Pregnant Pause: The Exclusion of Pregnant Women from Clinical Research as Sex Discrimination

Richard M Weinmeyer
ABSTRACT

Since the early 1990s, legislative and policy reforms have spurred the inclusion of women of childbearing potential in clinical research overseen by the National Institutes of Health and the U.S. Food and Drug Administration. Pregnant women have received no such help, however, despite the tremendous medical needs of this important demographic. This article argues that the exclusion of pregnant women from biomedical research in the United States constitutes sex discrimination as a matter of public policy given the interpretation of existing regulations governing human subjects protections. The current regulations that are in place guiding research on human subjects treat pregnant women as a vulnerable population, yet the regulations are themselves vague in their application. Because of this ambiguity, discretion is left to the individual researchers and institutional review boards on how to interpret and apply those regulations, and they have done so in a discriminatory manner that has systematically excluded pregnant women from clinical research. To end this discretion, two legislative recommendations are proposed that could shift the clinical research model from a presumptively exclusionary format to one that explicitly includes pregnant women in the design and development of medical trials that will be utilized by this important demographic. The remedies discussed have been effectively implemented by Congress in similar contexts in the past, and could very well prove fruitful for dissipating the barriers now faced by pregnant women in participating in research and receiving appropriate medical care.
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Richard Weinmeyer, JD, MPhil

**INTRODUCTION**

Kelli Tussey is an informed woman. The thirty-four-year-old resident of Columbus, OH wanted to have a second child, but there was one event in her medical history that made her particularly wary of jumping back on the pregnancy train: a heart attack following the birth of her first child.1 Because of her heart condition, Kelli was on a variety of medications, including a statin that she took to lower her cholesterol.2 The problem with statins, however, is that they are theorized to pose a teratogenic risk to fetuses, meaning that they increase the likelihood of physiological malformations during fetal development.3 In fact, the U.S. Food and Drug Administration (FDA) states “women who are pregnant or may become pregnant” are contraindications for statins, and therefore, should not take this class of drugs.4 Aware of the possible danger of continuing her medication regimen while pregnant, Kelli met with physicians at Ohio State University’s Adult Congenital Heart Disease in Pregnancy Program.5 The doctors

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2 Id.
3 See Aleksey Kazmin, Facundo Garcia-Bournissen & Gideon Koren, Risks of Statin Use During Pregnancy: A Systematic Review, 29 J. OBSTETRICS & GYNAECOLOGY CAN. 906, 906 (2007) ("Although statins have been identified as potential teratogens on the basis of theoretical considerations and small case series, the available evidence is far from conclusive.").
4 See Chaitany Patel, Lisa Edgerton & Donna Flake, What Precautions Should We Use with Statins for Women of Childbearing Age?, 55 J. FAM. PRAC. 75, 77 (2006) ("The Food and Drug Administration has given statin agents a pregnancy category of X (risks involved in use of the drug by pregnant women clearly outweigh potential benefits.").
at Ohio State took Kelli off of her statin and placed her on a blood thinner deemed safer for her potential child.\textsuperscript{6} Ms. Tussey is now approximately five months pregnant and reports to be doing just fine.\textsuperscript{7}

The surprising aspect of this story is that no one can say for certain whether statins \textit{actually} raise the chances of birth defects in a fetus. In a recent review of clinical studies conducted over the last two decades that examines the teratogenic potential of statins in women of childbearing age, the authors conclude “[h]uman teratogenic risk has not been proven nor has it been ruled out by the available data on statin use in pregnancy.”\textsuperscript{8} So why all the fuss? It seems that much of the cautionary warnings around statins stem from a fetal toxicity study in 1987 that included no humans; instead, the research design was based around animal models where mice and rats were given forty to eighty times the recommended human dose.\textsuperscript{9} The data available from studies where research subjects are pregnant women are few and far between, and the numbers of subjects per study are too small to have any real statistical power, and provide no conclusory determination on the impact of statins on fetal health.\textsuperscript{10}

If you think the lack of information on statin use in pregnancy is abysmal, it is sad to say, but it is actually one of the better examples of pharmacological research involving pregnant women. Although two-thirds of pregnant women in the United States will take a prescription medication during the course of their pregnancies (excluding prenatal pills), there is an alarming

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\textsuperscript{6} Neergaard, \textit{supra} note 1.
\textsuperscript{7} Id. (”‘They said my heart could take it . . . it seems everything’s fine.’”).
\textsuperscript{9} \textit{GERALD G. BRIGGS, ROGER K. FREEMAN & SUMNER J. YAFFE, Drugs in Pregnancy and Lactation} 855–57 (9th ed. 2011).
\textsuperscript{10} Kazmin, Garcia-Bournissen & Koren, \textit{supra} note 3, 906–08.
\end{flushleft}
dearth of data on the efficacy and safety of most medications in this population.\textsuperscript{11} And as many women who have endured the trials of pregnancy can attest, the myriad of physical and mental ailments that can strike during that nine month period are no joke. Whether it is hypertension, gestational diabetes, or the exacerbation of a preexisting condition, many women need medical interventions beyond those linked directly to their pregnancy and the fetus. Yet when it comes to the provision of this care, medical personnel are usually operating on little-to-no concrete clinical data, and instead applying evidence-based best guesses and theoretical hunches. This precarious practice of medicine stems from an often ignored trend in the arena of biomedical research and practice that has left pregnant women as a uniquely vulnerable class of the American general public.

Since the 1970s, pregnant women have been almost entirely excluded from biomedical research in the United States. Amidst a tumultuous wave of medical disasters, legal and political debates regarding abortion, and the protectionist actions of a public and private clinical research regime, pregnant women and their unborn offspring have been barricaded by explicit regulations and implicit practices intended to keep them out of harm’s way. This systematic omission has done quite the opposite, however. As scientific innovation in the areas of drugs, devices, and biologics has moved ahead at an ever increasing pace, the knowledge of how these novel discoveries will function in the bodies of pregnant women, as well as their fetuses, has only shown nominal blips of grudging progress in the last few years. In order to meet the underserved medical needs of this population, practical steps in law and policy are necessary to shift to a scientific culture where the incorporation of pregnant women is a norm of inclusion, not exclusion.

This article argues that the intentional exclusion of pregnant women from biomedical research in the United States constitutes sex discrimination as a matter of public policy. There is no statutory exclusion of pregnant women from clinical research. Instead, what exists is a set of regulations that have chilled biomedical researchers and institutions from going down this scientific avenue of investigation, culminating in a clinical culture where pregnant women have been left out in the cold. For decades, the medical needs of pregnant women have been disregarded in clinical trials research that seeks to test the safety and effectiveness of emerging drugs and medical therapies, placing pregnant women at a distinct and dangerous disadvantage relative to the rest of the population. This marginalization of the pregnant body is the lingering artifact of a discriminatory policy scheme that kept all women of childbearing age out of clinical research until the late 1980s. Although the reasoning behind such actions was cautionary and well meaning at one point in history, it is a regulatory practice that only interjects the possibility of unforeseen harms into the daily lives and reproductive choices of women.

Part I of this article details the severity of the knowledge gap on medical treatments for pregnant women that has come about because pregnant women have not been allowed to participate in biomedical research, and the quagmire of clinical uncertainty it has advanced. Part II then discusses how this communal anxiety around the inclusion of pregnant women in medical research is the product of several particularly notable medical mishaps that ultimately shaped the contours of regulations pertaining to this segment of the populace. Part III posits the claim for sex discrimination that exists because the regulatory system presumptively excludes pregnant women from clinical research. The current regulations that are in place governing research on human subjects treat pregnant women as a vulnerable population, yet the regulations are themselves vague in their application. Because of this ambiguity, discretion is left to the
individual researchers and institutional review boards on how to interpret and apply those regulations, and they have done so in a discriminatory manner that has systematically excluded pregnant women from clinical research. While the regulations certainly constitute state action in that they construct a research scheme that treats pregnant women differently, the claim for sex discrimination is not constitutional in nature because of the Supreme Court’s existing precedent on the matter of pregnancy discrimination as sex discrimination. The problem is one of sex inequality, however, and it is a problem that requires the intervention of Congress. Part IV offers two legislative recommendations that could shift the clinical research model from a presumptively exclusionary format to one that explicitly includes pregnant women in the design and development of medical trials that will be utilized by this important demographic. The remedies discussed have been effectively implemented by Congress in similar contexts in the past, and could very well prove fruitful for dissipating the barriers now faced by pregnant women in participating in research and receiving appropriate medical care.

I. THE PREGNANCY PROBLEM

a. Immense Demand But Little Supply

In the United States, roughly four million women give birth each year. While some of these women will have complication-free pregnancies, the majority of them will not. Pregnant women are often affected by any number of serious illnesses during their pregnancies, including: hypertension, diabetes, asthma, mental illnesses, autoimmune disorders, cancer, and a whole host of other health problems that will require urgent treatment or ongoing care.\footnote{Mary C. Blehar et al., Enrolling Pregnant Women: Issues in Clinical Research, 23 WOMEN’S HEALTH ISSUES e39, e40 (2013).} Chronic conditions are especially quite common during pregnancy. For example, chronic hypertension and diabetes
complicate five percent of 40,000 pregnancies each year, and an estimated 500,000 women experience a psychiatric illness during their pregnancy. Such chronic diseases are often present before a pregnancy occurs, but “gestation [also] engenders a host of pregnancy-specific conditions that range from difficult (extreme nausea and vomiting) to disabling (sciatic nerve compression) to life-threatening for the woman and her fetus (preeclampsia).” Whether suffering from a chronic condition or a pregnancy-specific illness, sixty-four percent of pregnant women will be prescribed one or more medications to treat their ailments.

Despite the clear need for effective medications to ameliorate the symptoms, discomforts, and dangers of these illnesses, there are presently only a dozen medications—approved by the FDA specifically for use during pregnancy—that are available on the market. The medications that have received the FDA’s stamp of approval have a very limited role, however, because all of them are used to treat gestation- or birth-related complications, such as regional anesthesia, nausea and vomiting, congenital malformation prevention, and delaying or inducing labor.

Outside of this rarified group of drugs, there are no medications that have been approved to treat illnesses during pregnancy. As one group of scholars has noted, “Pregnancy, it turns out, is an ‘off label’ condition.”

b. The Particulars of Pregnancy

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16 Andrade et al., supra note 11, at 403.
By name, the medical issues that come with pregnancy are certainly not always that different than the health problems that affect other adults in the general public (e.g., heart disease, depression), yet the unique physiological changes that happen to a woman’s body during pregnancy make it nearly impossible to ascertain how most medications will metabolize in her body. Furthermore, not only are there distinct differences between a pregnant woman’s body and the body of a non-pregnant woman, but the pregnant state is itself far from static throughout the duration of pregnancy because of the continuous physical demands a growing fetus presents. For instance, during pregnancy, the volume of blood flowing through a woman’s body doubles, significantly affecting how a drug will be metabolized if given during the first trimester (where there is comparatively less blood) as opposed to being provided during the third trimester (where there is comparatively more blood). Additional changes to a woman’s body include: increases in body weight and body fat composition, increased cardiac output, changes in regional blood flow, increased renal function, altered gastrointestinal motility, and countless hormonal shifts underlying the entirety of the pregnancy. The interaction between medications that have gone untested in the pregnant body, and the physical transformations that take place during pregnancy, have made it nearly impossible to determine what effect, if any, specific treatments will have.

Since 2001, several public health emergencies have demonstrated just how vulnerable pregnant women are given the absence of knowledge around drug metabolism. After the terrorist attacks of September 11th and the anthrax attacks that soon followed, the American College of Obstetrics and Gynecologists Committee of Obstetric Practice recommended that pregnant women take amoxicillin for post-exposure prophylaxis should they be exposed to the

deadly bacteria.\textsuperscript{21} As it turns out, this course of therapy would have been under-treatment in pregnant women. In 2007, a study partially funded by the FDA and the National Institutes of Health (NIH) revealed that the recommended dose of amoxicillin needed to prevent anthrax would have been unachievable in pregnant women because of the increased metabolism of the drug in their bodies.\textsuperscript{22} And in 2009, amidst the H1N1 pandemic, one of the first people to die from the disease in the U.S. was a pregnant woman who had only been taking prenatal vitamins until her death.\textsuperscript{23} The Centers for Disease Control and Prevention (CDC) and the World Health Organization (WHO) determined pregnancy to be a risk factor for succumbing to the virus, and Tamiflu was ultimately recommended by the CDC despite the risks the drug was believed to pose to pregnant women.\textsuperscript{24} Naturally, this recommendation was largely theoretical given that there was no dosing data and no pharmacokinetic data for any of the flu vaccines in pregnant women until just this year.\textsuperscript{25}

The apprehension about delving into the physiological responses of pregnant women to experimental (and traditional) therapies is not an elusive reason. There are justifiable concerns about exposing a fetus to risks that may irreversibly damage its growth and development, or worse, result in its death. But given the fact that many women use medications while they know

\begin{enumerate}
\item M.A. Andrew \textit{et al.}, Amoxicillin Pharmacokinetics in Pregnant Women: Modeling and Simulations of Dosage Strategies, 81 \textit{CLINICAL PHARMACOLOGY \& THERAPEUTICS} 547, 547–56 (2007).
\item \textit{Id.}
\end{enumerate}
they are pregnant, and that many women unknowingly expose their fetuses to the effects of over-the-counter and prescription drugs when the pregnancy is unplanned, they are pregnant, and that many women unknowingly expose their fetuses to the effects of over-the-counter and prescription drugs when the pregnancy is unplanned,\textsuperscript{26} the queasiness of researchers to begin filling this biomedical knowledge gap is an ethically and legally dubious justification for keeping pregnant women and their fetuses on the sidelines. History has given the research community ample fodder for their neglect of pregnant women’s medical needs, however, and the lessons learned from two tragic events has fueled regulation and a clinical culture where women and pregnant women have been unwelcomed.

II. \textbf{PREGNANCY PANIC}

a. \textbf{Thalidomide and DES}

In 1957, the German pharmaceutical company Grünenthal brought to market a new sedative, tranquilizer, and antiemetic that was lauded as an alternative to barbiturates—a class of drugs known to be addictive and containing many side effects.\textsuperscript{27} This new drug, Thalidomide, was marketed as being safe for adults, children, and “even during pregnancy for mother and child.”\textsuperscript{28} Thalidomide’s antiemetic qualities were especially attractive to pregnant women because of the drug’s ability to rid women of morning sickness during the first trimester.\textsuperscript{29} News of Thalidomide’s miraculous effects for easing sleepless nights, discomfort, and nausea went

\textsuperscript{26} Kate Greenwood, \textit{The Mysteries of Pregnancy: The Role of Law in Solving the Problem of Unknown But Knowable Material Maternal-Fetal Medication Risk}, 79 U. CIN. L. REV. 267, 276–77 (2010) (“There is also unintended drug use during pregnancy. Every year, an estimated 10\% of women between the ages of fifteen and forty-four become pregnant; nearly half of those pregnancies are unplanned. A 2002 survey found that 82\% of women eighteen to forty-four years old had used some type of medication during the preceding week. As these statistics suggest, many women unwittingly expose their fetuses to one or more medications before realizing that they are pregnant.”).


\textsuperscript{28} Michael Emanuel, Michael Rawlins & Gordon Duff, \textit{Thalidomide and Its Sequelae}, 380 LANCET 781, 781 (2012).

\textsuperscript{29} \textit{Id.}
global, and by the early 1960s, it was given to patients in forty-six countries.\textsuperscript{30} Thalidomide never made it to the American market, though, after a young medical officer, Dr. Frances Kelsey, refused to approve the drug’s FDA application for lack of sufficient safety and efficacy data, not to mention because of the badgering antics of the U.S. pharmaceutical company seeking the drug’s approval.\textsuperscript{31}

By the time Thalidomide was pulled from the international marketplace in 1962, more than 10,000 children would be born with horrible deformities such as abnormally short limbs, flipper-like arms, malformed internal organs, and hearing and sight disabilities.\textsuperscript{32} The cause of these deformities was the use of Thalidomide during the first trimester of pregnancy, which also caused many women to miscarry or lose their newborns within days of delivery.\textsuperscript{33} A stunned medical community was caught by surprise with the aftermath of the Thalidomide tragedy, sparking new calls for increased data on drug safety and effectiveness, and dramatic regulatory reforms, including in the United States, a country untouched by Thalidomide.

While pregnant women in the U.S. were spared the horrors of the Thalidomide episode, another drug made it into the American market that would have a similarly scarring result. Diethylstilbestrol (DES) is a synthetic nonsteroidal estrogen that was prescribed to pregnant women from 1938 until 1971.\textsuperscript{34} The use of DES was thought to lower the risk of pregnancy


\textsuperscript{31} Id. (noting how one drug representative from the company “made repeated phone calls and personal visits to Kelsey, and complained to her superiors that she was unreasonable and nit-picking, and that she was delaying the drug’s approval unnecessarily”).

\textsuperscript{32} Id.

\textsuperscript{33} Id.

\textsuperscript{34} Ctrs. for Disease Control & Prevention, \textit{DES History}, DES UPDATE HOME, http://www.cdc.gov/des/consumers/about/history.html (last visited May 9, 2013).
complications and miscarriages.\textsuperscript{35} Within those three decades, some five to ten million women were given DES during their pregnancies, despite evidence that came to light in 1953 that DES did not have the prophylactic qualities it had originally promised. In 1971, a study was published that prompted the FDA to inform all physicians to stop prescribing DES to their patients. The study revealed a cascade of serious health problems befalling the daughters of women who had taken DES while pregnant.\textsuperscript{36} “DES daughters,” as they have come to be known, were found to be at an increased risk for developing a rare vaginal and cervical cancer called clear cell adenocarcinoma, in addition to other harms such as reproductive tract structural deformities, ectopic pregnancy and pre-term deliveries, and infertility decades after their mothers had ingested DES.\textsuperscript{37}

The fallout from DES was enormous. An incredible amount of product liability litigation filled court dockets for over forty years as DES mothers and DES daughters sought damages from pharmaceutical companies given the subsequent health problems triggered by the drug.\textsuperscript{38} Most notably, in 1980 the California Supreme Court ruled in \textit{Sindell v. Abbott Laboratories}\textsuperscript{39} that a DES daughter was able to recover from Abbott Labs under the theory of market share liability, whereby a defendant with a substantial share of the marketplace for a product could be held liable for a faulty product, and therefore, payout damages equal to the defendant’s market

\textsuperscript{35} Id.
\textsuperscript{37} Id.
\textsuperscript{38} See, e.g., Cynthia Alice Feigin, \textit{Statutes of Limitations: The Special Problem of DES Suits}, 7 AM. J. L. & MED. 91, 91–106 (1981) (discussing the enormity of litigation from DES, and strategies for plaintiffs to overcome statutes of limitations that initially bar many from bringing suit against DES manufacturers).
\textsuperscript{39} 607 P.2d 924 (Cal. 1980).
share at the time the product was used. But outside the sphere of tort law, farther-reaching consequences emanated from the biomedical disasters shaking the United States research infrastructure.

b. Restrictions on Research

Amidst the wake of Thalidomide and DES tragedies, and the 1973 ruling by the U.S. Supreme Court in *Roe v. Wade*, regulators looked for ways to restructure the biomedical research arena in order to produce generalizable medical knowledge that was safe and effective for the American public, but simultaneously insulated pregnant women and fetuses from harm. Following decades of ethical breaches in medical research that had haunted the U.S. government and peaked in the acknowledgment of the Tuskegee syphilis study, Congress created the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research to oversee the construction of the ethical guidelines for biomedical research in the United States. Congress’s first assignment for the Commission was the creation of recommendations for research involving pregnant women and fetuses. After a hurried four-month timeline for completing the project, the Commission’s report, *Research on the Fetus*, laid out sixteen recommendations in which the commissioners agreed that the pursuit of both therapeutic and non-therapeutic medical research with pregnant women and fetuses should be allowed. Commentators note, however, that the recommendations have continuously operated

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40 *Id.* at 937.
41 410 U.S. 113 (1973).
43 Blehar et al., *supra* note 12, at e40.
45 *Id.* at 73–76.
on “a policy of . . . presumed exclusion”\textsuperscript{46} for reasons discussed below. Those recommendations, along with the other studies conducted by the Commission, are now the nation’s official human subjects protections regulations codified under 45 C.F.R. 46.

The FDA would follow the same path of exclusion with the release of its own guidelines in 1977. Under its new requirements for companies submitting clinical studies for federal oversight and approval, the FDA required that “females of childbearing potential” were to be excluded from the Phase I (drug safety) and Phase II (drug effectiveness) stages of clinical trials, with the only exceptions being for life-threatening or serious illnesses.\textsuperscript{47} The only way a drug could actually finds its way into a study population of pregnant women would be if the drug demonstrated minimal fetal risk in teratogenicity animal studies (usually performed while the clinical trial is already taking place),\textsuperscript{48} and if a drug could be shown as effective in men, older women, or both.\textsuperscript{49}

c. Removing Restrictions, But Not For All Women

All women of childbearing potential were effectively shut out of clinical research for twenty years. The disquieting lack of women in biomedical research placed the lives of millions of women in peril, and in the 1990s the anger over this discrimination was translated into congressional pressure from scientists, activists, and members of the public, men and women alike. A 1990 investigation undertaken by the General Accounting Office (GAO) revealed that the NIH had failed to fund external studies or oversee internal studies that consistently included women as human subjects, casting doubt on whether the findings of such research could provide

\textsuperscript{48} \textit{Id.}
\textsuperscript{49} Ellen Pinnow et al., \textit{Increasing Participation of Women in Early Phase Clinical Trials Approved by the FDA}, 19 WOMEN’S HEALTH ISSUES 89, 89 (2009).
scientific data to guide clinical decisions for women in health care.\textsuperscript{50} From the results of the study, along with additional pushback from Congress, the NIH dedicated itself to instituting enforceable guidelines for the inclusion of women in biomedical research, resulting in the translation of those standards into law via the 1993 NIH Revitalization Act.\textsuperscript{51} Under the Act, the NIH was required to “conduct or support outreach programs for the recruitment of women . . . as subjects in projects of clinical research,”\textsuperscript{52} and established a designated Office of Research on Women’s Health.\textsuperscript{53} Because of the requirements for including women in research, “[s]cientists could no longer categorically deny women access to clinical trials; instead they had to provide a scientific argument to justify women’s exclusion.”\textsuperscript{54}

Congress then set its sights on the FDA in 1992. That year the GAO reported that women were greatly underrepresented in clinical trials under the auspices of the agency, and in those studies where women were included, the data on women was seldom analyzed and compared to the data on men.\textsuperscript{55} GAO recommended that the FDA ensure companies going through the drug approval process provide “sufficient numbers of women in drug testing to identify gender-related differences in drug response and that such differences [be] explored and studied.”\textsuperscript{56} Under this scrutiny from Congress, the FDA removed its restrictions on women of childbearing potential in clinical trials and issued formal guidelines for analyzing data by sex.\textsuperscript{57}

\begin{thebibliography}{9}
\item \textit{Id.} at § 131.
\item \textit{Id.} at § 141.
\item Keitt, \textit{supra} note 47, at 258.
\item \textit{Id.} at 12.
\end{thebibliography}
As the research frontier has vacillated between inclusion and exclusion of women for decades, women now comprise approximately half of the human subject population for biomedical research trials.\textsuperscript{58} Pregnant women continue to remain on the periphery of scientific advancement. As medical knowledge expands and refines with each new day, treatments for pregnant women and their fetuses remain stagnant. There does exist the possibility of enforceable redress for expanding the clinical research opportunities for pregnant women, just how this progress can come about—either via the courts or regulation as a claim of sex discrimination—will be explored next.

III. A CLAIM FOR SEX DISCRIMINATION

a. Sex Discrimination as a Matter of Public Policy

There exists no specific statute or regulatory language that outright bars the participation of pregnant women in clinical research. What does exist is a confluence of evidence that this demographic has been shut out of research for decades because of how the regulations have been applied, and an acknowledgement by those agencies that oversee biomedical research (namely, the NIH and FDA) that pregnant women constitute a “vulnerable population,” or in the recent words of one FDA official, “a challenging population.”\textsuperscript{59} Guiding the research endeavors of both of these agencies, and the Department of Health and Human Services (DHHS) as a whole, are the regulations for the Protections of Human Subjects under 45 C.F.R. 46.

\textsuperscript{58} GEN. ACCT. OFF., NIH HAS INCREASED ITS EFFORTS TO INCLUDE WOMEN IN RESEARCH (2000).
\textsuperscript{59} FDA OFF. OF WOMEN’S HEALTH, DIALOGUES ON DIVERSIFYING CLINICAL TRIALS: SUCCESSFUL STRATEGIES FOR ENGAGING WOMEN AND MINORITIES IN CLINICAL TRIALS 66 (2012), available at http://www.fda.gov/downloads/ScienceResearch/SpecialTopics/WomensHealthResearch/UCM334959.pdf (providing the comments of Dr. Leyla Sahin, Medical Officer on the Maternal Health Team at FDA’s Center for Drug Evaluation and Research, who stated “Pregnant women are a challenging population to study due to concerns regarding potential adverse effects of medication exposure on the developing fetus”).

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The Regulations in Place

The exclusion of pregnant women from clinical research is sex discrimination as a matter of policy because it is based on an explicit federal policy that treats women differently because of their pregnant status, and has ramifications that applies only to women because of their innate childbearing potential. What is interesting about this discriminatory effect is that it stems from the interpretation and application of regulations that were intended not to harm pregnant women and their fetuses, but to guard them from the myriad of dangers implicit in medical research.

The research regulations pertaining to pregnant women are found at 45 C.F.R. 46, “Protection of Human Subjects.” Subpart A of this regulatory apparatus is generally known as “The Common Rule.” The Common Rule sets forth the basic policies of DHHS for institutional review boards (IRBs), informed consent, and Assurances of Compliance. Subpart B of the regulations, however, establishes “Additional Protections for Pregnant Women, Human Fetuses and Neonates Involved in Research.” In order to undertake research involving pregnant women and fetuses “conducted and supported by [DHHS],” ten conditions must be in place beyond those required by the Common Rule before the research commences. The two groups of conditions central to the argument for sex discrimination are included here.

The first group of conditions deals with the risks of the research. Each research study must be “scientifically appropriate” and based on data collected from “preclinical studies, including studies on pregnant animals, and clinical studies, including studies on nonpregnant

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60 45 C.F.R. § 46 (2009).
62 Id.
64 Id. at § 46.201.
women” in order to assess the potential risks to pregnant women and fetuses. All of the risks involved must be “the least possible for achieving the objectives of research,” and the risks to the fetus are allowable if:

[C]aused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus; or, if there is no such prospect of benefit, the risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge which cannot be obtained by any other means.

The second group of conditions addresses the direct benefits to the pregnant woman and the fetus, and the issue of informed consent. If the research demonstrates the possibility of a direct benefit to the pregnant woman, to the pregnant woman and the fetus, or no direct benefit to either, the research is guided by the following: “when risk to the fetus is not greater than minimal, and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means,” a pregnant woman must provide her informed consent under the requirements of the Common Rule. Should the research in question only hold out the potential for direct benefit to the fetus, “then the consent of the pregnant woman and the father” must be obtained according to the provisions of the Common Rule, unless the father cannot consent because of “unavailability, incompetence, or temporary incapacity or the pregnancy resulted from rape or incest.” All those who provide informed consent to the

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65 Id. at § 46.204.
66 Id.
67 Id.
68 Id.
69 45 C.F.R. § 46.204 (2009).
research are to be fully informed “regarding the reasonably foreseeable impact of the research on the fetus or neonate.”

As the regulations themselves demonstrate, the federal government has imposed heightened requirements that must be satisfied before any researcher under the guise of DHHS can enroll pregnant women. A researcher must be able to demonstrate that there has been ample data collected in pregnant and non-pregnant populations (animal and human), and that the risks associated with the science are minimized and balanced against the direct benefits of the research to the pregnant woman, fetus, or both. If there is no alternative to acquiring important biomedical knowledge, then the risks to the fetus still must be minimal. While there is state action, that action has not flatly banned the inclusion of pregnant women. Instead, what has grown from this clinical research regulatory body has been a reticence on the part of the actors legally bound by those rules that have obfuscated any and all medical research on the pregnant body and the fetus it holds.

**The Regulations in Practice**

Pregnant women are treated differently as a distinct class under the human subjects regulations, but just how and when those distinctions are applied is open to debate. The regulations for the inclusion of pregnant women, as they currently stand, provide little guidance on their operation in a clinical setting. In fact, their interpretation is typically left to case-by-case determinations by researchers overseeing the design and the implementation of the respective clinical trial, with additional controls exerted by the applicable IRB. Despite numerous reports, conferences, and calls to arms by researchers and government officials from across medicine, law, and ethics, most researchers and IRBs “continue to regard pregnancy as a near-automatic

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70 *Id.*

cause for exclusion, regardless of the costs of exclusion or the magnitude or likelihood of the risks of participation.”

A crude search of clinicaltrials.gov speaks to this continued practice. Of the 144,845 studies currently registered with the federal government, only 1,452 include pregnant women or study some medical aspect of pregnancy.

Critics of the existing regulations point to the numerous policy concerns that emanate from 45 C.F.R. 46 Subpart B. A dominant point of contention is that pregnant women are categorized as a vulnerable population, and that because of this, there is a implicit presumption of exclusion by researchers. By portraying a group as “vulnerable,” it is assumed that the group has a “compromised ability to protect their interests and provide informed consent.” This presumption is absurd, however, given that most pregnant women can surely provide their informed consent and take the time to evaluate their interests in participating in research. Therefore, this labeling of “vulnerable” cuts against their autonomy. Such a categorization jeopardizes “the pregnant woman’s primacy as the advocate for her and her fetus’s well-being and invite[s] incursions against maternal knowledge of roles and responsibilities and maternal decision making.” Pregnant women do not make decisions in a vacuum where their actions only impact them. If a pregnant women suffers from a life-threatening illness or a debilitating condition and chooses to enroll in a clinical trial that offers hope of a therapeutic benefit, she is

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72 Id.
73 Search for Studies on Pregnancy Registered with the Fed. Gov’t, CLINICALTRIALS.GOV (under “Search for Studies,” search for “pregnant”).
74 Blehar et al., supra note 12, at e41.
75 Id.
certainly aware that her health is closely linked to the health of her fetus, and it must be left to her discretion to weigh the costs and benefits of such a decision.\textsuperscript{77}

As the regulations currently stand, this risk-benefit calculation is left in the hands of researchers who must justify the inclusion of pregnant women in their research and demonstrate that all the required conditions of Subpart B are in place. There is no regulatory language requiring the justification of excluding pregnant women from a study’s protocol; an unusual regulatory absence because it is a requirement necessary for the exclusion of other populations that are considered to be (or were once considered to be) vulnerable. For research funded by the NIH, an investigator must specifically justify the exclusion of women, racial and ethnic minorities, and children from a grant application.\textsuperscript{78} In addition to this presumptive exclusion, research that only holds out a direct benefit to the fetus further chips away at a pregnant woman’s independence by requiring that the father provide his informed consent in order for the fetus to be included in the study.\textsuperscript{79} This is an antiquated requirement, to say the least.

Interpretations by IRBs have also fed the problem of excluding pregnant women from biomedical research. Again, because the regulations are ambiguous in how they are to be applied, IRBs have varied significantly from one another in their reading of 45 C.F.R. 46 Subpart

\textsuperscript{77} Blehar et al., \textit{supra} note 12, at e42.
\textsuperscript{79} 45 C.F.R. § 46.204 (2009). This is a highly contentious requirement that was slated for revision during the Clinton administration, however, with the change in administrations in 2001, the final language of the rule for this condition was kept in place. \textit{See} Keitt, \textit{supra} note 47, at 260.
B. Studies have shown that IRBs have typically taken a very conservative stance when it comes to reviewing research protocols that include vulnerable populations, lending the concept of “minimal risk” to become an elusive definition. For example, in one study on how IRB chairs perceive minor changes in risk to a study protocol on pediatric research, even the slightest modification to the research design (e.g., increased blood draws, an MRI scan, etc.) greatly shifted how the chairs defined minimal risk to the pediatric human subjects. And despite clarifications from the Institute of Medicine and the Secretary’s Advisory Committee on Human Subjects Research, the meaning of “minimal risk” has continued to be disputed and interpreted differently. Even the more basic task of determining how much pre-clinical (i.e., animals) and clinical (i.e., non-pregnant women) background research data is needed to support the inclusion of pregnant women in a clinical trial is a matter of disagreement across IRBs. Much of this conservatism understandably stems from a fear of exposure to legal liability because of the potential for injuries to the pregnant woman, her fetus, or both, despite the fact that there has been little litigation against IRBs as whole.

The regulations, which establish specific conditions for the inclusion of pregnant women in biomedical research, have been used by researchers and IRBs to place pregnant women at a

80 Blehar et al., supra note 12, at e42.
81 Levine, supra note 42, at 41.
85 Blehar et al., supra note 12, at e42.
86 Id.
disadvantage in terms of medical knowledge about how to treat the panoply of disease and disorders that can strike a pregnant women at any time during her pregnancy. This sex inequality has left women who are pregnant in a precarious position if and when an unexpected condition strikes, or if a known illness is further compounded by the inexcusable chasm of scientific insight into how the pregnant body responds to medications ranging from antidepressants to antiretrovirals. But because this discrimination has been derived from a cautionary and conservative approach from the medical research community, and not the regulations or explicit policies of DHHS on their face, it is a problem best resolved by the policy arena. This conclusion is further supported by the reality that a sex discrimination claim based on pregnancy would fail under prevailing constitutional doctrine, as would a claim under Title VII given the role of research subjects.

b. No Claim Under the Constitution or Title VII

Prohibited by the Precedent of Geduldig

The foundational case for determining whether the disparate treatment of pregnant women could qualify as sex discrimination is Geduldig v. Aiello.\(^88\) In Geduldig, California maintained a disability insurance program that provided benefits to employees from private companies in the event an employee experienced a disability not covered by worker’s compensation.\(^89\) Not all disabilities were covered, however, including “certain disabilities that [were] attributable to pregnancy.”\(^90\) The appellee in the case, a pregnant woman denied benefits because of disability stemming from her normal pregnancy, brought forth a claim of sex discrimination under equal protection arguing that the insurance program “invidiously discriminate[d] against [pregnant women] by not paying insurance benefits for disability that

\(^{88}\) 471 U.S. 484 (1974).
\(^{89}\) Id. at 486.
\(^{90}\) Id. at 489.
accompanies normal pregnancy and childbirth.” 91 The Court found otherwise, ruling that although only women can become pregnant, the program divided “potential recipients into two groups—pregnant women and non-pregnant persons,” and since “non-pregnant persons” included both men and women, the absence of pregnancy from the benefits scheme did not constitute sex discrimination. 92

The central holding of Geduldig is that discrimination based on pregnancy is not sex discrimination under the Equal Protection Clause. In the context of clinical research, where the pregnant woman has been precluded from gaining access to the arms of randomized controlled trial, the Court’s interpretation of what does qualify as sex discrimination as a matter of constitutional law prohibits pregnant women from arguing that the human subjects protections regulations, and their interpretation, discriminate on the basis of sex. The physical condition of pregnancy is certainly a matter that is only borne by women, and the existing regulations allow all men unfettered access to participate in clinical research. 93 But as it stands, 45 C.F.R. 46 Subpart B does not impose burdens on all women, nor does it technically bar pregnant women from contributing their bodies to scientific endeavors. As is explained above, it has been the clinical research culture and the actions of individual research investigators and IRBs as a collective that has relegated pregnant women to their disparate status among the human subjects population. Pregnant women have been distinguished from non-pregnant persons, both men and

91 Id. at 492.
92 Id. at 496–97 n.20.
93 The human subject protections regulations do impose additional requirements, similar to pregnancy, for research in prison populations. See Additional Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners as Subjects, 45 C.F.R. § 46.301–306 (2009). Given that men represent 93.5% of the prison population in the United States, these regulations primarily impact men, and less so women, who make up the remaining 6.5%. See FED. BUREAU OF PRISONS, U.S. DEP’T OF JUST., QUICK FACTS ABOUT THE BUREAU OF PRISONS (2013) available at http://www.bop.gov/news/quick.jsp.
women, and under *Geduldig*, such sex inequality is constitutionally tolerable because it is not sex-based state action, but pregnancy-based state action.

**Evidence of Evolution Under Johnson Controls?**

Human subjects can definitely derive a reasonable income by being compensated for participating in clinical research, especially if one supplements one’s income by aggressively enrolling in Phase I clinical trials. As to whether this type of compensatory arrangement constitutes employment, the answer is almost certainly “no.” Regardless, the reasoning in *Automobile Workers v. Johnson Controls* demonstrates that the Court’s view on pregnancy discrimination in employment could someday be applied to other areas of legal doctrine that would advance the conception of pregnancy discrimination as sex discrimination beyond the reasoning of *Geduldig*.

After the Supreme Court’s ruling in *Geduldig* in 1974, Congress enacted the Pregnancy Discrimination Act (PDA) of 1978 which amended Title VII of the Civil Rights Act of 1964 “to prohibit sex discrimination on the basis of pregnancy” in employment. The purpose of the Act was to protect pregnant women from being terminated from their employment while able to fully

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94 Carl Elliott, *Guinea-Pigging*, NEW YORKER, Jan. 7, 2008, http://www.newyorker.com/reporting/2008/01/07/080107fa_fact_elliott (detailing the underground world of artists and activists who regularly participate in Phase I clinical trials to support other facets of their life, despite the questionable research activities and medical dangers they are exposed to in the end).

95 See R. Alta Charo, *Protecting Us to Death: Women, Pregnancy, and Clinical Research Trials*, 38 ST. LOUIS U. L.J. 135, 156 (1993) (“But even compensated service as a research subject would not appear to meet the definition of ‘employee’ under Title VII.”). *But see* Elliott, *supra* note 94 (“The result is an uneasy compromise: guinea pigs are paid to test drugs, but everyone pretends that guinea-pigging is not really a job.”).


97 Pregnancy Discrimination Act of 1978, Pub. L. No. 95-555, 92 Stat. 2076 (Oct. 31, 1978) (stating that “because of or on the basis of pregnancy, childbirth, or related medical conditions; and women affected by pregnancy, childbirth, or related medical conditions shall be treated the same for all employment-related purposes, including receipt of benefits under fringe benefit programs, as other persons not so affected but similar in their ability or inability to work, and nothing in section 703(h) of this title shall be interpreted to permit otherwise”).

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perform their job duties. Under this section of Title VII, female employees of an automobile battery manufacturer brought suit against their employer, Johnson Controls, Inc., claiming that its gender-based fetal protection policy was discriminatory in that it banned fertile women from taking specific jobs that exposed them to lead “because of [the company’s] concern for the health of the fetus the woman might conceive[.]”98 With this differential treatment of female employees compared to male employees, and finding no bona fide occupational qualification (BFOQ) that carved out a sex-based safety exception for filling these specific manufacturing roles,99 the Court held that the “fetal-protection policy is sex discrimination forbidden under Title VII.”100 In its analysis, the Court noted that the policy conflicted with Congress’s intent in enacting the PDA, which allows that “the decision to become pregnant or to work while being either pregnant or capable of becoming pregnant [is] reserved for each individual woman to make for herself.”101

Despite the confinement of the holding from Johnson Controls to the employment arena, its reasoning helps to construct an argument for pregnancy discrimination as sex discrimination that could work in favor of the exclusion of pregnant women from clinical research. In Johnson Controls, the Supreme Court emphasized the autonomous decision-making capabilities of women in making informed choices as to whether or not to expose themselves to a harm in return for a job with higher pay, and this “notion that it is wrongfully discriminatory to exclude women from a benefit on grounds of fetal protection could apply by analogy to the context of

99 Id. at 204 (“Johnson Controls suggests, however, that we expand the exception to allow fetal-protection policies that mandate particular standards for pregnant or fertile women. We decline to do so. Such an expansion contradicts not only the language of the BFOQ and the narrowness of its exception, but also the plain language and history of the PDA.”).
100 Id. at 200.
101 Id. at 206.
clinical studies.”102 By leaving the crux of the decision to include pregnant women in clinical research in the hands of researchers and IRBs—who fear harm not only to the woman, but to the fetus as well—pregnant women are excluded from the potential benefits that can come directly from clinical research, not to mention the medical care innovations that grow from the application of this research data. Through the enactment of the PDA and the Court’s ruling in Johnson Controls, it is evident that both branches of the government support “a woman’s ultimate right to make the decision about accepting the risk that may be potentially harmful to her reproductive status.”103 Yet even with this acknowledgment by Congress and the Court that women, including pregnant women, are to be left to make their own informed determinations about what to do with their bodies, the behavior of the biomedical research community has struck against this realization. This is despite the existence of a clear regulatory framework for guiding informed consent, and the unlikely probability of litigation in the event of an injury or death occurs during the research process.104

The courts are not the suitable venue to remedy the dilemma of excluding pregnant women from clinical research. As the Supreme Court cases on this matter demonstrate, pregnancy discrimination is not sex discrimination under the Court’s understanding of the Constitution, and the reasoning of both Congress and the Court around pregnancy discrimination protections have been kept within the realm of Title VII employment discrimination prohibitions. This should not be of great concern, however, because the most effective way to remove the existing obstacles to the inclusion of pregnant women in biomedical research exists in the

102 INST. OF MED., supra note 83, at 149.
104 INST. OF MED., supra note 83, at 152 (“Because of the extensive disclosure involved in the informed consent process, those injured in research seldom have a basis to pursue legal action.”).
legislative powers of Congress. In the past twenty years, Congress has successfully bolstered research in two populations once deemed “untouchable” by the medical research community, and similar actions by Congress pertaining to pregnant women could very well provide the solutions to this problem of medical marginalization.

IV. **Acts of Congress**

The discrimination faced by pregnant women in clinical research, and the desert of data on drug effects in pregnant women, is a truly stunning circumstance, but it is certainly not a unique problem that has plagued U.S. biomedical research and medical care. As is discussed earlier, women as a whole were almost entirely prohibited from participating in clinical research until the early 1990s. It was not until the enactment of the NIH Revitalization Act of 1993 that scientific progress was actually made because Congress directed the agency to take concrete steps to include women (and minorities) in the external grants being funded by the agency and the internal studies taking place within NIH.\(^\text{105}\) While women of childbearing potential were once barred from research, females currently account for forty-nine percent of subjects in NIH-funded studies that include males and females.\(^\text{106}\)

An equally deleterious medical failure was the near complete absence of clinical data on safe and effective treatments for children in the U.S. health care system, and this problem continued for decades until Congress intervened.\(^\text{107}\) Through two acts that changed the relationships between the FDA and drug makers, Congress helped turn the tide of this dilemma.

\(^{105}\) See NIH Policy and Guidelines on The Inclusion of Women and Minorities as Subjects in Clinical Research, Nat’l Inst. Of Health, http://grants.nih.gov/grants/funding/women_min/guidelines_amended_10_2001.htm (last visited May 9, 2013) (discussing the legislative background of the NIH Revitalization Act and the actions the NIH was bound to pursue in terms of research on women and minorities).

\(^{106}\) Blehar et al., supra note 12, at e39.

through the enactment of the Best Pharmaceuticals for Children Act (BPCA) in 2002,108 and the Pediatric Research Equity Act (PREA) in 2003.109 The results of these congressional activities have been met with considerable enthusiasm from the medical and scientific communities. According to one estimate, more drugs have been studied in the pediatric population in the last decade than in the previous five decades combined.110 And because of the combined effects of the BPCA and the PREA, over 400 drugs already on the market have been relabeled with information on their suitability for pediatric patients, and approved as safe and effective for use in neonates, infants, children, and adolescents.111

When faced with the disparate treatment of women and children by the biomedical community in the United States, acts of Congress have sustained desperately needed progress in the areas of research and drug development. These acts have added greater clinical data on the conditions that impact women and children differently because of each group’s respectively distinct physiologies. Congress should address the plight of pregnant women in the exact same fashion. The human subject protections regulations governing pregnant women in research are not necessarily the obstacle to effectuating this change.112 What is needed, however, are

112 The main thrust of the argument presented here is that for truly effective change to take place, the agencies that oversee medical research in the U.S. must be at the forefront of implementing alterations to the manner in which the biomedical research community treats pregnant women. Clearly, change is needed in the way in which the regulations are interpreted, but the Acts that are proposed have been remarkably successful in bringing about the inclusion of other populations deemed “vulnerable.”
legislative enactments that will shift the clinical research culture from one of presumed exclusion to one of presumed inclusion when it comes to understanding the physiology of the pregnant body, and the drug interactions that take place within it. Proposed here are two congressional actions that should be pursued to begin ameliorating the harms perpetuated by the exclusion of pregnant women from research.

a. **NIH Revitalization Act for the Inclusion of Pregnant Women in Research**

To begin pushing for the inclusion of pregnant women in clinical research, Congress should enact legislation that strikes at the very institution that is the largest funder of biomedical and health-related research in the United States: the NIH. The purpose and requirements of this Act should follow the language of the 1993 Revitalization Act given its success in raising inclusion of women in research.113

The proposed Act should first begin by establishing an opt-out system where pregnant women are to be by default included in federally funded research. Based on the 1993 language, the proposed legislation should state, “In conducting or supporting clinical research for the purposes of this title, the Director of NIH shall . . . ensure that pregnant women are included as subjects in each project of such research.” This type of language explicitly counters the default exclusion of pregnant women, and falls in line with the automatic inclusion of women, minorities, and children that is built into every NIH-supported study.114 Obviously, not all research funded by the NIH will be applicable to pregnant women, and like the 1993 Act, there should exist a set of specific guidelines to help determine “the circumstances under which the

inclusion of pregnant women as subjects in projects of clinical research is inappropriate.” And in terms of explicit inclusion in clinical trials research, the proposed Act should state the following to certify that the inclusion of pregnant women will result in worthwhile data:

In the case of any clinical trial in which pregnant women will be included as subjects, the Director of NIH shall ensure that the trial is designed and carried out in a manner sufficient to provide for valid analysis of whether the variables being studied in the trial affect pregnant women, as the case may be, differently than other subjects in the trial.

These types of research specifications, like those found in other congressional actions, must be supported by outreach efforts on the part of the agency as a means to encourage the research community’s input, as well as the participation of members of the general public in the very research endeavors this type of Act aims to inspire. Within the 1993 Revitalization Act, the NIH was required to enhance its outreach programs in order to develop community buy-in, and to serve as a mechanism for recruiting subjects into clinical trials and for disseminating data collected from those studies.115 Congress ensured this by requiring the creation of the Office of Research on Women’s Health to oversee these types of activities.116 Unsurprisingly, there exists no specific office with the NIH dedicated solely to research efforts regarding pregnant women’s health, and this is certainly a much needed component of this proposed Act to keep the importance of this population on the forefront of medical research moving forward.117

115 NIH Revitalization Act of 1993 § 492B(a)(2) (“The Director of NIH, in consultation with the Director of the Office of Research on Women's Health and the Director of the Office of Research on Minority Health, shall conduct or support outreach programs for the recruitment of women and members of minority groups as subjects in the projects of clinical research.”).
117 It should be noted the Office of Research on Women’s Health at the NIH has set one of its year 2020 sub-goals to “Encourage research on safe and effective interventions for conditions affecting pregnant women.” OFF. OF RES. ON WOMEN’S HEALTH, MOVING INTO THE FUTURE WITH NEW DIMENSIONS AND STRATEGIES: A VISION FOR 2020 FOR WOMEN’S HEALTH RESEARCH
b. **Incentives for Drug Safety and Effectiveness Determinations in Pregnant Women**

Congressional actions towards the NIH to shift towards a framework of the explicit inclusion of pregnant women in clinical research will help to bolster the creation of federally funded scientific endeavors that factor in the health of pregnant women from the outset. Tackling those medical treatments that are already in existence will require a separate legislative action by Congress, however. In order to accomplish the goal of determining which FDA-approved medical treatments are both safe and effective for pregnant women and their fetuses, Congress should pursue legislative reform that mirrors that of the BPCA and PREA in unearthing which drugs can be given to this cohort. Just why that should be the case is explained below.

The BPCA, which amended the Food, Drug, and Cosmetic Act, was enacted to “improve the safety and efficacy of pharmaceuticals for children.” Under the BPCA, the FDA was charged with implementing a voluntary system whereby the agency could request pharmaceutical companies to investigate which of their marketed drugs could be studied and approved for use in pediatric populations, and to make publicly available the data and information stemming from this work. In order to entice drug manufacturers to participate in this area of research and manufacturing, the FDA offered “drug sponsors holding approved applications and existing patents . . . a six-month extension of market exclusivity for all of their

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119 Best Pharmaceuticals for Children Act §§ 2, 9. It should be noted that the BPCA, in addition to its research on existing drugs and their suitability for pediatric patients, established numerous advisory committees to oversee pediatric research initiatives within the FDA, created a new Office of Pediatric Therapeutics, and strengthened the pediatric research activities between the FDA and the NIH. Id. at §§ 6, 13-18.
drug products with the same active ingredient as the one studied.”120 The BPCA was made that much more attractive to pharmaceutical companies because “the FDA [could not] approve an abbreviated new drug application for generics relying on the safety and efficacy data from the original sponsor's new drug application.”121 In other words, the BPCA gave drug manufacturers additional market exclusivity by delaying the creation of generic drugs, and temporarily prevented other drug manufacturers from submitting applications for drugs with similar chemical compounds. Congress would follow up the BPCA a year later with its enactment of the PREA.122 Similar in its aims to the BPCA, the PREA was non-voluntary in its functioning and required drug makers to initiate pediatric studies early on in the drug development process, but allowed several forms of waiver in the event a drug manufacturer could demonstrate the drug was either unsafe or ineffective in pediatric populations, if the pediatric study requirements would delay the completion of adult safety and efficacy studies, and so forth.123

Because such a small set of existing drugs and biologics have been approved for their use in pregnant women, the plethora of medical interventions that could be adapted for use during pregnancy is undoubtedly promising. What the BPCA and PREA models have done in pediatric care is coax pharmaceutical manufacturers to reassess the safety and effectiveness for their existing products, and to include pediatric populations in those nascent drug studies currently under development. Pregnant women would greatly benefit from such a regulatory mechanism as well. With so few drugs having ever been tested in the pregnant body, an act of legislation that will financially reward drug makers to move beyond their exclusionary habits can only lead

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121 Id.
123 Fernandez Lynch, supra note 120, at 94.
to greater clarity on which drugs will work for pregnant women, and which will not. There will obviously be great discomfort and ethical doubts about using financial rewards to break into the pregnancy drug market, but those same doubts were raised with the enactments of BPCA and PREA,124 and those Acts have achieved the outcomes many had hoped they would.125 What is more damning, however, is the continued absence of pregnant women from the clinical research marketplace, and should a market-focused approach of greater drug exclusivity and less competition be the answer, so be it.

**CONCLUSION**

Pregnancy is a big deal. It is one of the most celebrated occurrences of the lifecycle, and its importance across cultures and time cannot be understated. Yet, the precarious position pregnant women have been placed in because of the discriminatory actions of the medical research community demeans what should be, for the most part, a joyous experience. It is almost inevitable that a pregnant woman will encounter an illness or condition during the term of her pregnancy that will require some form of medical treatment, and when a medical intervention is needed in the form of a drug or biologic, she and her health care professionals will largely be making decisions in the dark. This reality is inexcusable.

What has been argued here is that the exclusion of pregnant women from clinical research constitutes sex discrimination as a matter of policy. Pregnant women, because of their pregnant status, have been presumptively excluded from the medical research environment because they have been deemed a vulnerable population whose health and safety are intimately connected to the fetuses they carry. The human subjects protections regulations created to

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124 See INST. OF MED., SAFE AND EFFECTIVE MEDICINES FOR CHILDREN 89–110 (2012) (discussing the ethical concerns of the BPCA and the PREA in sparking greater research in pediatric populations).

125 Christensen, supra note 111, at 140.
include pregnant women have been left to the interpretation and determination of hesitant researchers and IRBs who fear repeating medical disasters of years gone by. While the courts will prove unsuitable for healing this health care wound, Congress has demonstrated its adeptness at resolving similar clinical quandaries in the last two decades through legislative acts that have pushed the NIH and FDA to do more in meeting the medical demands of those who need it most. Congressional intervention can almost certainly bring some relief to pregnant women by instigating change that will allow these women to engage in research, and overall, receive care that more accurately treats their varied conditions.

Women should be afforded the opportunity to enjoy their pregnancies with relative ease and comfort, knowing that an unforeseen medical complication can be treated safely and effectively. In a nation that places a high premium on women’s health, children, and the family, we at least owe them that.