Presidential Commission for Bioethical Issues and is not as comprehensive as the Research Participants Protection Modernization Act of 2011. As a result, the RPPMA is still needed to fully address the problems with the U.S. informed consent system.

Rather than relying on the DHHS' proposed rule alone, Congress should adopt the Research Participants Protection Modernization Act of 2011. Unlike the bills that Representative DeGette proposed in the past, news of the Guatemala study has created more public pressure to change modern informed consent laws. The financial incentives for IBRs as well as the goal to streamline federal regulations make the RPPMA an effective remedy to problems found in federal informed consent regulations because parties involved would better understand how the regulations work and have an incentive to follow the regulations. Moreover, the Office for Human Subject Protections' enhanced enforcement authority would centralize federal authority and provide clarity to researchers, many of which truly want to comply with informed consent procedures (unlike the researchers in the Guatemala study). The mandatory reporting requirements the RPPMA offers in combination with the enhanced enforcement authority granted to the Office for Human Subject Protections also creates a more transparent system and allows the IRB system to become a more effective enforcement mechanism.

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322. *See id.*

323. *See* Human Subjects Research Protections: Changing Protections for Research Subjects and Reducing Burden, Delay, and Ambiguity for Investigators, 76 Fed. Reg. 143 (proposed Jul. 22, 2011) (to be codified at 21 C.F.R. Parts 50 and 56) (seeking to establish better methods to uphold ethical principles in medical research).

V. Conclusion

Despite the protections that federal regulations and international guidelines impart, improvements are needed. The goals of current federal protections and modern international guidelines should be extended in the law to cover all situations involving research with human subjects. It is feasible to do this through adopting the Research Participants Protection Modernization Act of 2011 that extends the Common Rule, provides for greater enforcement of current protections, and reshapes the IRB oversight system into an effective enforcement mechanism.

The Guatemala study was horrendous, and the legal standards and guidelines of its day failed to protect Guatemalans who were infected with syphilis. Similar studies are being conducted by U.S. researchers in developing nations around the world, whether through grants from the U.S. government or by private U.S. companies. These problems must be remedied, and the Research Participants Protection Modernization Act of 2011 provides the impetus for the U.S. to do so. As Amy Gutmann, Chair of the Presidential Commission for the Study of Bioethical Issues stated, "a civilization can be judged by the way that it treats its most vulnerable individuals. There is no position of vulnerability that is greater than to be the subject of a medical experiment."[324]

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324. Gutmann, *supra* note 12.