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MISSING THE “TARGET”: PREVENTING THE UNJUST INCLUSION OF VULNERABLE CHILDREN FOR MEDICAL RESEARCH STUDIES

Ruqaijah Yearby†

I. INTRODUCTION

Nearly everyone has experienced a burn and the resulting pain. Now imagine that you suffer a third-degree radiation burn that injures all the layers of your skin as well as the tissue, causing you extreme pain. The burn turns your skin white, cherry red, or black and may produce blisters that are dry, hard, and leathery-looking. The burn can also be seen on the surface of your lungs and gastrointestinal tract. If the burn is big enough you will need skin grafts and surgery to replace the skin and tissue that will never grow back, as well as treatment to prevent infection. Assumedly, no human being would intentionally cause another human being to experience this type of pain and suffering. However, U.S. researchers did. Researchers at the Medical College of Virginia conducted radiation tests on healthy African American children, as young as 6 months old, deliberately causing third-degree burns to their skin. The tests not only damaged the skin of these children, causing them extreme pain, but it also required surgery and skin grafts.

Although the central purpose of medical research on children is to “generate new knowledge” that can improve children’s health, research “can never take precedence

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1 Harriet Washington, Medical Apartheid 236-37 (2007) (discussing a Medical College of Virginia experiment to determine “whether radiation inflicted different degrees of damage on the skins of black people than on that of whites”).

2 See id.
over the rights and interests of” children serving as research subjects.\(^3\) Unfortunately, medical research has too often taken precedence over the rights and interests of children, which is why many researchers and bioethicists have characterized the history of medical research on children as a history of child abuse.\(^4\) Usually, the debate regarding the use of children in medical research studies has centered on questions regarding the ethical principles of autonomy (informed consent)\(^5\) and beneficence (the best interest of the child based on a benefit risk analysis).\(^6\) The debate has rarely focused on the justice principle.\(^7\)

My article begins to fill this void by critically analyzing medical research studies conducted on children by discussing the requirements of the justice principle. The justice principle, used to determine who will serve as a research subject,\(^8\) is the most significant ethical principle governing medical research studies because the first thing that researchers must consider when designing their study is subject selection. Once it is decided who will serve as a research subject, the researcher can determine whether the study complies with the requirements of autonomy and beneficence.

When selecting research subjects, the justice principle prohibits targeting. Targeting is the systematic selection of research subjects who are from vulnerable populations, such as racial minorities, children, and the economically disadvantaged, “because of their easy availability, their compromised position, or their manipulability, rather than for reasons directly related to the problem being studied.”\(^9\) Additionally, even if the research is directly related to a condition suffered by the vulnerable population, researchers should not use these populations as research subjects if they are already overburdened due to lack of access to essential goods, such as food and housing. Consequently, research subjects should be chosen according to an order of

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6. 45 C.F.R. §§ 46.404-46.407 (2010); NAT'L INSTS. OF HEALTH, supra note 5; NAT'L COMM'N FOR THE PROTECTION OF HUMAN SUBJECTS OF BIOMEDICAL & BEHAV. RES., supra note 5. See also, Loretta Kopelman, Children as Research Subjects: Moral Disputes, Regulatory Guidance, and Recent Court Decisions, 73 MOUNT SINAI J. MED. 596 (2006); Michelle Oberman & Joel Frader, Dying Children and Medical Research: Access to Clinical Trials as Benefit and Burden, 29 AM. J.L. & MED. 301 (2003).
9. Id. The justice principle also requires that if vulnerable populations are used in medical research studies then the benefits of the research must be distributed to those vulnerable populations. See id. I discuss the justice principle’s requirement that the populations that participate in medical research studies must be the populations that benefit from the research in my forthcoming article entitled, Exploitation in Medical Research Forty Years After the Tuskegee Syphilis Study, 67 CASE W. RES. UNIV. L. REV. (2017) (forthcoming).
preference of subjects for research: the economically advantaged before the economically disadvantaged, the majority before minorities, and adults before children.

Notwithstanding the Justice Principle, researchers continue to target children for medical research studies. Since the late 1700s, children have repeatedly been targeted for participation in medical research studies because they were readily accessible and easy to manipulate. Using economically disadvantaged minority children as an example of the harm all children suffer when targeted for medical research studies, I argue that the justice principle must be redefined and new safeguards must be implemented to protect all child participants. Specifically, Section II provides a descriptive overview of the purpose and structure of medical research studies, as well as a brief history of medical research studies that targeted economically disadvantaged minority children. Section III examines the parameters of the justice principle and further defines what constitutes targeting. Section IV discusses the problems with the enforcement of the justice principle and provides examples of medical research studies that targeted and harmed economically disadvantaged minority children in the United States and abroad as a result of these problems.

In Section V, I propose several ways to end targeting in the United States and abroad. First, the justice principle must be redefined to mean equity in participation. Equity in participation would require researchers to use non-disadvantaged children as research subjects unless the study is a priority to and does not overburden economically disadvantaged minority children. To measure whether equity in participation is met, researchers should be required to use the proposed Vulnerability and Equity Impact Assessment (VEIA) tool, to determine whether the selection of children from particular groups as research subjects violates the redefined justice principle. Finally, I suggest the creation of a Board of Children to review all medical research studies regulated by the United States that use children as research subjects. If all of these recommendations are implemented, it will prevent economically disadvantaged minority children from being targeted in medical research studies for the benefit of an unworthy society.

II. MEDICAL RESEARCH STUDIES INVOLVING CHILDREN: THE STRUCTURE AND HISTORY

There are two types of medical research studies involving human subjects: Non-therapeutic and Therapeutic. Regardless of the type of medical research study, all

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10 Leonard Glantz, Research with Children, 24 AM. J.L. & MED 213, 215-18 (1998); Lederer & Grodin, supra note 4, at 12, 19. Children have also been exploited in medical research studies for conditions that were not limited to children. Id. Moreover, many medical research studies conducted on children produce minimal scientific benefits in comparison to their costs and are stigmatizing. See, e.g., Solomon R. Benatar, Global Health and Justice: Re-Examining Our Values, 27 BIOETHICS 297, 301-02 (2013); Iain Chalmers & Paul Glasziou, Avoidable Waste in the Production and Reporting of Research Evidence, 374 LANCET 86 (2009); Washington, supra note 1, at 271-96; Lainie Ross, Children in Medical Research: Access versus Protection 48-56 (2006).

11 The Vulnerability and Equity Impact Assessment tool is based on the Health Equity Impact Assessment tool. For a description and evaluation of the Health Equity Impact Assessment tool see Rebecca Haber, Health Equity Impact Assessment: A Primer (Wellesley Institute 2010) and Rainer Fehr, Environmental Health Impact Assessment, Evaluation of a Ten-Step Model, 10 EPIDEMIOLOGY 618 (1999) (analyzing various ways to assess health impacts).

12 Declaration of Helsinki (1964), 313 Brit. Med. J. 1448, 1448 (1996) (distinguishing between research “in which the aim is essentially diagnostic or therapeutic for a patient” and that which “is purely scientific and without implying direct diagnostic or therapeutic value to the person subjected”).
studies using children entail risk of psychological and physical harm, as well as the possibility of stigma. In fact, countless children have suffered harm as a result of study participation, often without any benefit in return. Economically disadvantaged minority children have been and continue to be overrepresented in medical research studies.

A. STRUCTURE OF MEDICAL RESEARCH STUDIES INVOLVING HUMAN SUBJECTS

A non-therapeutic medical research study is conducted to obtain generalizable scientific knowledge. This research is done to learn more “about the subjects' disorder or condition which is of vital importance for the understanding or amelioration of the subjects' disorder or condition.” An example of non-therapeutic research is a study to ascertain the effects of household pesticide use on children’s health.

A therapeutic medical research study tests a vaccine, drug, or medical device for the treatment of a disease. An example of a therapeutic medical research study is the testing of HIV/AIDS drugs. There are five Phases of therapeutic medical research studies: Phase 0, I, II, III, and IV. Using drug medical research studies as an example, each Phase is discussed below.

In a Phase 0 drug study, research is conducted using at most ten people and involves the administration of small doses of an experimental drug over a short period of time to determine if there is any pharmacological effect. The purpose of the study is to evaluate whether there is any effect in humans, before undertaking Phase I and II drug studies. Unlike Phase I drug studies, there is no therapeutic intent and little to no toxic effect in a Phase 0 drug study, which is primarily done for cancer drugs and therapies.

13 Glantz, supra note 10, at 215-18. See also Lederer & Grodin, supra note 4, at 12, 19.
14 Throughout the article, I use the term “economically disadvantaged” to discuss children who lack access to essential goods such as food, housing, and health care. Although the term can be over inclusive, for clarity, I have used the word accepted in the medical research community. For more discussion, see Carol Levine, Changing Views of Justice after Belmont: AIDS and the Inclusion of “Vulnerable” Subjects, in THE ETHICS OF RESEARCH INVOLVING HUMAN SUBJECTS: FACING THE 21ST CENTURY 105-24 (1996).
16 Declaration of Helsinki (1964), supra note 12. Children are allowed to participate in these studies where they present more than minimal risk to the subjects only if “[t]he risk represents a minor increase over minimal risk” and “[t]he intervention or procedure presents experiences to subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations.” 45 C.F.R. § 46.406 (2015).
17 45 C.F.R. § 46.406.
18 For an example of one such study, see Jack K. Leiss & David A. Savitz, Home Pesticide Use and Childhood Cancer: A Case-Control Study, 85 AM. J. PUB. HEALTH 249 (1995).
19 Declaration of Helsinki (1964), supra note 12.
22 Id.
In a Phase I drug study, research is conducted using a small number of subjects, less than 100 people, to obtain information regarding the safety and efficacy of the candidate drug on human subjects. Phase II studies obtain information from several hundred subjects regarding the subjects’ immune system’s response, the efficacy of the drug on different populations, and the effect of different doses on the population.

After preliminary evidence has been obtained suggesting effectiveness of the drug, a Phase III drug study is conducted “to gather additional information to evaluate the overall benefit-risk relationship of the drug and provide an adequate basis for physician labeling.” Researchers determine the efficacy of the drug in preventing the disease by following several thousand subjects. This is the last phase before the drug is marketed and distributed. Phase IV is the final step in drug studies. It includes “[p]ost-marketing . . . studies to delineate additional information about the drug’s risks, benefits, and optimal use.”

The main difference between each Phase is the purpose of the study and the benefit. In Phase 0, I, and II studies, the goal is primarily the attainment of scientific knowledge, whereas in Phase III and IV studies, the goal is treatment. Many patients, physicians, and scholars often misunderstand the difference between research and therapy. Although there is no potential for a benefit in Phase 0, I, and II medical research studies, many patients, providers, and even researchers believe that enrollment in these studies is beneficial for the patient because the patient will receive treatment. This therapeutic misconception is used to justify the targeting of vulnerable research subjects, such as economically disadvantaged minority children, for participation in medical research studies.

B. EASILY MANIPULATED SUBJECTS: A BRIEF HISTORY OF TARGETING

Although the definitions seem clear, ascertaining whether a study is non-therapeutic or therapeutic can be difficult because both studies may potentially benefit society through either generalizable knowledge or direct treatment. Nevertheless, no matter whether the study is non-therapeutic or therapeutic, some researchers have targeted economically disadvantaged minority children for use in medical research studies, causing lifelong disability and/or death.
Between 1936 and 1960, psychiatrists and neurosurgeons conducted lobotomies on healthy African American boys as young as five years old that obliterated their thought ability and personality. The psychiatrists and neurosurgeons used crude tools such as the icepickalon. Inserting the tools into the boys’ brains, the researchers “blindly swept [the tools] back and forth . . . cutting all the connecting nerves,” removing any chance for the once healthy boys to lead a normal life. From 1949 to 1960, the Medical College of Virginia conducted radiation tests on healthy African American children, as young as six months old, deliberately causing third-degree burns to their skin. In 1956, seventeen healthy African American infants were deprived of an essential nutrient, which researchers knew the body could not survive without. Ten of the seventeen suffered severe complications, in order for scientists to determine if canned milk caused skin rash, diarrhea, or slow weight gain. Notwithstanding the complications, the study was repeated with 428 infants and seven of the infants died.

The U.S. Atomic Energy Commission (AEC) “irradiated 235 African American newborns from 1953 to 1954 in various hospitals across the nation” for no recorded therapeutic purpose since the infants were healthy. Between 1960 and 1970, the AEC sponsored a study in which radioactive material was added to the oatmeal of thirty healthy orphans, some of which were African American. The government obtained the bodies of the research participants who died to measure the levels of radioactivity and biological damage.

These are just a few examples of the targeting of economically disadvantaged minority children in medical research studies for the benefit of society. The children who participated in these studies were chosen because they were readily accessible and in a compromised position, not because they were particularly affected by the condition being studied. These historical abuses were the foundation for the application of social justice to medical research studies and the protection of vulnerable populations, particularly economically disadvantaged minority children, from exploitation.

III. THE JUSTICE PRINCIPLE: SOCIAL JUSTICE IN MEDICAL RESEARCH STUDIES

The concept of social justice has been applied in the allocation of societal benefits and burdens, such as “punishment, taxation and political representation.” Before 1979, most scholars, bioethicists, and researchers did not view social justice as
relevant to medical research studies. The first discussion concerning the proper allocation of burdens and benefits of medical research studies appeared in the Belmont Report’s discussion of the justice principle. This report, mandated by the United States’ Congress, not only defined the term, but also provided the framework for which to apply the principle to medical research studies. Since 1986, when the Common Rule was enacted, the justice principle has been applied to all medical research funded by the federal government. Beginning in 1996, the justice principle was also applied to any medical research studies conducted outside the United States by a company seeking drug approval in the United States.

A. BELMONT REPORT

In the early 1970s, the U.S. Senate Committee on Labor and Human Resources held hearings on some of America’s most egregious medical research studies, such as the Willowbrook study and the Tuskegee Syphilis study. As a result of the

48 Lederer & Grodin, supra note 4, at 3, 18-19. The precursor to international protections of human subjects participating in medical research studies was the Nuremberg Code in 1947, which was developed in response to the Trials of War Criminals before the Nuremberg Military Tribunals. See Nuremberg Code (1947), 313 BRIT. MED. J. 1448 (1996).

49 Belmont Report, supra note 8, at 23,194. In fact, the justice principle was found only in the Belmont Report until 2000, when the World Medical Association added the principle to the Declaration of Helsinki, a renowned document of bioethics for medical research. See Robert V. Carlson, Kenneth M. Boyd & David J. Webb, The Revision and the Declaration of Helsinki: Past, Present, and Future, 57 BRITISH J. CLINICAL PHARMACOLOGY 695, 699-704 (outlining the 2000 revisions to the Declaration of Helsinki). For a discussion regarding the ethical documents that discuss the use of children in research trials, see Duane Alexander, Regulation of Research with Children: The Evolution from Exclusion to Inclusion, 6 J. HEALTH CARE L. & POL’Y 1, 1-3 (2002).

50 Belmont Report, supra note 8, at 23,196-97.


52 INTERNATIONAL CONFERENCE ON HARMONISATION OF TECHNICAL REQUIREMENTS FOR REGISTRATION OF PHARMACEUTICALS FOR HUMAN USE, GUIDELINE FOR GOOD CLINICAL PRACTICE 1 (1996) (providing “an international ethical and scientific quality standard for designing, conducting, recording and reporting trials that involve the participation of human subjects”).

53 For fifteen years (1956-1971) researchers conducted a non-therapeutic medical research studies on children at the Willowbrook State School, an institutional facility for mentally ill children on Staten Island, New York. Carl Coleman, et al, Historical Antecedents: Medical Research in the United States from 1900 to the Early 1970s, in THE ETHICS AND REGULATIONS OF RESEARCH WITH HUMAN SUBJECTS 39 (2005). Researchers infected healthy children, thus the study was not to treat a disease from which the children suffered. Early in the study the children were fed “extracts of stools from [Hepatitis-infected children] and injected with “more purified virus preparations” to determine “the natural history of hepatitis and the effects of gamma globulin in preventing or moderating its effects.” Id. While the study led researchers to develop a hepatitis vaccine and better understand the differences between Hepatitis A and B, healthy children were infected with life-long debilitating diseases. Id. The infected children could never use the new vaccine, and as a result of the studies were subject to costly treatment for the rest of their lives.

The researchers defended their work by noting hepatitis “was prevalent in the institution.” Id. They assumed the children would eventually acquire the disease. Id. Major medical journals (the Journal of the American Medical Association and the New England Journal of Medicine) published the results of the study, commending the researchers for their use of vulnerable children. Id. (noting that Franz Inglefinger argued in the New England Journal of Medicine that “the children benefited from being infected under carefully controlled research conditions and receiving expert attention.”) Furthermore, many scholars argue that parental consent forms were not entirely voluntary as due to overcrowding, the only way to have a child admitted to Willowbrook was through the hepatitis study. Id.

hearings, Congress created the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (Commission). In addition, Congress imposed a moratorium on research conducted or supported by the U.S. Department of Health and Human Services (HHS) on a living human fetus until adequate protections for such subjects were developed.

The Belmont Report was an outgrowth of the Commission’s deliberations regarding ethical protections and a 1976 conference at the Smithsonian Institute’s Belmont Conference Center. In the Belmont Report, the Commission selected justice as one of the three fundamental ethical principles to protect vulnerable groups from exploitation in medical research studies. The Commission noted that in the United States the burden of participating in medical research studies was borne principally by the economically disadvantaged while the rich enjoyed the benefits, as evidenced by the Tuskegee Syphilis Study.

From 1932 until 1972, researchers enrolled economically disadvantaged black men in a study to document the course of syphilis, even though the course of the disease was already known. In exchange for free meals, medical exams and burial insurance, the researchers promised the men that they would provide treatment for their “bad blood,” which could include “anemic blood to muscle aches, general malaise, disorders such as parasitic infections, gonorrhea, syphilis, and other venereal disease.” The researchers never informed the men that they were participating in a medical research study, and therefore, never told them about the purpose of the study. Researchers also intentionally deprived these men of “demonstrably effective treatment in order not to interrupt the project, long after such treatment became generally available,” causing the unnecessary disability and death of the men, their wives, and their children. The study was not a therapeutic study because it was not

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55 Belmont Report, supra note 8, at 23,192. The Commission was composed of eleven members appointed by the Secretary of HHS. Protection of Human Subjects of Biomedical and Behavioral Research Act, Pub. L. No. 93-348, § 201, 88 Stat. 348 (1974). The National Research Act advised the Secretary of HHS to choose the members of the Commission from distinguished individuals from the fields of medicine, law, ethics, theology, philosophy, humanities, health administration, government, public affairs, and the biological, physical, behavioral, and social sciences. Id. Five of the members of the Commission had to be individuals engaged in biomedical or behavioral research involving human subjects. Id. Members of the Commission included Dorothy I. Height, President of the National Council of Negro Women, Inc., Dr. Albert R. Jonsen, Associate Professor of Bioethics at the University of California at San Francisco, and Patricia King, Associate Professor of Law at Georgetown University Law Center. Office for Human Research Protections, The Belmont Report, HHS.GOV (March 15, 2016), http://www.hhs.gov/ohrp/regulations-and-policy/belmont-report/ [https://perma.cc/6665-WG3C].

56 Prior to 1980 and the enactment of the National Research Act, the U.S. Department of Health and Human Services was originally named the U.S. Department of Health, Education, and Welfare. See Department of Education Organization Act, Pub. L. No. 96-88, § 509(e), 93 Stat. 695 (1979) (codified at 20 U.S.C. § 3508 (2012). To avoid confusion when discussing events before and after the name change, I refer to the agency only as the U.S. Department of Health and Human Services.


58 Belmont Report, supra note 8, at 23,192.

59 Id. at 23,194. The two other principles were respect for persons and beneficence. These principles focus on ensuring that the subjects’ choices are voluntary (respect for persons) and that subjects are not sacrificed for the benefit of society (beneficence). Id. at 23,193-94.

60 Id. at 23,194.

61 JONES, supra note 54, at 4.

62 WASHINGTON, supra note 1, at 164.

63 See id. at 162-63.

64 Belmont Report, supra note 8, at 23,194. See also Deleso Alford Washington, Examining the “Stick” of Accreditation for Medical Schools Through Reproductive Justice Lens: A Transformative Remedy For Teaching the Tuskegee Syphilis Study, 26 J. OF CIV. RIGHTS & ECON. DEV. 153, 177, 193 (2011).
testing a possible treatment of syphilis and blocked any access to treatment.65 Additionally, the study was not a non-therapeutic study to attain generalizable knowledge because the medical community had already documented the disease process of syphilis.66 Thus, there was nothing gained from the study other than exploiting the economically disadvantaged and minorities.

To put an end to the exploitation of the economically disadvantaged and minorities, the Commission incorporated social justice into the ethical principles governing medical research studies using human subjects.67 Specifically, the Commission created the justice principle to determine “Who ought to receive the benefits of research and bear its burdens?”68 To answer this question and establish the contours of the justice principle, the Commission defined what is just and what is unjust in the selection of research subjects.69

In selecting research subjects, the justice principle requires that researchers ensure disadvantaged groups such as minorities, women, children, the institutionalized mentally infirm, prisoners, and the economically disadvantaged70 are not “being systematically selected simply because of their easy availability, their compromised position, or manipulability, rather than for reasons directly related to the problem being studied.”71 The Commission reasoned that:

whenever research supported by public funds leads to the development of therapeutic devices and procedures, justice demands both that these not provide advantages only to those who can afford them and that such research should not unduly involve persons from groups unlikely to be among the beneficiaries of subsequent applications of the research.72

According to the Commission, “the principle of justice gives rise to moral requirements that there be fair procedures and outcomes in the selection of research subjects” on two levels: Individual and Social.73 On the Individual level, researchers should include the disadvantaged in potentially beneficial research that is usually reserved for the rich, instead of using them for non-therapeutic and dangerous medical research studies.74 On the Social level, researchers must draw a distinction “between classes of subjects that ought, and ought not, to participate in any particular kind of research, based on the ability of members of that class to bear burdens and on the appropriateness of placing further burdens on [an already burdened group].”75 The Belmont Report noted that it was not fair for the economically disadvantaged, who rely on public funds for health care, to be considered as preferred research subjects for publicly funded research because of their need to access health care.76 Thus, there is an order of preference in the selection of research subjects, such that researchers should

65 See Washington, supra note 64, at 179-80.
66 After a lawsuit was filed on July 23, 1973, the government settled the case for approximately $10 million dollars ($37,500 to research participants with syphilis who were alive as of July 23, 1973, $15,000 to the heirs of research participants with syphilis, $16,000 to research participants without syphilis who were alive as of July 23, 1973, and $5,000 to the heirs of research participant without syphilis). JONES, supra note 54, at 217-19. Researchers directly involved the study never apologized. Id.
67 See Belmont Report, note 8, at 23,196.
68 Id. at 23,194.
69 See id.
70 Id. at 23,193-34 and 23,196-97.
71 Id. at 23,194.
72 Id.
73 Id. at 23,192.
74 Id. at 23,196.
75 Id.
use the rich before the economically disadvantaged, the majority before minorities, and adults before children.

On an Individual level, the justice principle requires inclusion of vulnerable groups for potentially beneficial research, while on a Social level this inclusion must be limited to protect vulnerable groups from being overburdened. Nevertheless, even after researchers balance the Individual and Social level requirements of the justice principle, the use of certain classes of people for research may be unjust because of “social, racial, sexual, and cultural biases institutionalized in society” that place a class of people in a vulnerable and compromised position, easily manipulated into participating in medical research studies.

For example, over three decades of empirical research studies show that racial bias institutionalized in society prevents many African Americans from receiving quality education, obtaining jobs, and accessing housing in safe, diverse, and environmentally-friendly neighborhoods. Studies show that African Americans seeking employment have a harder time obtaining employment because non-African American managers tend to hire more Caucasians. Also, African Americans with non-Caucasian names receive fifty percent less callbacks than African Americans with Caucasian sounding names. As a result, many African Americans are more likely to be unemployed or employed with no health insurance. Lacking health insurance or money to pay for health care, African Americans are left in a compromised position

77 See id. at 23,196.
78 Id.
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and easily manipulated into participating in medical research studies to obtain access to health care. Consequently, even if researchers fairly select African Americans as research subjects, without bad intent, these institutional racial biases, which place African Americans in a vulnerable and compromised position, easily manipulated into participating in medical research studies, make their use as research subjects a violation of the justice principle.\textsuperscript{83} To counteract these unjust social patterns the \textit{Belmont Report} requires researchers to consider distributive justice in selecting research subjects and follow the order of preference, using the rich before the economically disadvantaged, the majority before minorities, and adults before children.\textsuperscript{84}

\section*{B. Federal Regulation of Medical Research Studies and the Justice Principle}

In 1986, the \textit{Belmont Report} in its entirety, was adopted by sixteen federal agencies and departments, including HHS, and codified in 45 C.F.R Part 46 (the Common Rule).\textsuperscript{85} In fact, not only did the Common Rule make the justice principle law, but also it explicitly defined the groups protected by the justice principle as vulnerable populations that shall not be targeted.\textsuperscript{86} Vulnerable populations include minorities, children, prisoners, pregnant women, mentally disabled persons, and economically or educationally disadvantaged persons.\textsuperscript{87} It governs all research studies conducted by or funded by the federal government, except for those studies conducted in emergency settings.\textsuperscript{88}

Institutions receiving federal funding to conduct medical research must enter into a contractual agreement with the federal government, called an assurance, asserting that they will comply with the Common Rule.\textsuperscript{89} Once an institution’s assurance is approved and it receives federal funding, the federal government requires that all research conducted by the institution regardless of who funds it comply with 45 C.F.R Part 46. The Office for Human Research Protections (OHRP), a federal agency housed within HHS, is responsible for ensuring that institutions comply with their assurances and the Common Rule.\textsuperscript{90} To fulfill this task, OHRP may request additional information in writing, conduct telephone interviews, or conduct site visits.\textsuperscript{91} These visits can be random or in response to allegations of noncompliance with the Common Rule.\textsuperscript{92}

\textsuperscript{83} See \textit{Belmont Report}, supra note 8, at 23,196.
\textsuperscript{84} Id.
\textsuperscript{85} For list of agencies, see ROSS, supra note 10, at 23 n.101.
\textsuperscript{86} 45 C.F.R. § 46.111 (2015).
\textsuperscript{89} See generally id. at 137 (discussing different types of assurances).
\textsuperscript{90} Id.
\textsuperscript{91} Coleman et al., supra note 88, at 136-37; see also \textit{Memorandum from Director to OHRP Staff} (Dec. 4, 2000), \textit{in THE ETHICS AND REGULATIONS OF RESEARCH WITH HUMAN SUBJECTS} 138, 139 (2005) [hereinafter \textit{OHRP Memorandum}]. For government funded medical research studies in which there has been an allegation of noncompliance, Office of Human Rights Protections’ (OHRP) initiates an investigation. \textit{Id.} at 138-41. For a detailed sequence of events in compliance investigations, see \textit{id.} at 140-41.
\textsuperscript{92} Coleman et al., supra note 88, at 136-37.
When reviewing allegations of noncompliance, OHRP grants the institution an opportunity to refute the allegations. OHRP determines whether the institution has violated the law. OHRP issues corrective action for instances of noncompliance, which is in “the best interest of human research subjects, and to the extent possible, the institution, the research community, and HHS.” Corrective action may include restriction or withdrawal of approval for an institution’s assurance and suspension or permanent removal from participation in specific projects. Information regarding allegations and findings of noncompliance can be found on OHRP’s website.

OHRP is responsible for reviewing compliance at the institutional level. Every institution that has an assurance with OHRP is responsible for ensuring that individual medical research studies conducted by those affiliated with the institution comply with the Common Rule. To accomplish this task, all institutions and federal agencies that enter into an assurance with OHRP have an Institutional Review Board (IRB). There are an estimated 3,000 to 5,000 IRBs, which serve as the main protection for vulnerable populations in medical research studies.

Before researchers can conduct medical research studies using human subjects in the United States or be funded by the United States government to conduct medical research studies using human subjects, they must submit a research protocol to their IRB. A complete research protocol includes a statement of compliance with the ethical principles, such as the justice principle. The IRB reviews all written research protocols in application for medical research studies using human subjects to ensure that the proposed studies comply with the Common Rule, including the ethical requirements of the justice principle. If the IRB finds that the research protocol is ethical, they can approve the research to be conducted and/or submitted for funding to the United States government. The IRB can also require modifications in the research protocol or disapprove any research protocol.

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93 See OHRP Memorandum, supra note 91, at 139.
94 Id.
95 Id.
96 Id. at 140. Many, including the former Secretary of HHS, have argued that regulatory agencies have failed to issue meaningful sanctions. See L. Song Richardson, When Human Experimentation Is Criminal, 99 J. CRIM. L. AND CRIMINOLOGY 89, 126 (2008); Donna Shalala, Protecting Research Subjects – What Must Be Done, 343 NEW ENG. J. MED. 808 (2000). Usually, the only sanctions that OHRP imposes is posting a letter of violation on its website. See generally OHRP Determination Letters, DEP’T OF HEALTH AND HUMAN SERVS., OFFICE FOR HUMAN RESEARCH PROT., http://www.hhs.gov/ohrp/compliance-and-reporting/determination-letters/index.html [https://perma.cc/9C4X-KR8V]. However, in the past when the public pressure has become too much, some institution have voluntarily stopped the research studies, while others have continued the research studies. See generally David B. Resnik, Research Ethics Timeline, NAT’L INSTS. OF HEALTH, http://www.nihms.nih.gov/research/resources/bioethics/timeline/ [https://perma.cc/LX68-JKNP]. Yet, this is an erratic outcome that simply depends on how much media attention the study received.
97 See OHRP Determination Letters, supra note 96.
98 45 C.F.R. § 46.103(a).
99 Coleman et al., supra note 88, at 137.
100 45 C.F.R. § 46.101(a)(2).
102 45 C.F.R. § 46.101(a)(2).
103 45 C.F.R. § 46.103(b)(1).
104 45 C.F.R. § 46.101(a)(2).
105 See id.
In terms of the justice principle, the IRB is required to ensure that the “risks to subjects are minimized . . . by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk”\textsuperscript{107} and the selection of subjects is “equitable.”\textsuperscript{108} In order to determine if the selection of subjects is equitable the IRB is required to ensure that vulnerable populations are not targeted by taking into account the purposes of the research, the setting in which the research will be conducted, and the need to protect vulnerable populations.\textsuperscript{109} If the IRB allows vulnerable populations to be targeted, the institution is in violation of their assurance and subject to corrective action by OHRP. Not only does the justice principle apply to research conducted in the United States or funded by the United States government, but it also governs research used to seek drug approval in the United States.\textsuperscript{110}

C. ICH-GP

The International Council for Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) \textsuperscript{111} “is a unique project . . . [that] brings together the regulatory authorities of Europe, Japan and the United States and experts from the pharmaceutical industry in the three regions to discuss scientific and technical aspects of product registration.”\textsuperscript{112} The sole purpose of ICH is “to make recommendations on ways to achieve greater harmonisation in the interpretation and application of technical guidelines and requirements for product registration in order to reduce or obviate the need to duplicate the testing carried out during the research and development of new medicines.”\textsuperscript{113} The ICH developed the Good Clinical Practice guidelines (GCP), “an international ethical and scientific quality standard for designing, conducting, recording and reporting [medical research] trials that involve the participation of human subjects.”\textsuperscript{114} Researchers generating medical research study data to be submitted to regulatory authorities in the EU, Japan, and the United States, must comply with the ICH-GCP in order to have their drug approved in these countries.

Overall, “the objective of this ICH-GCP . . . is to provide a unified standard for the EU, Japan, and the United States to facilitate the mutual acceptance of clinical data by the regulatory authorities in these jurisdictions,” while protecting medical research subjects.\textsuperscript{115} Developed using ethical principles around the world to protect among other things, vulnerable populations from being targeted in medical research studies, the ICH-GCP defines vulnerable subjects as those who are economically disadvantaged, minority groups, and/or minors.\textsuperscript{116} To protect these vulnerable populations the ICH-GCP states that IRBs have to pay special attention to medical


\textsuperscript{109} Id.

\textsuperscript{110} 45 C.F.R. § 46.101(a).


\textsuperscript{112} Vision, INT’L COUNCIL ON HARMONISATION http://www.ich.org/about/vision.html [https://perma.cc/STF7-73C6].


\textsuperscript{114} Id.

\textsuperscript{115} Id. at 7. The clinical guidelines came from countries and organizations including countries in the European Union, Japan, United States, Australia, Canada, the Nordic countries and the World Health Organization (WHO). Id. at 1.
research studies that include subjects from vulnerable populations. Additionally, the ICH-GCP incorporates all of the principles of the Declaration of Helsinki.

The Declaration of Helsinki, drafted and adopted in 1964 by the World Medical Association, is a statement of ethical standards that was designed as a guide to physicians and others participating in medical research studies involving human subjects, in addition to the responsibilities imposed by their own countries. In 2000, thirty-six years after the adoption of the document, the World Medical Association amended the Declaration of Helsinki to include the justice principle.

Similar to the justice principle espoused in the Belmont Report, the Declaration of Helsinki advises medical researchers that vulnerable populations should not be targeted for medical research studies. Specifically, the Declaration of Helsinki states “[M]edical research with a vulnerable group is only justified if the research is responsive to the health needs or priorities of this group and the research cannot be carried out in a non-vulnerable group.” Hence, medical researchers cannot use human subjects from vulnerable populations just because they are readily available, easily manipulated into participating, or in a compromised position. Instead there is an order of preference in the selection of research subjects to use those from non-vulnerable groups first. The incorporation of the justice principle into the ICH-GCP demonstrates clearly the importance of the principle in protecting research subjects across the world.

Unfortunately, since the implementation of the justice principle in U.S. and international law, members of vulnerable populations continue to be targeted for medical research studies because of structural problems in the regulation process and a paradigm shift in the meaning of the justice principle. The regulatory problems, reasons for this shift, and examples of the egregious harm caused by both are discussed below.

IV. PRIVATE REGULATION AND INCLUSION: BARRIERS TO ENFORCEMENT OF THE JUSTICE PRINCIPLE

Structural flaws in the regulation of medical research studies have allowed researchers to often ignore the justice principle’s prohibition against targeting. Moreover, in 1990, only four years after being applied to medical research studies, there was a “paradigm shift” in the use of the justice principle that has allowed researchers to target economically disadvantaged minority children in the name of

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116 Id. at 10.
117 Id. at 1.
118 See Declaration of Helsinki, supra note 3.
120 Carlson, supra note 49, at 699-704.
121 See Declaration of Helsinki, supra note 3. Unlike the Common Rule, the Declaration of Helsinki does not define vulnerable populations using explicit characteristics. See id. Instead it states that “some groups and individuals are particularly vulnerable and may have an increased likelihood of being wronged or of incurring additional harm. All vulnerable groups and individuals should receive specifically considered protection.” Id. at Section 19.
122 Id. at Section 20. The Declaration of Helsinki also requires that if vulnerable groups are used in medical research studies, the “group should stand to benefit from the knowledge, practices or interventions that result from the research.” Id. In addition, the Declaration states that “[i]n advance of a clinical trial, sponsors, researchers and host country governments should make provisions for post-trial access for all participants who still need an intervention identified as beneficial in the trial. This information must also be disclosed to participants during the informed consent process.” Id. at Section 34.
123 See id. at Section 20.
inclusion. Specifically, instead of using the justice principle to protect economically disadvantaged minority children from researcher’s targeting, now researchers use the justice principle to grant economically disadvantaged minority children a ‘fair opportunity’ to participate in medical research studies. Proponents of inclusion have three main arguments.

First, they argue that inclusion provides economically disadvantaged minority children with access to innovative drugs. This argument misapprehends the true meaning and nature of medical research. Medical research is not treatment and can be a dangerous endeavor that causes significant harm and death. Second, they argue that the justice principle kept vulnerable populations, such as economically disadvantaged minority children, from participating in medical research studies. Empirical research shows that economically disadvantaged minority children never stopped participating in medical research studies. Third, proponents of inclusion argue that children are therapeutic orphans, meaning that they do not have drugs to address their specific health care needs, because the justice principle limits children’s participation in medical research studies. However, children have been therapeutic orphans since 1963, sixteen years before the creation of the justice principle. As a result of these regulatory and interpretation problems, economically disadvantaged minority children are still targeted for medical research studies.

A. ENFORCEMENT FAILURES IN THE REGULATION OF MEDICAL RESEARCH STUDIES

The current regulatory system is ineffective at protecting children from being targeted because the regulation of the justice principle has been left to the discretion of the very institutions that target vulnerable populations. The government delegated the authority to prevent targeting to IRBs, which are housed within the institutions that employ the researchers seeking grants. Because this money benefits the institution as well as the researcher, IRBs are often reluctant to deny approval of research protocols.

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125 Id. For more background regarding the conflict, see Michael Shevell, Ethics of Clinical Research in Children, 9 SEMINARS IN PEDIATRIC NEUROLOGY 46 (2002); Levine, supra note 13, at 116.
126 Harold Varmus & David Satcher, Ethical Complexities of Conducting Research in Developing Countries, 337 NEW ENGLAND J. MED. 1003, 1003-04 (1997).
127 The belief that medical research is treatment is called a “therapeutic misconception.” Oberman & Frader, supra note 6, at 308-10.
128 Ross, supra note 10, at 51, 56.
129 Id.
130 Id.
131 Id. at 61.
132 Donald Barlett & James Steele, Deadly Medicine, VANITY FAIR (Feb. 5, 2016), http://www.vanityfair.com/news/2011/01/deadly-medicine-201101 [http://perma.cc/4S8G-VFYD] (pointing out that independent contractors now run many drug medical research studies and select research subjects). Even though the same laws apply to these independent contractors and researchers from institutions with IRBs, the government does not even regulate these independent contractors. See id. Therefore, not only does the government need to regulate these contractors, but it should also apply the suggestions I have for preventing targeting discussed in Section V.
134 Beh, supra note 133, at 34-41.
In fact, scholars have noted that IRBs often fail to comply with federal law because they are “too weak, overburdened, ignorant, or conflicted.”\textsuperscript{135} The failure of IRBs to comply with the law is particularly troubling in instances concerning the justice principle because the IRB is the main protector of the vulnerable against targeting by researchers. Data also suggests that IRBs rarely review protocols for compliance with the justice principle compared to other requirements such as autonomy (informed consent).\textsuperscript{136}

Empirical evidence shows that IRBs returned “only 10 percent of research proposals . . . to investigators for clarification of subject selection,” while IRBs returned “the consent portion of proposal . . . for correction 25 percent of the time.”\textsuperscript{137} Moreover, if the proposed research subject is a pediatric patient in a hospital or clinic and a consenting parent or guardian is present, the researcher’s motives for including the child are never investigated.\textsuperscript{138} Additionally, the burdens borne by these children because of their socioeconomic and minority status are rarely measured.\textsuperscript{139} Thus, it is not surprising that some researchers continue to target economically disadvantaged minority children for use in medical research studies.

Another reason for the persistent targeting of vulnerable populations is lax federal oversight. Scholars note that OHRP barely reviews IRB compliance with the Common Rule.\textsuperscript{140} Furthermore, there is no mandatory public reporting of medical research studies conducted in the United States or in foreign countries.\textsuperscript{141} Consequently, IRB decisions regarding the selection of research subjects are never disclosed to the public unless there are allegations made to OHRP or to the media that the Common Rule has been violated. Even if IRBs and the OHRP enforced the Common Rule, there would still be issues with research subject selection because the regulations and government guidance are devoid of meaningful practical advice on how to ensure that subjects are selected equitably according to the justice principle.\textsuperscript{142}

The OHRP issued an IRB Guidebook, a non-binding guidance to assist IRBs in fulfilling their responsibilities in protecting the rights and welfare of human subjects.\textsuperscript{143} Chapter VI of the Guidebook addresses special classes of subjects, which includes all of the groups listed in the vulnerable population definition in the Common Rule.\textsuperscript{144} Even though the Guidebook was issued in 1993, it is telling that the only discussion regarding the selection of subjects is in response to cognitively impaired persons.\textsuperscript{145} There is no discussion about the equitable selection of children or minorities, the main groups whose targeting served as the basis for the creation of the justice principle.\textsuperscript{146} Furthermore, even though the Guidebook addresses the use of children and foster children in medical research studies, these guidelines only focus on

\textsuperscript{135} Id.
\textsuperscript{136} See id. at 32-33
\textsuperscript{138} Id.
\textsuperscript{139} Id.
\textsuperscript{140} Beh, \textit{supra} note 133, at 34.
\textsuperscript{141} Barlett & Steele, \textit{supra} note 132.
\textsuperscript{143} See OHRP GUIDEBOOK, \textit{supra} note 87.
\textsuperscript{144} Id.
\textsuperscript{145} Id.
\textsuperscript{146} Id.
autonomy (informed consent) and beneficence (the best interest of the child based on a benefit risk analysis), not the justice principle.147

The lack of guidance in applying the justice principle is highlighted in the medical research literature. As T. Howard Stone notes, “[T]here is a dearth of literature addressing how IRBs should approach the review of research involving persons who are economically or educationally disadvantaged.”148 Consequently, persons from vulnerable populations “remain unduly vulnerable to clinical research risks, and they have become the ‘invisible vulnerable.’”149 These regulatory failures are compounded by the shift in interpretation of the justice principle from protection to inclusion.

B. PROTECTION TO INCLUSION: THE PROBLEM OF INTERPRETATION

The justice principle was only in effect for four years, when the federal government shifted its view from protection of vulnerable populations, to inclusion of vulnerable populations to promote greater access to medical research studies.150 This campaign to change the meaning of the justice principle was a result of three things: 1) HIV/AIDS epidemic; 2) the perceived lack of participation of economically disadvantaged minority children in medical research studies; and 3) the therapeutic orphan problem. In response to these three events, civil rights organizations, patients, physicians, and researchers began advocating for the right of vulnerable populations, particularly economically disadvantaged minority children, to participate in medical research studies to gain access to potentially life-saving treatment. Unfortunately, inclusion has not provided the benefits that advocates were fighting for. Instead, it has provided the justification for targeting economically disadvantaged minority children for participation in medical research studies.

1. Therapeutic Misconception

In the 1990s, medical research became synonymous with treatment. Carol Levine notes that the HIV/AIDS epidemic is responsible for the paradigm shift.151 As a result of the HIV/AIDS crisis, people were dying with no hope for treatment. New HIV/AIDS drugs and therapies were being tested in medical research studies, but not available to the general public. Consequently, HIV/AIDS medical research was viewed as “cutting-edge medical treatment” not “experimental research” that could cause serious harm.152 Thus, some HIV/AIDS activists began to argue that medical research “served as an important means of access to otherwise unobtainable and theoretically helpful new therapies.”153 In fact, some HIV/AIDS activists began to argue that access to medical research studies for vulnerable populations should be considered an essential good, like food and housing, rather than a risk from which vulnerable populations should be protected.154 However, these arguments misinterpret the true nature of medical research.

147 Id.
149 Id.
150 See ROSS, supra note 10, at 25.
151 See Levine, supra note 14, at 109.
153 EPSTEIN, supra note 130, at 63 (emphasis added).
154 Id.
Medical research studies are not therapeutic and do not guarantee life-saving medicine. This is a therapeutic misconception. Although there is no potential for a benefit in Phase I and II medical research studies, many patients, providers, and even researchers believe that enrollment in these studies is beneficial for the patient because the patient will receive treatment. This therapeutic misconception is often used to justify the targeting of vulnerable populations to serve as research subjects, such as economically disadvantaged minority children, in medical research studies.

Participation in medical research studies is also not an essential good, like food, which economically disadvantaged minority children are often denied. Unlike an essential good, there are risks associated with participation in medical research studies including stigma, long-term disability, and death. For example, in the late 1980s, researchers in Los Angeles gave healthy African American infants five hundred times the approved dose of an experimental measles vaccine, which had already sickened and killed children in Senegal, Mexico, and Guinea-Bissau. Not only did this medical research study not provide any treatment, but it also caused harm.

In the 1990s, the Kennedy Krieger Institute researchers investigating cheaper lead abatement techniques partnered with landlords to partially abate lead tainted housing in Baltimore. In order to test the efficacy of the abatement procedures, the researchers in collaboration with the landlords ensured that only families with healthy children lived in the lead tainted housing by agreeing to pay for abatement procedures if the landlords rented to families with young children. Due to the racial makeup of the neighborhood, the young children participating in the study were all minorities. Even though the information given to parents “implied that the study was protecting their children from lead damage and promised to inform parents of any hazards,” such as abnormal tests showing high lead levels, the study was non-therapeutic because it provided no benefit to the participants. In fact, the researchers did not notify the parents of their children’s elevated lead levels or lead hot spots in the house. As a result, many of the healthy children suffered exposure to lead, which can cause inattention, irritability, hyperactivity, learning and reading delays, delayed growth and hearing loss, permanent brain damage, and even death. Thus, this study did not provide treatment or a benefit to society, and it caused harm.

155 Francis, supra note 30, at 228-29; Oberman & Frader, supra note 6, at 308-10.
156 Francis, supra note 30, at 228-29; Oberman & Frader, supra note 6, at 308-10.
157 Francis, supra note 30, at 229-30.
158 Bridget Pratt, & Bebe Loff, Linking International Research to Global Health Equity: The Limited Contribution of Bioethics, 27 BIOETHICS 208, 209-10 (2013); Bridget Pratt, Deborah Zion & Bebe Loff, Evaluating the Capacity of Theories of Justice to Serve as a Justice Framework for International Clinical Research, 12 AM J. BIOETHICS 30, 32 (2012); Varmus & Satcher, supra note 126, at 1003. There is a moral conflict between pursuing medical discoveries through medical research to find cures that will benefit society and protecting subjects from exploitation. The theory that medical research is conducted for the common good becomes corrupted when pursuing medical discoveries is suffused with a profit motive. Therefore, before medical research is conducted the social and economic needs of the society must be considered. Daniel Callahan, What Price Better Health?: Hazards of the Research Imperative 57, 62 (2003).
159 Washington, supra note 1, at 295.
161 Id. Washington, supra note 1, at 292.
162 Grimes, 782 A.2d at 811-17; Washington, supra note 1, at 292.
163 Grimes, 782 A.2d at 824; Washington, supra note 1, at 292.
164 Grimes, 782 A.2d at 823-33.
From 1992 to 1997, researchers at Columbia University’s Lowenstein Center for the Study and Prevention of Childhood Disruptive Behaviors and New York City’s New York State Psychiatric Institute conducted research to try to show a link between genetics and violence, using only healthy and non-violent African American and Latino children.\textsuperscript{166} The researchers administered fenfluramine to 126 boys between the ages of six and ten, even though the drug had already been shown to cause heart-valve damage, pulmonary hypertension (a life-threatening form of high blood pressure), brain damage, and death in adults.\textsuperscript{167}

As a result of participating in the study, children suffered physical harm including but not limited to anxiety, fatigue, headaches, lightheadedness, difficulty concentrating, visual impairment, diarrhea, and nausea.\textsuperscript{168} No generalizable knowledge was obtained from this study because the premise of the research was that genetics was linked with violence had been disproven by over a century of research.\textsuperscript{169} Furthermore, the researchers’ use of only minorities in the study, even though Caucasians also commit acts of violence, sent the message that minorities are more violent than Caucasians and thus must be studied.\textsuperscript{170} Thus, inclusion of minority children in the study did not grant them access to new medicine or treatment and it caused harm.

These studies are not outliers. In fact, empirical data shows that in comparison with their percentage in the U.S. census, African American children continue to be overrepresented in non-therapeutic medical research studies and underrepresented in Phase III therapeutic medical research studies.\textsuperscript{171} This means that when compared to Caucasians, African American children participate in medical research studies that may not add to scientific knowledge beneficial to society, but not in medical research studies that will be beneficial for them as a group by providing treatment.

Hence, the justice principle must mean more than a ‘fair opportunity’ for economically disadvantaged minority children to participate in medical research studies that are meaningless or can cause long-term disability or death. This holds true especially for economically disadvantaged minority children, who have already been denied the essential goods of food, housing, education, and access to health care.

2. The Myth of Protection: Participation in Medical Research Studies Never Stopped

In the 1990s HIV/AIDS disproportionately affected vulnerable populations allegedly protected from the harms of medical research (women, minorities, and children); these vulnerable populations, civil rights organizations, physicians, and researchers advocated for the populations’ right to participate in medical research studies to gain access to potentially life-saving treatment. The argument for the need for inclusion was further bolstered by media reports that minorities and children lacked access to HIV/AIDS drug studies.

For example, using National Institutes of Health (NIH) documents, a reporter noted in a front page Los Angeles Times article that African Americans, Latinos, and groups disproportionately afflicted with HIV/AIDS were significantly underrepresented in federally-sponsored HIV/AIDS clinical trials.\textsuperscript{172} Advocates of inclusion also argued that children with HIV/AIDS in the United States did not receive

\begin{itemize}
  \item \textsuperscript{166} WASHINGTON, supra note 1, at 272.
  \item \textsuperscript{167} Id. at 274-78.
  \item \textsuperscript{168} Id. at 278-79.
  \item \textsuperscript{169} Id. at 275-76.
  \item \textsuperscript{170} Id.
  \item \textsuperscript{171} ROSS, supra note 10, at 48-50.
  \item \textsuperscript{172} EPSTEIN, supra note 130, at 61.
\end{itemize}
AZT until three years after adults gained access to AZT because children were denied participation in medical research studies as a result of the justice principle.\textsuperscript{173} The theory of inclusion is based on an incorrect assumption that economically disadvantaged minority children were not participating in medical research studies, including those related to HIV/AIDS.\textsuperscript{174} However, even once the justice principle was adopted, economically disadvantaged minority children were being targeted for, and as a result, participating in medical research studies.

For example as discussed in more detail in subsection C, economically disadvantaged healthy African American and Latino children in the United States and abroad were used as research subjects in Phase I and II HIV/AIDS drug studies.\textsuperscript{175} Research shows that not only did some of these healthy children experience long-term disability or die as a result of their participation in these studies,\textsuperscript{176} but it also shows that many economically disadvantaged minority children in the United States and abroad still do not have access to this medicine.\textsuperscript{177}

Continuing lack of access to HIV/AIDS drugs is illustrated by a medical research study conducted by a U.S. researcher. Funded by the U.S. government, the research study used economically disadvantaged HIV-positive children in the Dominican Republic “to determine if massage therapy would boost the immune systems” of the children.\textsuperscript{178} “The children were ‘randomized’ into two groups. One received therapeutic massage; the other, made up of twelve HIV-positive children, met with a nurse for ‘reading, talking, playing quiet games’ as part of the friendly visit control group.”\textsuperscript{179} The results from the study were reported in The Journal of Alternative and Complementary Medicine.\textsuperscript{180} In this study, the inclusion doctrine was used to give economically disadvantaged minority children a ‘fair opportunity’ to participate in medical research studies that did not provide them with any access to HIV/AIDS drugs.\textsuperscript{181} The research did not address the problem of children as therapeutic orphans.\textsuperscript{182} Instead, it continued the practice of targeting minority children already living in poverty for medical research studies.\textsuperscript{183}

\textsuperscript{173}See id. at 63-64.
\textsuperscript{174}See id.
\textsuperscript{176}See Solomon, supra note 175.
\textsuperscript{179}Id.
\textsuperscript{180}Gail Shor-Posner et al., Massage Treatment in HIV-1 Infected Dominican Children: A Preliminary Report on the Efficacy of Massage Therapy to Preserve the Immune System in Children Without Antiretroviral Medication, 10 J. ALTERNATIVE & COMPLIMENTARY MED. 1093, 1095 (2004) (reporting that massage therapy as a complementary treatment may “have a positive impact on immune function in HIV+ children not receiving antiretroviral medications”).
\textsuperscript{181}Id. at 1094.
\textsuperscript{182}Id. at 1094-95.
\textsuperscript{183}Id.
3. Therapeutic Orphans

In the 1990s, the federal government, health care providers, and parents were worried about the fact that children were ‘therapeutic orphans’ because “more than 75 percent of drugs marketed to children” in the United States had never been tested in children. Arguing for the inclusion of children in medical research studies, “patient advocates and some clinicians have noted that, in the interest of good medical care, drugs should be tested on the populations that will use them.” Although this lack of testing is definitely a problem, the failure to test drugs on children was not a result of the four years of protection from targeting granted by the justice principle.

Children have been ‘therapeutic orphans’ since 1963, at a time when researchers were putting radioactive material in healthy children’s oatmeal, cutting out parts of the brain of healthy children, injecting healthy children with Hepatitis, and using radiation to cause third-degree burns on healthy children as young as six months old. Hence, the therapeutic orphan problem was not a result of the protections required by the justice principle. It is not surprising that the shift to inclusion did not increase medical research studies using children. In fact even after the shift to inclusion, the U.S. government had to encourage pharmaceutical companies to conduct medical research studies on children.

In 1997, Congress passed the Food and Drug Administration Modernization Act (FDAMA) to incentivize pharmaceutical companies to conduct medical research on children by providing an additional six months of patent exclusivity to the companies even if the results were negative or inconclusive. The government hoped that the medical research would provide safety and efficacy information for drugs and therapies used on children, ensuring that they were no longer therapeutic orphans. In 2000, Congress passed the Children’s Health Act, which included the Pediatric Research Initiative. The law made medical research studies of childhood illness and conditions a priority, however, funding for research using children still lagged behind funding for all other medical research. In 2002, Congress extended the FDAMA incentives in the Best Pharmaceuticals for Children Act (BPCA), which provided government subsidies for medical research studies testing drugs no longer under patent. A year later, Congress passed the Pediatric Research Equity Act, which requires that all new pharmaceuticals be tested on children.

Federal agencies and groups have also tried to increase the use of children in medical research studies. In 1998, the NIH issued policy guidelines requiring all NIH-funded research to “include a plan for the inclusion of children, unless there is good justification to exclude them.” The Institute of Medicine (IOM) also issued a report about the use of children in medical research studies in response to a mandate in the

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184 EPSTEIN, supra note 130, at 61; see also ROSS, supra note 10, at 24.
185 Levine, supra note 14, at 110. In response to these campaigns, Congress enacted Section 492B of the 1993 NIH Revitalization Act, mandating the inclusion of some vulnerable populations, including women and minorities, in all research projects funded by the NIH. Id. at 112.
186 EPSTEIN, supra note 130, at 61.
187 WASHINGTON, supra note 1, at 233, 236-37, 284, and 294; Carl Coleman et al., supra note 53, at 39.
189 Id.
190 Id.
192 ROSS, supra note 10, at 27.
The purpose of the IOM report was to increase the participation of children in medical research studies. Consequently, the IOM recommendations focused on access instead of protection including paying children to participate in medical research studies and permitting waivers of consent.

As a result of these efforts, between 1987 and 2006, 135 drugs were granted extended patent exclusivity and approximately 150 new drugs were approved through studies using children. Notwithstanding these incentives, children still remain therapeutic orphans. Pharmaceutical companies have focused on conducting medical research studies on children for drugs with a large adult market. Sometimes these studies have resulted in death or long-term disability. For example, in 2013, the U.S. Food and Drug Administration (FDA) halted all pediatric medical research studies of a calcium-lowering drug used in adults because of the death of a fourteen year old participating in the study. The drug was not geared to treat a childhood specific illness. Thus, inclusion of children in medical research studies has not fixed the therapeutic orphan problem.

C. RESULTING HARM: TARGETING FOR INCLUSION

Even when included in medical research studies conducted to find pediatric drug uses, many children are still targeted for medical research studies, resulting in serious harm. Below is a brief summary of the most notable studies.

1. Studies in the United States

For thirteen years (1988-2001), Illinois, Louisiana, Maryland, New York, North Carolina, Colorado, and Texas enrolled foster children, between the age of three months to nineteen years old, in Phase I and II drug studies for the treatment of the HIV/AIDS. Many of the foster children used for the study were African American or Latino and were economically disadvantaged. The medical research tested various drugs including protease inhibitors, Ritonavir therapy, and the live-attenuated Varicella vaccine. See Letter from Karena Cooper, Compliance Oversight Coordinator, Office for Human Res. Protections to Harvey Colten, Vice President & Senior Assoc. Dean for the Faculties of Health Sciences & Med., Columbia Univ. Med. Ctr. and Laura Forese, Vice President & Chief Med. Officer, N.Y. Presbyterian Hosp. (May 23, 2005), http://archive.hhs.gov/ohrp/detrm_letrs/YR05/may05c.pdf [https://perma.cc/H95W-X82K].

Solomon, supra note 175. In response to reports of ethical violations, the New York City Administration for Children’s Services (ACS) commissioned a study by the Vera Institute of Justice. Khabir Ahmad, Ethics of AIDS Drug Trials on Foster Children Questioned, 5 LANCET INFECT. DIS. 333, 333 (newsdesk) (2005). Some questioned the credibility of the investigation since “ACS lied about the number of children involved, stating in April 2004 that only 76 children were involved; later the number increased to 100, and now 465.” Id. The report is at Vera Institute of Justice, THE EXPERIENCES OF NEW YORK CITY FOSTER CHILDREN IN HIV/AIDS CLINICAL TRIALS 75 (January 2009) (a state-sponsored, independent review of New York City’s involvement in the medical research revealed that “sixty-four percent of the children were non-Hispanic blacks, 30 percent were Hispanic of varying races and fewer than 2 percent were non-Hispanic whites.”).
to be safe in adults. Funded in part by the NIH, the trials exposed the drug toxicity and adverse side effects of potential HIV/AIDS drugs not yet proven to be safe for children. There were a plethora of problems with the studies, including the targeting of economically disadvantaged minority foster children because of their manipulability and compromised position.

In response to innumerable complaints and newspaper exposés, OHRP finally investigated the use of economically disadvantaged minority children in HIV/AIDS drug studies and found that their use was inequitable. Seventeen years after the HIV/AIDS drugs studies started, OHRP issued a letter to the head of the IRB at Columbia University Medical Center, noting that some of the HIV/AIDS drug studies conducted at their institution violated the law. Specifically, the IRB approved research protocols in which researchers had inequitably targeted economically disadvantaged minority children in foster care to participate in the studies. In 2006, OHRP sent letters of violation to fourteen other universities conducting HIV/AIDS drug studies. Each letter noted that the universities had targeted economically disadvantaged minority foster children in violation of the justice principle and the Common Rule.

Nevertheless, OHRP did not put an end to the studies, did not impose any sanctions, and its findings failed to directly address the actions of the researchers who violated the justice principle. Consequently, the researchers who conducted the studies were able to publish their findings in medical journals without repercussions. In issuing its findings, OHRP did not even explain why they found that the studies targeted economically disadvantaged minority children as research subjects, but I suggest several reasons.

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204 Id.
205 Solomon, supra note 175.
206 In addition to this subjection of economically disadvantaged minority children to hazardous drug trials, some researchers failed to obtain proper consent from participants in the trials. There were two common practices that violated the informed consent laws. First, five children participating in the New York drug trials between five and ten years of age were asked to sign consent forms once they were told of the risks and benefits. See Solomon, supra note 175. Second, many of the researchers failed to obtain consent from an authorized person, such as an independent advocate, for each child. Id. The only consent researchers obtained for participating foster children were blanket consents from child welfare agencies. Id. None of the 200 Illinois foster children were appointed independent monitors even though researchers signed a document guaranteeing “the appointment of an advocate for each individual ward participating in the respective medical research.” Id. In New York, monitors were only appointed to less than one-third of the 465 foster children participating in the medical research studies. Id.
207 See Letter from Karena Cooper, supra note 202.
208 Id. at 2.
209 The following institutions received letters determining that they had selected foster children inequitably: Bellevue Hospital Center, Bronx-Lebanon Hospital Center, Children’s Hospital of King’s Daughters, Children’s Hospital Association, Children’s Hospital of Philadelphia, Children’s Hospital and Research Center at Oakland, Children’s Hospital and Regional Medical Center, Cook County Bureau of Health Services, Drexel University College of Medicine, Duke University School of Medicine, Johns Hopkins University/Johns Hopkins Health System, State University of New York-Upstate Medical University, University of Chicago, and University of Miami. See, e.g., Letter from Kristina C. Borror, Dir., Div. of Compliance Oversight, Dept. of Health & Human Servs., to Lynda D. Curtis, Senior Vice President & Exec. Dir., Bellevue Hosp. Ctr. (June 19, 2006), http://www.hhs.gov/ohrp/compliance-and-reporting/determination-letters/index.html; Letter from Julia Gorey, Div. of Compliance Oversight, Dept. of Health & Human Servs., to Steve Anderman, Senior Vice President & Chief Operating Officer, Bronx-Lebanon Hosp. Ctr. (June 19, 2006), http://www.hhs.gov/ohrp/compliance-and-reporting/determination-letters/index.html. Additional letters available at http://www.hhs.gov/ohrp/compliance-and-reporting/determination-letters/index.html.
210 See OHRP letters, note 209.
211 Id.
First, the selection of the children for participation in the HIV/AIDS drug studies violated the justice principle’s order of preference for selecting subjects. The preference requires that adults are used before children, the rich before the economically disadvantaged, and the majority before the minority. Some of the drugs tested in children were simultaneously being tested in adults. Second, the children were public wards and according to the justice principle, researchers are not allowed to use the economically disadvantaged, who rely on public funds for health care, to be used as research subjects for publicly funded research.

Third, not all the children used in the HIV/AIDS drug studies were even tested for HIV/AIDS. The states gave blanket consent for the use of these children instead of reviewing the files of each child to see if the child was even infected with HIV/AIDS. Thus, it can be argued that the children were selected simply “because of their easy availability, their compromised position, or manipulability, rather than for reasons directly related to the problem being studied.”

Fourth, the healthy children were unnecessarily “exposed . . . to risks of medical research and drugs that were known to have serious side effects in adults and for which the safety for children was unknown.” The drugs tested were failed cancer drugs that had severe side effects including rashes, vomiting, sharp drops in infection-fighting blood cells, and death. Hence, yet again, healthy minority children were subjected to medical research studies that lead to disability and death.

The dangers of participation in these studies for healthy children are best illustrated by an Illinois study of Dapsone, a drug to prevent AIDS-related pneumonia. “Researchers reported some children had to be taken off the drug because of ‘serious toxicity,’ others developed rashes, and the rates of death and blood toxicity were significantly higher in children who took the medicine daily, rather than weekly.” The researchers noted that for the period of the study “[a]t least 10 children died from a variety of causes, including four from blood poisoning, and researchers said they were unable to determine a safe, useful dosage. They said the deaths didn’t appear to be ‘directly attributable’ to Dapsone but nonetheless were ‘disturbing.’”

Finally, the HIV/AIDS drug studies continued even after 1990 when Azidothymidine, better known as AZT, was shown to be an effective treatment for HIV/AIDS without severe side effects. Children who participated in these HIV/AIDS drug tests were prohibited from taking AZT in order to determine if the new drugs were effective. This would have been acceptable if each foster child enrolled in the study had been tested to see if AZT was not an option. If AZT was not
MISSING THE “TARGET”: PREVENTING THE UNJUST INCLUSION OF VULNERABLE CHILDREN FOR MEDICAL RESEARCH STUDIES

an option for treatment, then and only then, would it be just for the children to participate in medical research.

Advocates of the research have argued that the inclusion of these children in the research benefited the children by increasing their access to new and effective HIV/AIDS drugs. However, it is unclear how many children participating in the study actually needed access to HIV/AIDS drugs, because none of the children were actually tested for HIV/AIDS. Furthermore, as discussed in Section IV.B.1, the presumption that participation in medical research studies, particularly Phase I and II studies, provides access to life-saving treatment is a therapeutic misconception. These phases only test safety and toxicity. Hence, participation in medical research studies at these stages does not provide the participant with a direct health benefit, especially when compared to the dangers of the research.

Furthermore, economically disadvantaged minority children who have HIV/AIDS and participated in the early phases of HIV/AIDS drug studies were not provided with access to the drugs that were approved in the United States and abroad. In fact, many of these children with HIV/AIDS still do not have access to HIV/AIDS drugs because they cannot afford them. Harms caused by the inclusion doctrine are not just limited to the United States. Researchers have used this doctrine to grant economically disadvantaged minority children in developing countries a ‘fair opportunity’ to participate in medical research studies that have not increased access to treatment and have resulted in serious harm and death.

2. Inclusion Theory Internationally

In 2008, researchers conducted vaccine trials on infants in Santiago del Estero, a province of Argentina. The trials were testing Synflorix, a new vaccine, “to prevent pneumonia, ear infections, and other pneumococcal diseases,” which would compete against a vaccine already approved and proven safe and effective. That year, seven babies died from Synflorix, and a total of fourteen children died during the testing. Because there was no evidence that children in this region disproportionately suffered from ailments Synflorix was intended to treat, there was no reason to use these children for the study other than their compromised position and easy manipulability.

Over a thirty-month period, children in New Delhi were enrolled in medical research studies testing a wide range of drugs “from high blood pressure to chronic focal encephalitis, a brain inflammation that causes epileptic seizures and other neurological problems.” Approximately, two-thirds of the children studied were less than one year old, of which forty-nine died as a result of participation in these medical research studies. Again there was no evidence that children in this region

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224 Levine, supra note 14, at 117.
225 Solomon, supra note 175; Ahmad, supra note 203, at 333.
226 Oberman & Frader, supra note 6, at 308.
227 See generally Bayer, supra note 175, at 569.
229 See, e.g., Shor-Posner et al., supra note 180, at 1094.
230 Barlett & Steele, supra note 132.
231 Id.
232 Id.
233 Id.
234 Id.
disproportionately suffered from these conditions, so there was no reason to use them for the study other than their compromised position and easy manipulability.

In 1996, researchers traveled to Kano, Nigeria to test Trovan, an antibiotic, on pediatric patients suffering from bacterial meningitis.\footnote{Adriana Petryna, When Experiments Travel: Clinical Trials and the Global Search for Human Subjects 38-39 (2009).} The objective of the study was to determine whether an oral version of Trovan, one of the United States’ best selling antibiotics, worked better than ceftriaxone, a fast-acting antibiotic already proven effective for treating bacterial meningitis.\footnote{Id. at 39.} Two hundred children waiting for ceftriaxone, the proven therapy, participated in the study.\footnote{Id.} Instead of receiving ceftriaxone, some children were given an oral version of Trovan, which had never been tested before in humans.\footnote{Id.} Others were given a dose of ceftriaxone that was below the dosage prescribed to treat bacterial meningitis.\footnote{Id.} Eleven children died unnecessarily.\footnote{Id. A two-billion-dollar lawsuit was filed in the United States against the U.S. based pharmaceutical company alleging that the low dosing of ceftriaxone caused the children’s death. Id. The case has been moved to Nigeria. Id. at 40. In 2006, a panel of judges in Nigeria found that Pfizer’s studies violated international law. Joe Stephens, Panel Faults Pfizer in ’96 Clinical Trial in Nigeria, WASH. POST (May 7, 2006), http://www.washingtonpost.com/wp-dyn/content/article/2006/05/06/AR2006050601338.html [https://perma.cc/36B9-2QF6].} Advocates of the research and the inclusion doctrine argued that the research did not violate the justice principle because it provided access to medicine as “a ‘massive epidemic [of bacterial meningitis] killing more than 11,000 people’” spread across Nigeria.\footnote{Petryna, supra note 235, at 40.} However, this study inequitably targeted Nigerian children in violation of the justice principle.

Comparable to the HIV/AIDS drug studies discussed above, the antibiotic medical research studies violated the order of preference for selecting research subjects because children were used to test oral Trovan before being proven safe in humans.\footnote{Id. at 39.} Second, the study was conducted during an epidemic although there was already a proven treatment.\footnote{Id.} Thus, it can be argued that the children were selected because the bacterial meningitis was an epidemic, which put the children in a compromised position to participate in medical research studies that promised potentially life-saving treatment.\footnote{Id.}

Third, the study caused harm because it prevented all participants from obtaining the proven therapy. Even though some children were given ceftriaxone, the dosage was below that needed to treat bacterial meningitis.\footnote{Id.} Moreover, the oral form of Trovan was never used outside of the study and three years later the United States limited the use of the non-oral form of Trovan because it was linked to liver damage and deaths.\footnote{Id.}

As evidenced by the aforementioned studies, the inclusion doctrine has been used as a justification for ignoring the requirements of the justice principle to target economically disadvantaged minority children for participation in medical research. The time has come to redefine justice, to measure the impact of research on vulnerable populations, and to implement a new regulatory structure for approving medical
research studies conducted using children, particularly economically disadvantaged minority children.

V. JUSTICE AS EQUITY IN PARTICIPATION: USING THE VULNERABILITY AND EQUITY IMPACT ASSESSMENT TO STOP TARGETING

Although arguments for inclusion were based on altruistic notions of providing everyone with a ‘fair opportunity’ to participate in medical studies, some researchers have used this interpretation of the justice principle to target economically disadvantaged minority children. As a result, numerous children have died or been seriously harmed. Consequently, the justice principle must be redefined in a manner that ensures equity and fairness in the use of all children.

I suggest that justice should be defined as “equity in participation,” which demands that economically disadvantaged minority children are only selected for medical research studies if their participation allows them to reach their highest attainable standard of health, by granting them continued access to health care and/or the alleviation of some burdens placed on them. This is accomplished when the medical research study focuses on conditions that are a priority to this population, eliminates some social disadvantage, and does not place additional burdens on them.

To ensure that there is equity in participation in medical research studies using economically disadvantaged minority children, I propose the use of the Vulnerability and Equity Impact Assessment (VEIA), which I created based on the Health Equity Impact Assessment (HEIA) tool. Under the VEIA, the researcher must complete an introspective summary of their research that includes the study’s purpose, the affected population, whether the research is a priority to the affected population, and any disparities (age, race, or class) in the treatment of the condition. Researchers must also identify the social disadvantage of, and burdens on, these vulnerable children being considered for participation, the adverse impacts from participating in the study, and how participation will outweigh these burdens and adverse impacts. If researchers determine that because of their status (age, social class, or race) children are easily manipulated, in a compromised position, or overburdened, then the researchers cannot use the children as research subjects.

Using the VEIA, a newly created Board of Children (Board) would be responsible for approving all medical research studies that include children and are seeking federal funding or drug approval in the United States. The completed tool should be posted on ClinicalTrials.gov and used by the Board to determine if the researcher is targeting economically disadvantaged minority children in violation of the redefined justice principle. Redefining justice to mean equity in participation, implementing the VEIA, and creating a Board to review all medical research studies using children will provide the analytical and regulatory framework currently missing from the IRB process.

A. JUSTICE AS EQUITY IN PARTICIPATION

To put an end to targeting, there must be a shift in the interpretation of the justice principle from the inclusion doctrine to the “equity in participation” doctrine, which I created based on equity in health definitions. The justice principle should include a definition of equity, which requires that everyone have a fair opportunity to attain his

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247 HABER, supra note 11 (explaining the Health Equity Impact Assessment).
Specifically, equity in participation will require researchers to use the order of preference to select research subjects and prevent them from overburdening economically disadvantaged minority children by further restricting their limited access to health care. Hence, I propose that the justice principle be defined as equity in participation based on Drs. Braveman and Gruskin’s definition of equity in health. Braverman and Gruskin’s definition states that, “[e]quity in health is an ethical value, inherently normative, [and] grounded in the ethical principle of distributive justice.” Equity in health has been used to “guide operationalization and measurement” of the right to the “highest attainable standard of health as indicated by health status of the most socially advantaged group.” According to Drs. Braveman and Gruskin, equity in health is “the absence of systematic disparities in health (or in the major social determinants of health) between [race and class] social groups who have different levels of underlying social advantage/disadvantage—that is different positions in a social hierarchy.” “Inequities in health systematically put groups of people who are already socially disadvantaged (for example, by virtue of being economically disadvantaged, female, and/or members of a disenfranchised racial, ethnic, or religious group) at further disadvantage with respect to their health.” “The concept of health equity focuses attention on the distribution of resources and other processes that drive a particular kind of health inequity.” “A health disparity between more and less advantaged population groups constitutes an inequity . . . because the disparity is strongly associated with unjust social structures,” which “put disadvantaged groups at generally increased risk of ill health and also generally compound the social and economic consequences of ill health.”

Not only does equity define what is fair, it imposes duties. According to the government of Ontario, equity in health requires the state to reduce “systemic barriers to equitable access to high quality health care for all; [to address] the specific health needs of people all along the social gradient, including the most health disadvantaged populations; and [to ensure] that the ways in which health services are provided and organized contributes to reducing overall health disparities.” Health equity also imposes a duty on the state to work to “reduce or eliminate socially structured health inequalities and differential health outcomes.”

Using these theories of equity and duty as a guide, I suggest that the justice principle be defined in terms of equity in participation. In particular, equity in participation should mean that vulnerable populations, such as economically disadvantaged minority children, can only serve as research subjects when the medical research study will allow the participants to reach their highest attainable standard of health. This is accomplished when the medical research focuses on conditions that are a priority to the vulnerable population, eliminates some form of social disadvantage,

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250 Braverman & Gruskin, supra note 248, at 256.
251 Id. at 254.
252 Id.
253 Id.
254 Id. at 255.
255 Id.
257 Id.
and does not add burdens to the vulnerable population. Even if the study fulfills these requirements, researchers should not use these populations if they are in a compromised position and participation can exacerbate the problems that these vulnerable populations experience because of their race, class, and age.

For example, institutionalized class and racial biases predict differential access to essential goods, such as health care, which cause disparities in disease, disability, and death.258 Burdened by an increase in disease, disability, and death, these children are a panacea for researchers investigating treatment and obtaining generalizable scientific knowledge, not usually relevant to their health condition.259 Powerless these children are invited to participate in medical research studies that provide minimal access to health care and will not alleviate their increased rate of disease, disability, or death.260 By doing this, researchers perpetuate the continued unequal distribution of access to health care when they use those without access for studies not even focused on issues suffered by their children.

Under the equity in participation doctrine, researchers would not be able to take advantage of the fact that economically disadvantaged minority children lack access to health care, as a means to enroll them in medical research studies. The researchers could only use them as subjects if the study focused on issues that are a priority to economically disadvantaged minority children and eliminated some social disadvantage, like lack of access to health care. To measure whether the equity in participation requirement is being met, I suggest that researchers be required to use VEIA.261

B. HEALTH IMPACT ASSESSMENT TOOLS

In 1970, the United States became the first country to require impact assessments to predict and assess the impact of policies on environmental health.262 Since then, several countries (Germany, Switzerland, and Canada) and international organizations (World Health Organization and the European Union) have required Environmental Impact Assessments to be completed in response to “highways, train lines, airports, industrial plants, waste disposal facilities, and many other development projects.”263 Since 1999, many countries, such as Germany, Switzerland, the Netherlands, Australia, New Zealand, Canada, and the United States have adopted this tool for use in the health field to avoid or minimize negative impacts on health.264 Impact assessment tools put the burden on those researchers completing the tool to show that their actions will not negatively impact the health of the population.

The Health Impact Assessment (HIA) is “a combination of procedures, methods and tools by which a policy, programme or project may be judged as to its potential effects on the health of a population, and the distribution of those effects within the population.”265 There are two main functions of the HIA: 1) “to support policy making

258 Washington, supra note 1, at 236-37, 284; Ross, supra note 10, at 48.
259 Washington, supra note 1, at 236-37, 284; Ross, supra note 10, at 48.
261 See generally Fehr, supra note 11.
263 Fehr, supra note 11, at 618.
265 Id. at 3.
in choosing between options” and 2) to predict “the future consequences” of implementing different policy options.266 There are six key stages in using a HIA: “screening, scoping, data collection, impact appraisal, reporting/recommendations, and monitoring/evaluation.”267 By using the HIA, policymakers can adopt the most beneficial policy for the population’s health. Attaining equity in health can be one of the priorities in completing an HIA. However, equity is not the main focus of the HIA.268 Although the HIA can determine if the policy will have different impacts on different social groups, the process does not provide information concerning whether these differential impacts are a result of unfair and biased policies.269 Consequently, the HEIA was created to ensure that assessments about a policy’s impact would include an evaluation of fairness and equity as well as root causes of inequities.270 The HEIA identifies the root causes of health inequity, such as wealth, income, knowledge, and power imbalances.271 The World Health Organization’s Commission on the Social Determinants of Health has recommended the use of the HEIA in all global, national, and local policy making.272 New Zealand, Australia, Canada, the United Kingdom, the United States, and other countries currently use the HEIA.273 There are five purposes of a HEIA:

- Help identify potential health impacts (positive or negative) of a plan, policy or program on vulnerable or disadvantaged groups within the general population.
- Help develop recommendations as to what adjustments to the initiative might mitigate negative impacts as well as maximize positive impacts on the health of vulnerable or disadvantaged groups.
- Embed equity across an organization’s existing and prospective decision-making models, so that it becomes a core value and one criterion to be weighed in all decisions.
- Support equity-based improvement in program/service design: ‘How does this program need to be adjusted to meet the needs of specific populations?’ ‘Could this program benefit some, but not others?’
- Raise awareness about health equity as a catalyst for change throughout the organization, so planners and managers develop ‘stretch goals’: How can we include more people in this program, especially those often missed? What barriers do we have to look for? Are we as effective as we could be, especially those with the greatest and most complex health needs?274

When completing a HEIA, the following five steps must be completed:

**Screening:**
Determine if the initiative requires a HEIA. If the initiative has the potential to impact the health of vulnerable or disadvantaged groups, HEIA is applicable. It is desirable that all initiatives be screened.

**Scoping:**
Identify affected populations or groups and predict key impacts (positive or negative) on those groups. Consider a wide range of vulnerable or disadvantaged groups to avoid overlooking unexpected or unintended consequences of an initiative.

266 Id.
267 Povall et al., supra note 249, at 622.
268 Id. at 621-22.
269 Id. at 624 (explaining that one study found that even when equity was a central theme of the HIA, the impact analysis did not go beyond identifying vulnerable populations and the differential effects of the policy on these populations).
270 Id. at 631.
271 Id. at 631-32.
272 Id. at 631.
273 ONTARIO MINISTRY OF HEALTH, supra note 256, at 3.
274 Id. at 5.
Impact Assessment:
Use available data/evidence to prospectively assess the impacts on vulnerable or disadvantaged groups in relation to the broader target population. It is both useful and important to consider a broader range of evidence including consultation findings and grey literature (including project or program reports, informal practice guidelines, recommended or promising practices). These sources of evidence should be weighed based on their strength and quality.

Where there is very limited data/evidence available, note the lack of evidence in the assessment or, where possible, implement other strategies to gather evidence. Strategies could include conducting surveys, focus groups, or consultation with experts or members of the affected groups where time permits.

Mitigation Strategy
Develop evidence-based recommendations to minimize or eliminate negative impacts and maximize positive impacts on vulnerable or disadvantaged groups. These recommendations comprise your mitigation strategy. Uptake of these recommendations in the roll out of the initiative will help to ensure that the initiative contributes to equity and does not perpetuate or widen existing health disparities. Where possible, recommendations should be informed by diverse members of the affected communities.

Monitoring and Evaluation
Determine how the rollout of the initiative will be monitored to determine its impacts on vulnerable or disadvantaged groups in comparison to other subpopulations or the broader target population. The resulting data will enhance the overall evidence base for equity-based interventions and can be fed back into the planning, policy or program development process.275

Once these steps have been completed, the organization must decide whether or not to implement the policy.276

A Racial Equity Impact Assessment (REIA) tool has also been created to identify the impacts of policies on racial and ethnic groups.277 Governments in Seattle, Washington, St. Paul, Minnesota, and the United Kingdom have adopted the REIA.278 Although the primary focus of the HEIA and REIA are to reduce health inequities, I believe that with some modification these tools can be used to create a tool to address inequities in medical research, such as the targeting of economically disadvantaged minority children.

C. VULNERABILITY AND EQUITY IMPACT ASSESSMENT TOOL

Based in part on the HEIA and the REIA, the VEIA should be used to assess whether a proposed research study is targeting vulnerable populations for use in medical research in violation of the redefined justice principle. The VEIA would require researchers to review the “social, racial, sexual, and cultural biases institutionalized in society” that place a class of people in a compromised position and easily manipulated into participation in medical research studies. The VEIA will require researchers to identify these institutionalized biases and determine whether the problems from these biases bar vulnerable populations from participating in medical research studies because it keeps them from attaining their highest standard of health. In this article I focus on how the VEIA can be used to protect disadvantaged children;

275 Id. at 6-7.
276 Id. at 7.
278 Id. at 29.
however, the VEIA can be used to protect all children and other vulnerable populations.279

1. The VEIA

First, the researcher must screen the research proposal to identify the purpose of the research, what the research seeks to accomplish, and whether the research has the potential to negatively affect economically disadvantaged minority children. If the research has a potential to burden this population or prevent them from attaining their highest standard of health, the researcher must discuss in their research proposal, why they feel that the use of these vulnerable children is necessary. Additionally, the researcher must discuss whether the research is a priority for the children. This review can be incorporated into the current requirement of showing that research will add to generalizable scientific knowledge.280

In order to answer these questions, the researcher must engage economically disadvantaged minority children or someone who represents their interests, such as Marian Wright Edelman, the President and Founder of the Children’s Defense Fund,281 or community leaders who focus on children’s health issues. This screening dovetails with procedures used by researchers when they conduct international research to ensure that research is culturally competent.282 Once this introspective review, or screening, has occurred and is noted in the research proposal, then the researcher must complete the scoping, impact assessment, and mitigation strategy steps.

To complete the scoping step, the researcher must answer the following questions:

1. What populations are most affected by the condition being studied?
2. Even if economically disadvantaged minority children are most affected by the condition, are there other less vulnerable populations that can be used for the research?

If economically disadvantaged minority children are most affected by the condition, then the researcher must assess whether the impacts on this population are negative or positive. To complete the impact assessment step, a researcher must use all available data, such as empirical research studies. If there is limited data available, then the researcher should collect data by “conducting surveys, focus groups, or consultation[s] with experts or members of the affected groups where time permits.”283

The evidence should be used to answer the following questions:

1. Disparities:
   a. Are there race, class, and/or age disparities in the number of people who suffer from the condition?
   b. Are there race and/or class disparities in the number of people who survive the condition?

279 The VEIA can also be used to measure whether researchers are complying with informed consent. Ruqaiijah Yearby, Involuntary Consent: Conditioning Access to Health Care on Participation in Clinical Trials, 44 J.L. MED. & ETHICS 445 (2016) (discussing how certain participants may be unduly influenced into participating in clinical trials).
280 See OHRP GUIDEBOOK, supra note 87.
282 See OHRP GUIDEBOOK, supra note 87.
283 Ontario Ministry of Health, supra note 256, at 7.
c. “What quantitative and qualitative evidence of inequality exists?”  

d. Which racial/ethnic groups are currently most advantaged and most disadvantaged by the issues this research seeks to address?  

e. Which socioeconomic groups are currently most advantaged and most disadvantaged by the issues this research seeks to address?  

f. Which age groups are currently most advantaged and most disadvantaged by the issues this research seeks to address?  

g. How are groups affected differently?  

h. What evidence is missing or needed?  

i. Will the research exacerbate these disparities?  

j. Will the research address these disparities?  

2. Burdens:  

a. What are the burdens on economically disadvantaged minority children who are potential research subjects?  

b. Will participation in medical research studies exacerbate these burdens?  

c. What are the root causes of the burdens, such as racial and class biases?  

d. Will the research address these root causes?  

3. Adverse Impacts:  

a. What potential adverse impacts or unintended consequences could result from participation in this research?  

b. Will the impacts or unintended consequences further burden economically disadvantaged minority children?  

c. How could adverse impacts be prevented or minimized?  

d. Can the research provide a solution to address the burdens faced by economically disadvantaged minority children?  

4. “Equitable Impacts:  

a. What positive impacts on equality and inclusion, if any, could result from this proposal?  

b. Which racial/ethnic groups could benefit?  

c. Which socioeconomic groups could benefit?  

d. Which age groups could benefit?  

e. Are there further ways to maximize equitable opportunities and impacts?”  

Using the answers from these questions, the researcher must provide an evidence-based determination of whether economically disadvantaged minority children should be used as subjects because there are no additional burdens and/or the research will eliminate burdens for this population. If the researcher decides to use economically disadvantaged minority children as research subjects even though there is a possibility for targeting, the researcher must develop a mitigation strategy that will minimize or eliminate the institutionalized biases that prevent economically disadvantaged minority children from equal access to essential goods such as food, education, and health care. If there is a mitigation strategy, the researcher must monitor the strategy throughout the study. Additionally, once the research is conducted, the researcher must monitor the actual impact the research has on economically disadvantaged minority children in  

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284 Keleher, supra note 277, at 30.  
285 Id.
comparison to advantaged groups. One way to monitor the impact is to determine whether there is a decrease in survival rate disparities between economically disadvantaged minority children and the advantaged population once the research is conducted.

2. Applying the VEIA

If researchers are required to apply the VEIA, many of the studies that targeted vulnerable populations in violation of the law would never have been funded.

For example, if the researchers who used African American and Latino foster children to test HIV/AIDS drugs, completed a VEIA, the tool would have shown the research violated the justice principle. First, the researchers would have been required to screen the research to identify the purpose of the research, what the research sought to accomplish, and whether the research had the potential to affect economically disadvantaged minority children.

Clearly, the screening would have shown that the medical research study had the potential to impact economically disadvantaged minority children if they were used as subjects, and it is unclear why healthy children had to be used to test HIV/AIDS drugs. Furthermore, there is no evidence that this research was a priority to healthy vulnerable children in foster care. If researchers were able to show that HIV/AIDS was a health priority, the research would still be prohibited under the scoping step. There is no evidence that at the time of the research, economically disadvantaged African American and Latino children were the group most affected by HIV/AIDS. Therefore, other children should have been used. Moreover, the impact assessment would have shown that the research was too dangerous to conduct on this population because the drugs had severe side effects for otherwise healthy children.

Additionally, the researchers discussed in Section IV.C.2 who traveled to Nigeria to test Trovan on pediatric patients suffering from bacterial meningitis would not have been able to show that their study complied with the justice principle using the VEIA. If researchers had screened the study, VEIA would have shown that the Nigerian children, who were vulnerable, would be negatively impacted by the research. The scoping step would have shown that other children were also affected by bacterial meningitis. Because these other groups were not in the middle of an epidemic, they would have been better subjects.

Furthermore, VEIA would have shown that the negative impact of the research outweighed any benefits from participation in the medical research study and could not be mitigated. First, there was already a proven therapy for the disease that children participating in the study were barred from taking. Second, the children could have died, an unreasonable impact that cannot be mitigated by any benefit. Thus, the researchers never should have used economically disadvantaged minority children.

These are just a couple of examples of how using the VEIA will protect economically disadvantaged minority children from being targeted. However, the adoption of justice as equity in participation and implementation of the VEIA will not put an end to targeting without changes to the current regulatory structure governing medical research studies using children.

D. A NEW REGULATORY STRUCTURE

287 Id. at 39.
In the past, OHRP and individual IRBs have been responsible for ascertaining whether the selection of economically disadvantaged minority children violated the justice principle. The examples discussed in Section I.V.C. suggest that neither OHRP, nor individual IRBs have been successful in accomplishing this task. Thus, I suggest the creation of a federal Human Research Protection Review Board for Children (Board for Children or the Board) using the authority granted by the Common Rule to review medical research studies otherwise unapprovable and the creation of an International Board of Children (IBOC) to review medical research studies using the authority granted by the Common Rule.

The Board for Children and the IBOC would be in charge of determining whether domestic and international medical research studies involving children were ethically based upon the redefined justice principle. Before a medical research study was conducted the Board of Children and/or the IBOC would be required to review the research proposal to evaluate whether the research targets economically disadvantaged minority children for studies in violation of the redefined justice principle.

To accomplish this task for research governed by the Common Rule, the Board for Children needs to have adequate community participation and specific requirements for the approval of research. The Board for Children must include at least two members of each group identified as a vulnerable population in the Common Rule. The Board for Children must also consist of at least two physicians that conduct research. However, these physicians cannot be from institutions that have been cited for violations by the OHRP. Finally, the Board for Children should include three bioethicists, two child advocates, and two government employees.

The Board must review the VEIA for all medical research studies using children governed by the Common Rule to ensure the studies comply with the redefined justice principle. This review must occur before the researcher submits the proposal for funding and drug approval. The Board would be responsible for reviewing the VEIA for each research proposal to make sure that the study was not targeting economically disadvantaged minority children for medical research studies. If the VEIA shows that there is no targeting and the study was necessary and safe, then the Board should approve the study and post the VEIA on ClinicalTrials.gov.

The IBOC should review proposals for medical research studies using children that are governed by the ICH-GCP. Using the VEIA to enforce the ICH-GCP, the IBOC would review all proposals for pediatric studies to ensure they comply with the redefined justice principle. The membership of the IBOC would include members of each group identified as a vulnerable population group in the ICH-GP. The IBOC would also consist of at least two physicians that conduct research. However, these physicians cannot be private contractors or from organizations that have conducted illegal and unethical research in the past. Finally, the IBOC should include three bioethicists, two child advocates, and three government employees (one from each regulatory authority in the EU, Japan, and the United States). The IBOC’s review would be similar to the Board of Children’s review. The review would take place before the researcher submits the proposal for drug approval.

Specifically, if a researcher planned to seek drug approval under the ICH-GCP, the researcher would need to complete a VEIA and submit it to the IBOC before

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289 In addition, the Board can review issues regarding autonomy and beneficence.
290 The Board would also be responsible for ensuring that the researchers comply with the other requirement of the justice principle, that members of the vulnerable population participating in the study directly benefit from the study.
conducted studies on children. The IBOC would review the VEIA for each research proposal and ensure that the study was not unfairly targeting economically disadvantaged minority children for medical research. If the VEIA shows that there is no targeting and the study was necessary and safe, then the IBOC should approve the study.

The creation of these Boards is just the beginning of the structural changes that need to be made to regulate pediatric medical research. Additionally, new penalties need to be imposed if a researcher and/or an institution violates the justice principle. Currently, OHRP just issues letters and suspends researchers from federally-funded research. Violations of the justice principle should also result in fines, loss of federal funding, and denial of drug approval. Researchers that violate the requirements should also face criminal fines. Furthermore, victims of research conducted in violation of the justice principle should be granted a private right of action against the institution and the researcher.

As more and more pediatric research is conducted overseas and outside of the public eye, it is imperative that the U.S. government, in cooperation with other governments, begins to aggressively enforce laws to protect all children, especially economically disadvantaged minority children, from being targeted for participation in medical research. Otherwise, these children will continue to suffer long-term disability or death.

VI. CONCLUSION

Children are vulnerable beings who we try to protect by limiting their access to alcohol, guns, and employment. Moreover, we limit their autonomy because, although we believe children are sacred, we question their decision-making capacity. We impose these limitations seemingly to protect children because they are vulnerable and susceptible to exploitation. Yet, some researchers willingly exploit children by targeting them to participate in medical research studies because it has the potential to benefit society.

Some bioethicists and researchers argue that all children are morally required to participate in medical research studies to provide a benefit to the society that benefits them. However, for economically disadvantaged minority children who lack access to essential goods, one must ask what benefit are the children receiving that they need to pay back? For many countries, including the United States, do not provide, nor guarantee a right to food, education, housing or health care for these children. So what duty do these children have to society? This is not a new question. As Patricia King noted, “American bioethics has tended to focus its attention on ethical issues associated with scientific and medical advances without recognizing that these developments occur in a social context that must be taken into account if the ethical issues are to be adequately addressed.”

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291 The IBOC would need to ensure that members of the vulnerable population participating in the study will directly benefit from the study.
292 For an example of a study in which researchers would face criminal fines, see Richardson, supra note 96, at 126.
Therefore, the time has come to put an end to this exploitation by enforcing the justice principle and prevent the targeting of all children, but especially economically disadvantaged minority children, from participation in medical research studies. This will only happen if the justice principle stands for more than inclusion. The justice principle must be a measurable standard that ensures fairness, equity, and the right of children to reach their full health potential without interference. Otherwise, children will continue to be sacrificed for the benefit of an unworthy society.