COVID RESEARCH INEQUALITIES: HIGHLIGHTING THE NEED FOR INCREASED MINORITY PARTICIPATION IN CLINICAL TRIALS

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I. INTRODUCTION

In March 2020, the world came to a screeching halt: people stopped going to work and children stopped going to school; grocery and drug stores displayed empty shelves where paper goods, cleaning supplies, medicines, and pantry items were once fully stocked. Big cities, like New York, felt almost post-apocalyptic: subways were empty, traffic had thinned, and the piercing wail of ambulance sirens echoed through the otherwise empty streets. Less than two months after the first confirmed COVID-19 case in the United States, the World Health Organization (WHO) declared COVID-19 a pandemic on March 11, 2020.[1] COVID-19, the disease caused by the novel coronavirus SARS-CoV-2, brought the economy to a grinding halt, pushed the healthcare systems beyond capacity, and as of October 2021, has caused more than 700,000 deaths in the United States alone.[2]

Experts noted early on in the pandemic that certain factors, such as preexisting conditions and geographic location, were associated with greater infection and death rates.[3] Data also shows that race or ethnicity plays a role in susceptibility to COVID-19 and that racial and ethnic

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[1] AJMC Staff, *A Timeline of COVID-19 Developments in 2020*, AJMC (Jan. 1, 2021), https://www.ajmc.com/view/a-timeline-of-covid19-developments-in-2020.

[2] *Id.*; Nat'l Ctr. for Health Statistics, *Daily Updates of Totals by Week and State*, CTRS. FOR DISEASE CONTROL & PREVENTION, https://www.cdc.gov/nchs/nvss/vsrr/COVID19/index.htm.

[3] Winston Morgan, *Will the COVID-19 Pandemic and Black Lives Matter Change Science and Society?*, MED. NEWS TODAY (Aug. 20, 2020), https://www.medicalnewstoday.com/articles/will-the-covid-19-pandemic-and-black-lives-matter-change-science-and-society; *see* Julius M. Wilder, *The Disproportionate Impact of COVID-19 on Racial and Ethnic Minorities in the United States*, 72 CLINICAL INFECTIOUS DISEASES 709 (2021), https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa959/5869621.

disparities exist for both morbidity and mortality rates of COVID-19.[4] A review of COVID-19 cases in England found that Black and Asian individuals are at a higher risk of COVID-19 mortality even when controlling for factors such as age and comorbidity.[5] This is consistent with general knowledge of racial health disparities in the United States.[6]

In addition to the COVID-19 pandemic, 2020 saw widespread support for the Black Lives Matter movement, sparked by outrage over the public murder of George Floyd by Minneapolis police officers.[7] Worldwide protests have called for an end to systemic racism, and the protests have had some success with finally pressuring individuals, politicians, and companies to recognize and reflect upon the injustices and abuses faced by Black Americans.[8] The convergence of the COVID-19 pandemic and the power and prominence of the Black Lives Matter movement provides the perfect sociopolitical climate to re-examine the landscape of our healthcare system through the lens of racial equality, particularly the field of clinical research.

Although minority communities are disproportionately affected by COVID-19, both treatment and vaccine clinical trials have failed to enroll sufficiently diverse participants.[9] While the National Institutes of Health (NIH) has issued regulations *requiring* minorities to be represented in Phase III clinical trials receiving NIH funding, the U.S. Food and Drug Administration (FDA), which oversees clinical trials of drugs and medical devices, has merely issued non-binding guidance *encouraging* diversity in clinical trial participants.[10] These efforts have been largely unsuccessful.[11] This Comment will argue that to reduce racial

[4] Morgan, *supra* note 3; Wilder, *supra* note 3, at 709 ("[Coronavirus] . . . has caused a global pandemic and has highlighted the glaring impact of social determinants of health and racism in the United States.").

[5] Morgan, *supra* note 3.

[6] *See infra* Section II.A.

[7] Austa Somvichian-Clausen, *What the 2020 Black Lives Matter Protests Have Achieved So Far*, HILL (June 10, 2020), https://thehill.com/changing-america/respect/equality/502121-what-the-2020-black-lives-matter-protests-have-achieved-so.

[8] *Id.*

[9] Wayne A. I. Frederick et al., Opinion, *We Need to Recruit More Black Americans in Vaccine Trials*, N.Y. TIMES (Sept. 11, 2020), https://www.nytimes.com/2020/09/11/opinion/vaccine-testing-black-americans.html ("[T]he largest population being killed by Covid-19 should have a significant role in development of a treatment."). Moderna has reported 26 percent diversity despite minorities making up 32 percent of the population, earning a "C" from Dr. Fauci. *Id.*

[10] *See infra* Section IV.A.

[11] *See* Vassia Barba, *Female Participation Up, Diversity Rates Down in 2019 Approved Drugs' Trials*, OUTSOURCING-PHARMA.COM (Feb. 26, 2020), https://www.outsourcing-pharma.com/Article/2020/02/26/FDA-release-of-clinical-trials-participation-demographics (The FDA's Drug Trials Snapshots report for 2019 "show[s] decreased

disparities in clinical trials effectively, the FDA must promulgate binding regulations requiring drug developers to increase diversity of clinical trial participants, especially when the disease that the drug or intervention targets disproportionately affects minority populations.

Part II of this Comment will briefly review the history of healthcare disparities in minority populations and the medical and social significance of these disparities. This Part will also examine how racial disparities have played out in the context of the COVID-19 pandemic. Part III will provide a brief overview of the FDA's role in regulating clinical trials to provide context for why the FDA is the correct entity to address the lack of minority inclusion in clinical trials. Part IV will review initiatives that the government has taken in the past to address this issue. This Part will also provide examples of initiatives taken by non-profit organizations, industry, and other private actors to increase diversity in clinical trials. Finally, Part V will propose an FDA regulation to increase diversity in clinical trials more effectively than the guidance it has issued in the past. This Part will also provide suggested guidance that can accompany the regulation to help members of the medical and health care professions increase their access to diverse patient populations. These suggestions will be similar to actions that non-profit organizations and industry actors have taken in the past and consider suggestions from experts in the field.

II. CAUSES AND SIGNIFICANCE OF RACIAL DISPARITIES IN HEALTHCARE

A. *Racial Disparities in Healthcare and Clinical Trials*

Healthcare disparities are systemic and consistent differences, such as greater health risks and worse health outcomes, in disadvantaged social groups such as racial and ethnic minorities.[12] For example, mortality rates from heart disease, stroke, and certain cancers are much higher in Black populations; diabetes rates in Native Americans and Latinx are 30 percent higher than White Americans; and Black Americans' life expectancy is nearly ten years less than White

ethnic diversity compared to last year's approved drugs' clinical trials, which included 69% White participants, 11% Black or African American, 10% Asian and 14% Hispanic."); Hala T. Borno et al., *COVID-19 Disparities: An Urgent Call for Race Reporting and Representation in Clinical Research*, CONTEMP. CLINICAL TRIALS COMMC'NS (July 30, 2020), https://www.sciencedirect.com/science/article/pii/S2451865420301149 ("In the United States, racial/ethnic minorities remain underrepresented in clinical research with Black and Hispanic patients comprising approximately three and six percent of clinical trial participants, respectively.").

[12] *Racial and Ethnic Health Care Disparities*, CTR. FOR MEDICARE ADVOC., https://medicareadvocacy.org/medicare-info/health-care-disparities/.

Americans.[13] There are a number of structural issues that prevent many minority communities from having equal or even adequate access to health care, including economic factors; linguistic, cultural, or religious barriers; and geographic barriers.[14]

In addition to structural factors, some scholars indicate that physicians' implicit racial biases are another cause of racial healthcare disparities.[15] In 2005, the National Academy of Medicine (NAM) found that even when controlling for factors such as insurance status, income, age, comorbidities, and access to healthcare services, racial and ethnic minorities still received lower-quality care than White patients.[16] The report concluded that some people are more likely to die from common diseases like cancer and heart disease "simply because of their race or ethnicity."[17] Physicians may be unaware that implicit biases negatively impact the care they provide to minority patients. Still, experiments have shown that physicians whose Implicit Association Test (IAT) results showed anti-Black bias were less likely to prescribe pain medications and specific (effective) treatments for heart disease to Black patients compared to White patients.[18] In conjunction with structural factors, healthcare providers' implicit biases dramatically compromise the quality of care and health outcomes for racial and ethnic minorities.

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[13] Wayne J. Riley, *Health Disparities: Gaps in Access, Quality and Affordability of Medical Care*, 123 TRANSACTIONS AM. CLINICAL AND CLIMATOLOGICAL ASS'N 167, 168 (2012), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3540621/pdf/tacca123000167.pdf. For detailed life expectancy data over the last century by race, see generally CTRS. FOR DISEASE CONTROL & PREVENTION, LIFE EXPECTANCY AT BIRTH, AT AGE 65, AND AT AGE 75, BY SEX, RACE, AND HISPANIC ORIGIN: UNITED STATES, SELECTED YEARS 1900–2016 (2017), https://www.cdc.gov/nchs/data/hus/2017/015.pdf.

[14] *Racial and Ethnic Health Care Disparities, supra* note 12. For a visualization of the model of health disparities from the Institute of Medicine (IOM), see Riley, *supra* note 13 at 167–68.

[15] Riley, *supra* note 13, at 169; Khiara M. Bridges, *Implicit Bias and Racial Disparities in Health Care*, AM. BAR ASS'N, https://www.americanbar.org/groups/crsj/publications/human_rights_magazine_home/the-state-of-healthcare-in-the-united-states/racial-disparities-in-health-care/ (last visited Oct. 24, 2021).

[16] For example, Black patients have higher rates of limb amputation than White patients; Black patients are typically discharged from hospitals after surgery earlier than White patients, often when discharge is inappropriate; and Black patients are more likely to be treated with antipsychotics for bipolar disorder compared to White patients, despite evidence that these medications are ineffective and cause long-term negative effects. Bridges, *supra* note 15.

[17] Bridges, *supra* note 15.

[18] *Id*.

Minority communities also face widespread distrust of the medical profession rooted in a history of mistreatment and abuse.[19] Perhaps one of the most well-known examples of this exploitation is the Tuskegee Syphilis Study, where Black men with syphilis were "enrolled" in a clinical study without their knowledge or consent.[20] Because the study's purpose was to track the natural progression of untreated syphilis, the men did not receive treatment for the disease even when penicillin became a widely accepted cure.[21] To this day, historical distrust is reinforced by the fact that Black patients tend to have worse clinical outcomes than White patients.[22]

Many of the barriers that racial and ethnic minorities face in healthcare generally create obstacles to accessing and participating in clinical trials. Because enrolling in a clinical trial is voluntary, patients must be willing to participate.[23] If minority patients do not trust their doctors, it will be difficult to recruit minority patients even with the best outreach programs.[24] A survey study of men with prostate cancer found that White men were far more willing to discuss clinical trials with their doctors than Black men.[25] The study found that the White men were less likely to believe that they should be suspicious of the healthcare system based on their race, while the Black men demonstrated greater group-based medical suspicion.[26] This is just one example of how increasing trust in the medical system may reduce healthcare disparities and improve equity in clinical research. Without representation in trials, minority patients have no reason to trust experimental interventions or newly approved treatments.[27]

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[19] This Comment will not expand upon the full history of unethical, inhumane, and cruel abuses against Black bodies which remain in the collective consciousness of Black Americans to this day. For a detailed history, see generally HARRIET A. WASHINGTON, MEDICAL APARTHEID: THE DARK HISTORY OF MEDICAL EXPERIMENTATION ON BLACK AMERICANS FROM COLONIAL TIMES TO THE PRESENT (2006).

[20] *The Tuskegee Timeline*, CTRS. FOR DISEASE CONTROL & PREVENTION, https://www.cdc.gov/tuskegee/timeline.htm (last visited Oct. 24, 2021).

[21] *Id*.

[22] J. Corey Williams, *Black Americans Don't Trust our Healthcare System—Here's Why*, HILL (Aug. 24, 2017), https://thehill.com/blogs/pundits-blog/healthcare/347780-black-americans-dont-have-trust-in-our-healthcare-system.

[23] U.S. FOOD & DRUG ADMIN., FDA ACTION PLAN TO ENHANCE THE COLLECTION AND AVAILABILITY OF DEMOGRAPHIC SUBGROUP DATA 11 (2014) [hereinafter FDA ACTION PLAN], https://www.fda.gov/media/89307/download.

[24] Frederick et al., *supra* note 9.

[25] Nicole Senft et al., *Willingness to Discuss Clinical Trials Among Black vs White Men With Prostate Cancer*, 6 J. AM. MED. ASS'N ONCOLOGY 1773, 1774 (Nov. 2020), https://jamanetwork.com/journals/jamaoncology/article-abstract/2770256.

[26] *Id.* at 1773.

[27] Frederick et al., *supra* note 9.

In addition to the structural issues and physician biases discussed above, the participant recruitment and referral processes inhibit minority access to clinical trials.[28] A paper from the Endocrine Society noted that,

> [P]harmaceutical companies and CROs [(Contract Research Organizations)] only recruit physicians with a track record of clinical research. Therefore, physicians with an interest in clinical research, but with little experience, lack the opportunities to participate in enough clinical trials to maintain the infrastructure that they have worked so hard to build. This results in *minority physicians being under-represented in clinical research and, as a consequence, their patients, many of whom belong to ethnic minority groups, are also under-represented*.[29]

Minorities are largely underrepresented in drug and disease treatment research even when a particular disease disproportionately affects a minority group or groups. For example, one in five Americans diagnosed with multiple myeloma is Black, yet in 2015, the FDA approved a study drug for multiple myeloma treatment after a trial in which only 1.8 percent of the participants were Black.[30]

B. *Importance of Minority Representation in Clinical Trials*

Clinical trials must include members of minority populations to ensure that the results of those trials are relevant to those populations. Many diseases disproportionately affect minority populations,[31] and clinical trials should include members of such populations to ensure the interventions developed will benefit the populations who are most affected by the disease.[32] One of the most common justifications for including minority populations in clinical trials is genetics. Genetics can

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[28] *See generally* ENDOCRINE SOCIETY, INCREASING MINORITY PARTICIPATION IN CLINICAL RESEARCH (2007), https://www.endocrine.org/~/media/endosociety/files/advocacy-and-outreach/important-documents/increasingminorityparticipationinclinicalresearch.pdf?la=en.

[29] *Id.* at 5–6 (emphasis added).

[30] Balt. Sun Editorial Bd., Editorial, *African Americans and Hispanics Must Be a Part of Vaccine Trials, and It's Up To Doctors and Researchers to Earn Their Trust*, BALT. SUN (Sept. 18, 2020, 5:53 AM), https://www.baltimoresun.com/opinion/editorial/bs-ed-09-covid-vaccine-african-americans-hispanics-20200918-yxea5t5qwng5njr5lhcpyk-aobm-story.html.

[31] *See supra* Section II.A.

[32] FDA ACTION PLAN, *supra* note 23, at 11 ("FDA fully supports efforts to encourage participation of underrepresented ethnic and racial subgroups participating in clinical trials in applications for all FDA-regulated medical products, *so that knowledge about the safety and effectiveness of these products is informative to patients who may use the products*.") (emphasis added).

affect how our bodies metabolize drugs and medications.[33] This is particularly true for vaccines, which work by manipulating the immune system.[34] Further, some diseases manifest differently depending upon a person's race or ethnicity.[35]

Because racial categories are social constructs rather than biological facts, membership in a self-defined racial group does not define one's genetic makeup. In fact, looking at genetics alone, scientists cannot distinguish between races.[36] Even when certain genetic features can be grouped and associated with "quasi-distinct" categories, these categories do not align with socially-constructed racial groups.[37] For example, there could be more genetic similarities between a racially Asian individual and a racially White individual than between two racially Black individuals.[38] And while certain genes can impact rates of disease and pharmaceutical metabolism, these genes "do not align neatly with reductive racial categories often employed to represent geographic origin."[39] Consequently, making health decisions based upon race can lead to more mistakes and thus worse health outcomes.[40]

Nevertheless, there is sometimes a correlation between self-identified racial groups and genetic characteristics, given that racial categories often are based on the geographic location of a person's ancestors. For example, from observational studies and pharmacogenetics (the study of how an individual's genetics affect his or her drug response), we know that responses to medications can vary

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33 Frederick et al., *supra* note 9.

34 Frederick et al., *supra* note 9; *see also* Daniel S. Streetman, *Pharmacogenomics and Race: Can Heritage Affect Drug Disposition?*, WOLTERS KLUWER (Apr. 18, 2017), https://www.wolterskluwer.com/en/expert-insights/pharmacogenomics-and-race-can-heritage-affect-drug-disposition ("[W]hen it comes to how our bodies metabolize and react to medications, we should not all be viewed as the same.").

35 Balt. Sun Editorial Bd., *supra* note 30.

36 Selin Ege Yalcindag, *There is No Biological Meaning for 'Race,'* ILL. SCI. COUNCIL (Sept. 7, 2020), https://www.illinoisscience.org/2020/09/there-is-no-biological-meaning-for-race/.

37 *Id.*

38 *Id.*; Jennifer Tsai, *What Role Should Race Play in Medicine?*, SCI. AM. (Sept. 12, 2018), https://blogs.scientificamerican.com/voices/what-role-should-race-play-in-medicine/ ("Research demonstrates that genetic differences are higher within racial groups than between racial groups—that two black patients sitting in the waiting room will have less genetic overlap with each other than with their white, Asian, or Hispanic neighbors.").

39 Tsai, *supra* note 38.

40 *See Scientists Call for the Removal of Race in Genetics Research*, WHYY (Feb. 18, 2016), https://whyy.org/segments/scientists-call-for-the-removal-of-race-in-genetics-research/ ("[B]ecause of the myth that sickle cell is a black disease, or cystic fibrosis is a white disease, white patients may be under diagnosed for sickle cell and other hemoglobin diseases, and black patients have been under diagnosed for cystic fibrosis.").

among individuals of different races or ethnicities.[41] A 2015 study concluded that about 20 percent of newly approved drugs have different responses based on the user's race or ethnicity.[42] For example, individuals of African or Mediterranean descent more commonly have a G6PD deficiency (a type of genetic abnormality) that places them at higher risk of hemolysis when exposed to certain medications such as antimalarial medications and sulfa drugs.[43] While the reasons for these varying responses are not entirely understood, some are attributed to specific genetic differences.[44] For many race-specific disposition differences, however, a specific genetic difference is not known.[45]

Aside from genetics, race is also relevant because of social determinants of health.[46] Differences in access to healthcare, employment, and clean, safe living conditions can lead to data that reflect racial differences in health outcomes.[47] These disparities "are engineered from a great number of social inequalities that disproportionately impact certain groups."[48] Negative healthcare outcomes are not a result of racial differences—rather, the healthcare disparities themselves are forms of "racial inequities driven by injustice."[49] With so many social factors at play, conclusions cannot always be accurately drawn about racial or genetic predispositions to health outcomes.[50] In a perfect world, doctors would consider their patients' social conditions rather than race, especially when caring for minority populations.[51]

Some scholars argue that "racial categories are weak proxies for genetic diversity [that] need to be phased out."[52] Jennifer Tsai, an

41 Streetman, *supra* note 34.

42 *Id.*

43 *Id.*

44 *Id.*

45 *Id.*

46 See *infra* Section II.C.i. for a more in-depth discussion of social determinants of health.

47 Yalcindag, *supra* note 36; Tsai, *supra* note 38 ("While African-American women fight to endure appalling rates of maternal mortality, white men are most likely to die from opioid overdose. These are not biological predispositions.").

48 Tsai, *supra* note 38.

49 *Id.*

50 Yalcindag, *supra* note 36.

51 *Scientists Call for the Removal of Race in Genetics Research*, *supra* note 40.

52 Megan Gannon, *Race is a Social Construct, Scientists Argue*, SCI. AM. (Feb. 5, 2016), https://www.scientificamerican.com/article/race-is-a-social-construct-scientists-argue/ ("[M]odern genetics research is operating in a paradox, which is that race is understood to be a useful tool to elucidate human genetic diversity, but on the other hand, race is also understood to be a poorly defined marker of that diversity and an imprecise proxy for the relationship between ancestry and genetics.").

emergency physician, disagrees, arguing, "[r]ather than a risk *factor* that predicts disease or disability because of genetic susceptibility, race is better conceptualized as a risk *marker*—of vulnerability, bias or systemic disadvantage."[53] She argues that because of the ubiquity of racial disparities in healthcare, we should not be asking whether or not to use race in medicine; rather, we should consider "how [to] use race well."[54] When used effectively, race should not be used as a proxy for genetics—except where racially-correlated genetic differences are known—or as an independent risk factor that is itself a cause of worse health outcomes; instead, race should be used as an indicator of potential risks caused by external social determinants.[55]

Social determinants affect responses to drugs or vaccines and should be considered during the clinical trial process by enrolling diverse trial participants. Differences in people's underlying medical conditions, for example, can affect vaccine effectiveness.[56] In individuals with preexisting conditions such as diabetes or HIV infection, both of which affect Black Americans at a higher rate than White Americans, vaccines have proven to be less effective.[57] Behavioral factors, such as smoking, alcohol consumption, exercise, sleep, and psychological stress, and nutritional factors, such as body mass index and nutritional status, also contribute to variations in vaccine responses—both the protection's efficacy and duration.[58] Because vaccine effectiveness can be impacted by differences in underlying conditions and can vary in groups of people not included or well-represented in clinical trials, vaccines that the FDA approves for emergency use must continue to be studied to determine their effectiveness under real-world conditions.[59] Including racially diverse participants in clinical trials would better ensure that vaccines are safe and effective for real-world populations at the time of approval, rather than relying upon post-approval studies that effectively force

53 Tsai, *supra* note 38.

54 *Id.*

55 *Id.*

56 *Ensuring COVID-19 Vaccines Work*, CTRS. FOR DISEASE CONTROL & PREVENTION (Dec. 13, 2020), https://www.cdc.gov/coronavirus/2019-ncov/vaccines/effectiveness.html.

57 Ananya Mandal, *Vaccine Effectiveness*, NEWS MED. (June 5, 2019), https://www.news-medical.net/health/Vaccine-Effectiveness.aspx.

58 For example, both adults and children who are infected with HIV show lower responses to various vaccines, including tetanus and measles, and patients with diabetes mellitus are associated with lower responses to Hepatitis B vaccination. Petra Zimmermann & Nigel Curtis, *Factors That Influence the Immune Response to Vaccination*, 32 AM. SOC'Y FOR MICROBIOLOGY, Mar. 13, 2019, https://cmr.asm.org/content/32/2/e00084-18.full.

59 *Ensuring COVID-19 Vaccines Work*, *supra* note 56.

disadvantaged populations to participate in a post-approval "clinical trial" without their knowledge or consent.

C. *Racial Diversity in COVID-19 Clinical Trials*

While a lack of diversity and inclusion in clinical trials is nothing new, the COVID-19 pandemic highlights how much more work still needs to be done. Because COVID-19 disproportionately affects minority communities, treatment and vaccine clinical trials need to include diverse populations to ensure the interventions developed will benefit the populations who are most affected by the disease. Vaccine trials proceeded quickly, and the lack of diversity illustrates the urgency of the ongoing challenge to improve inclusion in clinical trials.

1. Why COVID-19 Disproportionately Affects Minority Populations

Healthcare disparities and structural and societal factors, such as living and working conditions, reinforce these disparities, placing minority communities at a disadvantage during the COVID-19 pandemic.[60] The disproportionate impact that the pandemic has on racial and ethnic minority groups highlights relevant issues in medical, social, economic, and political contexts that have existed since long before the pandemic.[61]

Minority groups that are disproportionately affected by chronic medical conditions and lower access to health care have worse COVID-19 infection and mortality rates.[62] In cities like New York and San Francisco, Black and Hispanic Americans face higher rates of mortality, infection, and death from COVID-19.[63] Compared to White Americans, Black Americans are disproportionately burdened by chronic preexisting conditions such as diabetes mellitus, hypertension, and obesity, all of which increase a patient's risk of severe COVID-19 infection and mortality; this longstanding disparity directly contributes

[60] CDC data shows that 20.1 percent of COVID-19 cases were Black Americans, though they make up only 13.4 percent of the population. Similarly, 33.5 percent of cases were Hispanic individuals, who make up only 18.5 percent of the population. Borno et al., *supra* note 11.

[61] Wilder, *supra* note 3, at 709–10, refers to the combination of factors discussed in Tai, et al., *infra* note 62, as a second pandemic: "The pandemic of social determinants" ("Our unwillingness to confront the issue of racism in healthcare head-on will continue to impede our ability to achieve true health equity.").

[62] Don Bambino Geno Tai et al., *The Disproportionate Impact of COVID-19 on Racial and Ethnic Minorities in the United States*, 72 CLINICAL INFECTIOUS DISEASES 705 (2021), https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa815/5860249.

[63] Borno et al., *supra* note 11, at 1.

to disproportionately high infection rates and negative outcomes for Black Americans with COVID-19.[64] Chronic preexisting medical conditions are further exacerbated by less access to quality healthcare.[65] Black Americans, Hispanic Americans, and Native Americans have higher uninsured rates compared to White Americans (12 percent, 19 percent, and 22 percent, respectively, compared to 8 percent), in addition to living in areas with lower quality medical care.[66] If infected with COVID-19, these minority individuals will likely receive lower-quality care, which could lead to worse health outcomes.

Economic factors also contribute to the disparities in preexisting medical conditions and healthcare access. Compared to only 9 percent for Whites, the pre-COVID-19 poverty rates for Black Americans, Hispanic Americans, and Native Americans were 22 percent, 19 percent, and 24 percent, respectively.[67] Lower-income individuals lack the financial security to make necessary "healthful decisions" during the pandemic.[68] In New York City, 75 percent of frontline "essential" workers are people of color who were unable to work from home, many of whom even continued to use public transportation as their only means of getting to work.[69] Minority communities also frequently have higher housing density and are more likely to live with multiple generations of family members, circumstances that make social distancing much more difficult, if not impossible.[70] Other social determinants, such as language barriers and health illiteracy, prevent essential health information about the pandemic from being communicated to some minority populations.[71] As a result, the risk of COVID-19 spreading through these communities is higher than other communities because of the "relative lack of credible COVID-19 information."[72]

64 Tai et al., *supra* note 62, at 705.

65 Borno et al., *supra* note 11, at 1.

66 Tai et al., *supra* note 62, 705–06.

67 *Id.* at 706.

68 *Id.*

69 *Id.*

70 *Id.*

71 *Id.*

72 Tai et al., *supra* note 62, at 706. For how the factors described in this section are relevant to the efficacy of COVID-19 vaccines, see *infra* Section II.B. beginning with note 46.

2. COVID-19 Clinical Trials

Researchers and drug developers have historically failed at achieving inclusiveness in clinical trials, and the clinical trials for COVID-19 treatments and the development of a COVID-19 vaccine are no different.[73] So far, COVID-19 treatment trials have not included sufficiently diverse populations, despite the fact that Black and Latinx communities have been disproportionately affected by the disease.[74] A study conducted by researchers at the University of California San Francisco assessed the race representation in COVID-19 treatment studies through July 10, 2020.[75] The results found that race and ethnicity were inconsistently collected and reported and that "Black patients were consistently underrepresented relative to their disease burden."[76] In one New York-based retrospective study of Hydroxychloroquine in COVID-19 patients, Black patients made up only 11 percent of the study population—meanwhile, Black Americans made up 30.5 percent of New York's COVID-19 cases.[77] Interestingly, in the same study, Hispanic patients were vastly overrepresented—51 percent of the study population, but 32.7 percent of all cases—and race/ethnicity data was missing for 23.2 percent of the study participants.[78] Black and Hispanic patients were also underrepresented compared to the relative affected population in studies in Boston and Minneapolis.[79]

Knowing the history of clinical research with minority communities, scientists realize their obligation to create a vaccine that works for the diverse populations who will need it. One of the leading scientists on the Pfizer vaccine study understands the importance of diversity in understanding how a drug or vaccine will work in the general population:

> A question we always ask ourselves, when we do clinical trials, are how generalizable will results be to people who suffer from the disease? . . . If you did a study in a majority-White population with very little Black individuals, when we do get results from the study, it will always be a question: Does it

73 Balt. Sun Editorial Bd., *supra* note 30.

74 *See generally* Borno et al., *supra* note 11.

75 *Id.* at 1.

76 *Id.* at 3.

77 *Id.* at 2.

78 *Id.*

79 *Id.*

> work the same in Black [people] as compared to others? And that's even more so for covid.[80]

Yet by the end of August 2020, when Moderna's and Pfizer's vaccine trials had enrolled more than half of the target study population, just below one-fifth of the participants were Black or Hispanic.[81] In early October 2020, Moderna had still not recruited sufficient Black, Latinx, or Native American participants, leading the company to slow trial enrollment to prioritize minority recruitment.[82] Investigators working on the clinical trial reported that while minority recruitment lagged, trial quotas were quickly filled by "overwhelming interest in participation from [W]hite volunteers."[83] And in an online registry used for expressing interest in vaccine trials as of late August, Black and Hispanic people made up only 10–11 percent of volunteers.[84]

While current enrollment does not even mirror the demographic breakdown of the U.S. population as a whole (about 33 percent Black, Hispanic, and Native American), many experts argue that this target is too low: instead, enrollment efforts should "reflect the disproportionate burden of disease."[85] As evidenced by current enrollment, these goals would be difficult to achieve, largely because of minority populations' distrust of the medical community caused by a history of being subjects for experimentation without knowledge or consent.[86] The scientific and medical communities owe it to minority populations to address these fears. Only by addressing these fears can we hope to lessen the death

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[80] Carolyn Y. Johnson, *Large U.S. COVID-19 Vaccine Trials are Halfway Enrolled, but Lag on Participant Diversity*, WASH. POST (Aug. 27, 2020), https://www.washingtonpost.com/health/2020/08/27/large-us-covid-19-vaccine-trials-are-halfway-enrolled-lag-participant-diversity/.

[81] *Id.* ("Creating vaccine trials that, at minimum, mirror the racial and ethnic breakdown of the American population, which is about one-third total Black, Hispanic and Native American, has been a major focus — a necessity to make sure any vaccine works for everyone and is broadly accepted."); Balt. Sun Editorial Bd., *supra* note 30.

[82] Justine Coleman, *Moderna Vaccine Trials Slowed by Insufficient Minority Participants: Report*, HILL (Oct. 6, 2020), https://thehill.com/policy/healthcare/519807-moderna-vaccine-trials-slowed-by-insufficient-minority-participants-report.

[83] *Id.*

[84] Johnson, *supra* note 80 (quoting James Kublin, executive director of the federal HIV Vaccine Trials Network, which is currently being repurposed to test coronavirus vaccines ("We are working a bit uphill . . . to get the studies representing the diversity [of the U.S.] — and that goes into the historical legacy of not just discrimination, but of outright unethical medical practices . . . .") (alteration in original)).

[85] *Id.* (quoting Hala Borno, a medical oncologist at the University of California at San Francisco who studied coronavirus clinical trials that disclosed racial data and found that Blacks were underrepresented ("[T]he way that scientific research goes, is you need a sufficient sample to power your analysis, to determine there is a real difference for that population. You need to oversample racial and ethnic minorities.")).

[86] Coleman, *supra* note 82.

toll of COVID-19 in hard-hit communities.[87] We must increase inclusion in clinical research, especially trials related to COVID-19, to address disparities in health outcomes.[88] The COVID-19 pandemic has given medical and healthcare professionals a more powerful voice in society. These professionals now have the opportunity to unravel the old system, filled with social inequities, to design a "more equitable system that promotes health for all Americans irrespective of social or economic background."[89]

III. THE ROLE OF THE FDA IN REGULATING CLINICAL TRIALS

The FDA is the federal agency responsible for regulating clinical trials. The FDA derives much of its statutory authority from the Food, Drug, and Cosmetics Act, which states that missions of the FDA include "promot[ing] the public health by promptly and efficiently reviewing clinical research," and "ensuring that . . . human . . . drugs are safe and effective."[90] These missions should be carried out "in consultation with experts in science, medicine, and public health, and in cooperation with consumers, users, [and] manufacturers . . . of regulated products."[91] Further, the FDA's programs and policies should encourage collaboration with "the National Institutes of Health, and other science-based Federal agencies, to enhance the scientific and technical expertise available . . . with respect to the development, clinical investigation, [and] evaluation . . . of emerging medical therapies."[92] The FDA has promulgated numerous regulations to execute its statutory missions relating to clinical trials.[93] For example, one way the FDA regulates clinical trials is by requiring sponsors to submit an Investigational New Drug Application (IND) to the FDA before conducting a clinical trial.[94]

New, untested drugs typically go through three phases of investigation, referred to as Phases I, II, and III.[95] Phase I investigations are closely monitored, as they primarily focus on determining the maximum dose of a drug that can be administered safely without causing severe side effects.[96] Phase II investigations study the effectiveness of the new intervention and also further evaluate risks and

87 Balt. Sun Editorial Bd., *supra* note 30.
88 *See* Borno et al., *supra* note 11.
89 Tai et al., *supra* note 62, at 707.
90 Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 393(b)(1), (b)(2)(b) (2020).
91 21 U.S.C. § 393(b)(4).
92 21 U.S.C. § 393(c).
93 *See generally* 21 C.F.R. §§ 312.1–312.320 (2019).
94 21 C.F.R. § 312.20.
95 § 312.21.
96 *See id.*

short-term side effects associated with the drug.[97] Phase III investigations collect "additional information about effectiveness and safety that is needed to evaluate the overall benefit-risk relationship of the drug and to provide an adequate basis for physician labeling."[98] As a trial moves through the phases, the number of subjects included in the trial increases from approximately twenty to several thousand.[99]

The FDA has the power to place a clinical hold to suspend an ongoing investigation,[100] and utilizes this power to enforce compliance with regulations related to clinical trials. In existing regulations, the FDA lists a number of specified grounds for issuing a clinical hold at each phase of the trial process.[101] For example, the FDA may place Phase II or III studies on hold if the "plan or protocol for the investigation is clearly deficient in design to meet its stated objectives."[102] If the FDA identifies a study deficiency, it will "attempt to discuss and satisfactorily resolve the matter with the sponsor before issuing the clinical hold order."[103] If a hold order is issued, the trial may not resume until the FDA lifts the order because the sponsor has either (1) corrected the cited deficiency, or (2) "otherwise satisfie[d] the agency that the investigation(s) can proceed."[104]

IV. PAST AND CURRENT EFFORTS TO INCREASE RACIAL DIVERSITY IN CLINICAL TRIALS

A. *Government Initiatives*

1. NIH Revitalization Act of 1993

The NIH is a federal agency within the Department of Health and Human Services responsible for medical research.[105] The NIH conducts biomedical research projects and funds research projects conducted by public and private entities.[106] The NIH Revitalization Act of 1993 required the NIH to create a policy that would increase the inclusion of

97 *Id.*
98 *Id.*
99 *Id.*
100 § 312.42(a).
101 § 312.42(b).
102 *Id.*
103 § 312.42(c).
104 § 312.42(e).
105 *Who We Are*, NAT'L INSTS. HEALTH, https://www.nih.gov/about-nih/who-we-are (last visited Oct. 24, 2021).
106 *Mission and Goals*, NAT'L INSTS. HEALTH (July 27, 2017), https://www.nih.gov/about-nih/what-we-do/mission-goals.

women and minorities in clinical research.[107] The Act states that "[t]he Director of NIH . . . shall conduct or support outreach programs for the recruitment of . . . members of minority groups as subjects in projects of clinical research," and that "the costs of such inclusion in the trial is not a permissible consideration in determining whether such inclusion is inappropriate."[108] The Act also provides exceptions to the requirement for inclusion of minorities in clinical trials when "there is substantial scientific data demonstrating that there is no significant difference between" the effects of the intervention on minority groups and other trial subjects.[109]

> Following this directive, the NIH issued a policy that requires,
>
> [M]inority groups and their subpopulations [to] be included in all NIH-funded clinical research, unless a clear and compelling rationale and justification establishes to the satisfaction of the relevant Institute/Center Director that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research . . . . The inclusion of . . . members of minority groups and their subpopulations must be addressed in developing a research design or contract proposal appropriate to the scientific objectives of the study/contract.[110]

Mirroring the statute, the policy states that "[c]ost is not an acceptable reason for exclusion except when the study would duplicate data from other sources."[111] Policy exceptions may be permitted based on "compelling rationale and justification" at the NIH Director's discretion.[112] Evidence showing whether or not "race/ethnicity differences in the intervention effect are to be expected" must be reviewed during the proposal of an NIH-defined Phase III clinical trial.[113]

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[107] Nat'l Insts. Health, *NIH Policy and Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research*, NIH GRANTS & FUNDING (Dec. 6, 2017), https://grants.nih.gov/policy/inclusion/women-and-minorities/guidelines.htm. An amendment to the policy was made on November 28, 2017. The only significant change to the policy is the requirement that sex/gender, race, and/or ethnicity analysis are submitted to clinicaltrials.gov for applicable NIH-defined Phase III clinical trials. Because this Comment focuses on minority communities, efforts to include women in clinical research will not be discussed, though it is worth noting that efforts to increase gender-based diversity in clinical trials have been largely successful.

[108] National Institutes of Health Revitalization Act of 1993, Pub. L. No. 103–43, § 492B, 107 Stat. 122, 134 (1993).

[109] *Id.* at 135.

[110] Nat'l Insts. Health, *supra* note 107.

[111] *Id.*

[112] *Id.*

[113] *Id.*

If data supports "the existence of significant differences," the Phase III trial design must accommodate this.[114]

2. FDA Guidance Documents & Drug Trials Snapshots

The FDA has undertaken various initiatives to increase diversity in clinical trial participants and standardize the collection and reporting of race and ethnicity data.[115] Many of these initiatives have focused on broadening eligibility criteria, including "characteristics such as age, sex, medical history, current health status, presence or absence of certain genotypes, blood pressure or other physiologic parameter, and absence of certain diseases," to promote enrollment of participants that better reflect the population.[116]

In 2014, the FDA released the "FDA Action Plan to Enhance the Collection and Availability of Demographic Subgroup Data" ("Action Plan").[117] The Action Plan was published in response to Section 907 of the Food and Drug Administration Safety and Innovation Act of 2012 (FDASIA), which directed the FDA to provide Congress information regarding demographic subgroup participation in clinical trials and the availability of safety and efficacy data for specific subgroups.[118] Section 907 also mandated the FDA to issue an action plan making recommendations to improve,

> the completeness and quality of analyses of data on demographic subgroups in summaries of product safety and effectiveness data and in labeling; . . . the inclusion of such data, or the lack of availability of such data in labeling; . . . [and] the public availability of such data to patients, health care providers, and researchers.[119]

The Action Plan acknowledged that certain subgroups, including Blacks, Hispanics, and U.S. Asians, are less likely to participate in clinical trials compared to the population as a whole, and further acknowledged that "[p]articipation in clinical trials is voluntary, so in order to have

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114 *Id.*

115 *See, e.g.*, U.S. FOOD & DRUG ADMIN., COLLECTION OF RACE AND ETHNICITY DATA IN CLINICAL TRIALS: GUIDANCE FOR INDUSTRY AND FOOD AND DRUG ADMINISTRATION STAFF 1 (2016) [hereinafter 2016 GUIDANCE DOCUMENT]; *see generally Clinical Trials Guidance Documents*, U.S. FOOD & DRUG ADMIN., https://www.fda.gov/regulatory-information/search-fda-guidance-documents/clinical-trials-guidance-documents (last visited July 29, 2021).

116 U.S. FOOD & DRUG ADMIN., ENHANCING THE DIVERSITY OF CLINICAL TRIAL POPULATIONS — ELIGIBILITY CRITERIA, ENROLLMENT PRACTICES, AND TRIAL DESIGNS: GUIDANCE FOR INDUSTRY 2 n.2 (2020) [hereinafter 2020 GUIDANCE DOCUMENT].

117 FDA ACTION PLAN, *supra* note 23.

118 *See* Food and Drug Administration Safety and Innovation Act, Pub. L. No. 112–144, § 907, 126 Stat. 993, 1092–93 (2012).

119 *Id.* at 1093–94.

clinical trials with diversity among participants, a diverse population of people has to be willing to participate."[120]

One priority of this Action Plan was to encourage greater subgroup participation in clinical trials by identifying barriers to enrollment and implementing strategies to work around those barriers.[121] The Action Plan noted several barriers to participating, including a shortage of investigators who have access to patients who belong to demographic subgroups; "patients and families with negative attitudes about medical research and concerns about risk"; patient inconvenience, such as transportation requirements and geographic location; and insurance or socioeconomic status affecting access to trials and healthcare.[122] The Action Plan stated that the "FDA fully supports efforts to encourage participation of underrepresented ethnic and racial subgroups participating in clinical trials . . . so that knowledge about the safety and effectiveness of these products is informative to patients who may use the products."[123]

To address these participation barriers, the Action Plan contained several "Action Items," such as acknowledging that the issue "is not one of race and ethnicity alone" and introducing a plan to work with experts to better understand contemporary barriers to participation.[124] The Action Plan also proposed increasing effective communication with demographic subgroups about clinical trial participation, including distributing information in both English and Spanish, as well as establishing a "joint working group" that would "explore educational tools and outreach mechanisms to more broadly engage subgroups that consistently have low participation rates in clinical trials" and increase awareness about the value of participating in clinical trials.[125] Even with these Action Items, the Action Plan acknowledged that increasing subgroup participation in clinical trials is a complex issue that requires coordination with the NIH, advocacy groups, and industry and increased focus on community-based research.[126]

In 2015, the FDA's Center for Drug Evaluation and Research (CDER) began publishing Drug Trials Snapshots to make available to consumers and healthcare providers demographic information about

120 FDA ACTION PLAN, *supra* note 23, at 11.

121 *Id.*

122 *Id.* at 11–12.

123 *Id.* at 11.

124 *Id.* at 12.

125 *Id.* at 13–14.

126 FDA ACTION PLAN, *supra* note 23, at 13. See *infra* Section IV.B. for more information about industry initiatives to increase minority participation in clinical trials.

who participated in the clinical trials for newly approved drugs.[127] Each Snapshot indicates any differences in efficacy or side effects based on sex, age, or race, and provides a breakdown of the percentages of participants based on sex, age, and race.[128] At the end of each year, the FDA releases the "Drug Trials Snapshots Summary Report," which further breaks down demographic subgroups of all participants in trials for approved drugs.[129] In the annual report, demographic subgroups are broken down into White, Black or African American, Asian, and Hispanic.[130] For some drugs, certain demographic information is not reported.[131]

The Snapshots' purpose is to enhance transparency and "promote dialogue on the appropriate representation of different subgroups in clinical trials."[132] While a thoughtful initiative, the Snapshots have two major limitations: (1) conclusions regarding differences in safety and efficacy among different demographic groups "cannot always be made," and by looking at a few different snapshots, it appears that the inability to form conclusions happens often; and (2) Snapshots are posted within thirty days of drug approval and are not updated to reflect new information as it may become available.[133] Because the FDA typically approves drugs following Phase III,[134] the post-approval period—sometimes called Phase IV or a "post marketing surveillance" study—often produces additional safety or efficacy data that was not detected prior to FDA approval.[135] The "true safety profile" of a drug often is not fully developed until the drug has been made available on the market.[136] Because new information is not added to the Snapshot profile, a consumer or healthcare provider may not be considering the complete safety or efficacy information available for a certain drug when looking at Snapshot data.

In a complement to the Drug Trials Snapshots initiative, the FDA issued a guidance document in 2016 to establish a "standardized

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127 *Drug Trials Snapshots*, U.S. FOOD & DRUG ADMIN. (Apr. 9, 2021) [hereinafter *Snapshots*], https://www.fda.gov/drugs/drug-approvals-and-databases/drug-trials-snapshots.

128 *See, e.g.*, *Drug Trials Snapshots: ACCRUFER*, U.S. FOOD & DRUG ADMIN. (Aug. 15, 2019), https://www.fda.gov/drugs/drug-approvals-and-databases/drug-trials-snapshots-accrufer.

129 *See* U.S. FOOD & DRUG ADMIN., 2020 DRUG TRIALS SNAPSHOTS SUMMARY REPORT 2 (2021).

130 *Id.* at 3.

131 *Id.*

132 *Id.* at 2.

133 *Snapshots*, *supra* note 127.

134 *See supra* Part III.

135 Viraj Suvarna, *Phase IV of Drug Development*, 1 PERSPS. CLINICAL RSCH. 57, 57 (2010).

136 *Id.*

approach for collecting and reporting race and ethnicity data in submissions for clinical trials," because the use of standardized methods and terminology ensures that data is collected uniformly and consistently.[137] Per FDA regulations, trial sponsors are expected to "enroll participants who reflect the characteristics of clinically relevant populations with regard to age, sex, race, and ethnicity."[138] The guidance document provides that,

> A plan to address inclusion of clinically relevant subpopulations should be submitted . . . to the Agency at the earliest phase of development and, for drugs and biologics, no later than the end of the phase 2 meeting. Inadequate participation and/or data analyses from clinically relevant subpopulations can lead to insufficient information pertaining to medical product safety and effectiveness for product labeling.[139]

The most recent guidance document, titled "Enhancing the Diversity of Clinical Trial Populations—Eligibility Criteria, Enrollment Practices, and Trial Designs: Guidance for Industry," was introduced for public comment in June 2019 and finalized in November 2020.[140] This guidance document was issued to comply with Section 610 of the FDA Reauthorization Act of 2017 (FDARA), which required the FDA to "convene a public meeting to discuss clinical trial inclusion and exclusion criteria to inform the guidance" and issue a report on the matter.[141] This guidance document focuses primarily on how sponsors can increase underrepresented populations' enrollment in clinical trials using inclusive trial practices.[142] It also discusses "improving trial recruitment so that the participants enrolled in trials will better reflect the population most likely to use the drug."[143]

Obstacles to enrolling in clinical trials include the burden of frequent visits to specific sites, financial costs from traveling or missing work, and distrust of clinical research among certain populations.[144] The FDA suggests sponsors can improve the diversity of study

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137 2016 GUIDANCE DOCUMENT, *supra* note 115 at 1.

138 2020 GUIDANCE DOCUMENT, *supra* note 116, at 5; *see* 21 C.F.R. §§ 314.50(d)(v), (vi)(a) (Safety and efficacy data in NDAs "must be presented by . . . racial subgroups and must identify any modifications of dose or dose interval needed for specific subgroups.").

139 2016 GUIDANCE DOCUMENT, *supra* note 137, at 3.

140 2020 GUIDANCE DOCUMENT, *supra* note 116.

141 FDA Reauthorization Act of 2017, Pub. L. No. 115–52, § 610, 131 Stat. 1005, 1051 (2017).

142 *See generally* 2020 GUIDANCE DOCUMENT, *supra* note 116, at 4–7.

143 *Id.* at 3.

144 *See supra* Section II.A.

participants by considering these logistical barriers when designing the clinical trial and provides a number of potential approaches.[145] For example, the section titled "Make Trial Participation Less Burdensome for Participants" suggests that trial sponsors should take note of recruitment challenges that the study's planned visit schedule may cause and consider reducing the number of visits, increasing flexibility in visit windows when possible, using technology to replace in-person visits, or providing financial reimbursements for travel or lodging expenses.[146] Another section titled "Adopt Enrollment and Retention Practices That Enhance Inclusiveness" urges trial sponsors to work with communities to better understand why participants may be reluctant to enroll in a clinical trial to better address participants' needs and to involve the participants, their families, and patient advocates in the trial design process; to select trial sites located in areas with higher concentrations of minority populations; to consider diversity when selecting health care providers; and to make further efforts to increase diversity through public outreach and education within the industry, in partnership with patient advocacy groups and medical associations.[147]

It is worth noting that while guidance documents represent the "current thinking" on a topic, the guidance is "not binding on the FDA or the public" and creates no legally enforceable responsibilities.[148] Despite these various FDA initiatives, diversity in clinical trials is not significantly improving.[149]

B. *Non-Profit Organizations, Industry, and Other Private Actors*

Despite the lack of binding diversity requirements from the FDA, private actors often implement their own plans to increase diversity in their clinical trials, though the success of these initiatives is sometimes unclear.

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145 2020 GUIDANCE DOCUMENT, *supra* note 116, at 9.

146 *Id.* at 9–10.

147 *Id.* at 10.

148 2016 GUIDANCE DOCUMENT, *supra* note 137, at 2 ("FDA's guidance documents . . . do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.").

149 Barba, *supra* note 11; Luther T. Clark et al., *Increasing Diversity in Clinical Trials: Overcoming Critical Barriers*, 44 CURRENT PROBLEMS IN CARDIOLOGY 148, 150 (2019) ("[D]espite major efforts, including those from the US FDA and the Revitalization Act of 1993, which required that clinical trials funded by the National Institutes of Health include women and minority participants, diversity in clinical trials has not substantially improved.").

For example, the Center for Information and Study on Clinical Research Participation (CISCRP) is "dedicated to educating and informing the public, patients, medical/research communities, the media, and policy makers about clinical research and the role each party plays in the process."[150] CISCRP offers a number of services and programs to help consumers find trials that are relevant to their specific needs and learn more about clinical trials by providing "plain language translation" of research documents.[151] CISCRP also focuses on community engagement by increasing awareness about clinical trials through media campaigns and hosting educational events in diverse communities to further enable individuals to make informed decisions about participation in clinical trials.[152] Perhaps most importantly, CISCRP collects information about patient perceptions and experiences with clinical research.[153] Listening to patients and understanding their concerns allows for the development of new initiatives which are more likely to achieve the goal of increased diversity efficiently and effectively.

Pharmaceutical companies, as sponsors of clinical trials, are also taking steps to increase minority participation. Biogen, for example, is undertaking various initiatives to increase diversity in their clinical trials by providing "diversity and cultural sensitivity training" for its clinical trial sites; focusing on opening its trials at sites that serve a diverse patient population and underserved communities; forming a Community Advisory Board to help develop educational materials about clinical trials and develop new initiatives for working with underserved communities; including participant race and ethnicity goals in the trial design which reflect the patient population affected by a specific disease; and collaborating on a study with the Tufts Center for the Study of Drug Development (Tufts CSDD) to learn more from patients, healthcare experts, and community members about the obstacles patients face in clinical trial participation.[154] These initiatives reflect Biogen's commitment to "putting the weight of our business, our employees, and our collaboration partners to help close the disparity gap in clinical trials and access to healthcare."[155]

150 *About Us*, CISCRP, https://www.ciscrp.org/about-us/ (last visited Sept. 12, 2021).

151 *Services and Programs*, CISCRP, https://www.ciscrp.org/services/ (last visited Sept. 12, 2021).

152 *Id.*

153 *Id.*

154 *Increasing Diversity in Clinical Trials: A Collaboration with Tufts Center for the Study of Drug Development*, BIOGEN, https://www.biogen.com/en_us/stories/tufts-clinical-trial.html (last visited Sept. 12, 2021).

155 *Id.*

Pfizer also acknowledges that diversity in clinical trial participants is "critical to public health and well-being through increased representation of the populations who experience a condition."[156] To increase minority patient recruitment, Pfizer is employing community outreach programs in churches, schools, town halls, and other community centers to raise awareness and increase education about clinical trials.[157] Realizing the importance of investigator training, Pfizer also developed a recruitment tracking system to "help establish diversity as a key scientific variable across [its] research portfolio."[158]

While these initiatives represent a good start, to most effectively increase diversity in clinical trials, the medical community must be rebuilt to invite trust and confidence from minority populations.[159] Members of the medical and healthcare professions must remember the medical field's legacy of exploitation and experimentation and its lasting effects when caring for patients from minority communities. Patients often have racial preferences in healthcare, and providers should strongly consider these preferences to optimize care quality.[160] Studies have shown that the effects of implicit bias may be countered when providers accommodate patients' physicians' racial preferences.[161]

V. PROPOSAL FOR A NEW REGULATION

Since the guidance documents are nonbinding,[162] drug developers have no legal obligation to comply with the FDA's suggested courses of action. Demographic data shows that despite various FDA guidances, diversity in trials still fails to adequately represent the demographics of those impacted by specific diseases.[163] Utilizing its power to regulate

156 Tina Pavane, *Diversity in Clinical Trials: Why It's Important*, PFIZER, https://www.pfizer.com/news/featured_stories/featured_stories_detail/diversity_in_clinical_trials_why_it_s_important (last visited Sept. 21, 2021).

157 *Id.*

158 *Id.*

159 Frederick et al., *supra* note 9.

160 Kimani Paul-Emile, *Patients' Racial Preferences and the Medical Culture of Accommodation*, 60 UCLA L. REV. 462, 486–87 (2012) ("A patient must be willing to speak candidly about personal and potentially uncomfortable or embarrassing information; to submit to bodily examination, including attention to all manner of injury and abuse; to confide in and communicate openly with the physician; to rely on the physician's recommendations; and to feel confident in the belief that the physician is acting to advance the patient's best interest. In fact, the absence of these elements may mean the difference between life and death for some patients. To this end, the AMA has consistently and unequivocally maintained that a patient's ability to choose a personal physician is a 'prerequisite of optimal care and ethical practice.'" (Citations omitted.)).

161 *Id.* at 490.

162 2020 GUIDANCE DOCUMENT, *supra* note 116.

163 *See supra* Part II.

clinical trials from the Federal Food, Drug, and Cosmetic Act, the FDA should issue a rule mandating increased diversity in clinical trial participants when feasible and clinically appropriate as a condition of obtaining marketing authorization.

Many have criticized the FDA's attempts to address diversity in clinical trials and have urged for more compelling action. In a white paper report about increasing minority participation in clinical trials, the Endocrine Society asserted that the FDA should require rather than recommend adherence to its guidelines.[164] During the public comment period following the issuance of the Draft Guidance for the 2020 Guidance Document,[165] many of the comments from drug developers, clinical trial organizations, and patients criticized the document for its lack of "definition and depth," insisting that the FDA needs to provide more clarity about how to determine a clinically appropriate participant sample.[166] One organization specifically "lamented the fact that 'there is no direct mention of race and ethnicity' in the draft guidance, leaving it to the industry to guess what the FDA means by underrepresented and minority groups."[167] The organization further said that "[t]he guidance should provide direction specific to involving African Americans, Latin[x] and Asians."[168]

In 2017, the National Black Church Initiative (NBCI) called upon the FDA to require diverse participation before approving new drugs or medical devices.[169] Writing to the FDA Commissioner, the NBCI asserted that "the pharmaceutical community is not going to improve minority participation in clinical trials until the FDA compels them to do so via regulations."[170] In a 2008 report, the Eliminating Disparities in Clinical Trials (EDICT) Project, a collaboration of representatives from public, private, and non-profit sectors argued that the FDA should "strengthen its policy to require appropriate inclusion of underrepresented populations in all clinical trials; [i]mplement penalties for non-compliance with inclusion policies in clinical trials; [and] [i]mplement incentives for appropriate inclusion of all underrepresented

164 ENDOCRINE SOCIETY, *supra* note 28, at 27.

165 *See supra* Section IV.A.ii.

166 Colin Stoecker, *Industry Seeks More Detail from FDA Guidance on Trial Diversity*, CENTERWATCH (Aug. 19, 2019), https://www.centerwatch.com/articles/12265-industry-seeks-more-detail-from-fda-guidance-on-trial-diversity.

167 *Id.*

168 *Id.*

169 Caroline Chen & Riley Wong, *Black Patients Miss Out on Promising Cancer Drugs*, PROPUBLICA (Sept. 19, 2018, 5:00 AM), https://www.propublica.org/article/black-patients-miss-out-on-promising-cancer-drugs.

170 *Id.*

populations in clinical trials."[171] An FDA spokeswoman maintained that the FDA "'does not have the regulatory authority to require specific levels of minority representation in clinical trials'"—which, while true—does not prevent the FDA from demanding more generalized requirements.[172]

For these reasons, the FDA should promulgate an administrative rule that will place a legally enforceable duty on drug developers to increase diversity in clinical trials when feasible and clinically appropriate. The procedural requirement would be an expansion of the NIH policy requiring the inclusion of minority groups not just in studies funded by the NIH, but to all clinical trials under FDA purview.[173] The procedure would be as follows: when an IND is submitted to the FDA for a drug to advance from Phase II to Phase III of development, data must be submitted to the FDA detailing any significant demographic-based differences in safety or efficacy. In addition to demographic-based safety and efficacy information, the IND must identify the demographics of the trial participants compared to the demographics of those generally affected by the disease. If there is a significant lack of diversity compared to the demographics of those generally affected by the disease, then the drug developer must provide reasons why and explain what steps were taken (community outreach, site diversification, etc.) to enroll diverse trial participants. Alternatively, the drug developers can show that although they consulted with members of minority communities about participating in the trial, these individuals made the choice not to participate.[174] The FDA can use its power to place a clinical hold and suspend an ongoing trial[175] if it believes that the sponsor failed to make sufficient attempts to enroll diverse trial participants.

Proportionate diversity levels need not be reached if enrolling diverse participants proves too difficult despite best efforts, or if participants opt not to enroll in trials despite recruitment efforts. Sponsors, however, will bear the burden of proving that they made a "good faith effort" to recruit diverse trial participants. To do so,

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171 ARMIN D. WEINBERG, THE EDICT PROJECT: POLICY RECOMMENDATIONS TO ELIMINATE DISPARITIES IN CLINICAL TRIALS 11 (2008), https://www.researchgate.net/publication/320036453_The_EDICT_Project_Policy_Recommendations_to_Eliminate_Disparities_in_Clinical_Trials.

172 Chen & Wong, *supra* note 169.

173 *See supra* Section IV.A.i.

174 Participating in a clinical trial is a patient's choice, and drug developers should not feel incentivized to use coercive tactics to enroll diverse participants. *Informed Consent for Clinical Trials*, U.S. FOOD & DRUG ADMIN. (Jan. 4, 2018), https://www.fda.gov/patients/clinical-trials-what-patients-need-know/informed-consent-clinical-trials.

175 *See supra* Part III.

sponsors should generally be required to open their trials at facilities that largely serve minority communities. Sponsors should also have a certain budget dedicated to community outreach. Evidence showing a "good faith effort" may also be supported by an increased number of principal investigators from minority communities or proof that minority patients were counseled or signed consent to participate in a clinical trial, but subsequently were found ineligible or for another reason decided not to participate in the trial. Once that burden is met, the FDA may continue with its current review procedures.

Of course, there needs to be a balance between increasing diversity and maintaining an expeditious drug approval process. With COVID-19, for example, the government has a significant interest in fast tracking the vaccine development process. Called "Operation Warp Speed," the goal was to manufacture and deliver 300 million doses of a safe and effective vaccine by January 2021.[176] Though adding a diversity requirement may initially slow a study's progress due to minorities' distrust of the medical community,[177] there will be no "shortages" of potentially eligible patients that would dramatically slow drug development. After all, instances of COVID-19 and other diseases are much higher in minority communities. Even so, as a safeguard, lack of diversity would not necessarily impede approval: the FDA could discharge the requirement at its discretion in light of other competing interests.

This regulation would be an important first step towards removing health disparities and generally improving health outcomes for minority communities. We cannot undermine the importance of knowing that the government is looking out for minority communities' best interests and no longer standing passively by. By failing to introduce any binding regulations, government agencies have sent a clear message that the battle for equality is not one they will help fight. This deepens the disparities and feelings of isolation among minority communities.

VI. CONCLUSION

Pre-existing health disparities have worsened during the COVID-19 pandemic, which continues to disproportionately affect minority communities, including Black Americans, Latinx, and Natives Americans. Despite this fact, COVID-19 treatment and vaccine trials did

176 *Explaining Operation Warp Speed*, U.S. DEP'T OF HEALTH & HUM. SERVS., https://www.nihb.org/covid-19/wp-content/uploads/2020/08/Fact-sheet-operation-warp-speed.pdf (last visited Sept. 12, 2021).

177 *See supra* Section II.C.ii.

not reflect the diversity of infected individuals. This is consistent with the fact that clinical trials generally lack diversity compared to the population as a whole, with minorities being consistently underrepresented. As a result, safety and efficacy data frequently do not reflect racial and ethnic differences and may not provide useful information for many people using a drug or intervention. COVID-19 treatment and vaccine trials that do not include minority participants may not be safe or effective in these populations. Understandably, minority patients may not feel safe pursuing treatment or receiving a vaccination that has not been proven safe or effective in their demographic class.

To reduce these health disparities, diversity of clinical trial participants must increase. While government agencies, including the NIH and the FDA, have taken some steps towards increasing inclusion in clinical trials, the FDA is in the best position to enforce change because the FDA ultimately controls which drugs and vaccines are approved for commercial use. So far, the FDA has primarily issued non-binding guidance documents that encourage drug developers to increase diversity in their trials. These documents suggest steps that drug developers can take to increase diversity during the participant recruitment process, as well as how to re-design trials to be more inclusive. Since this guidance is non-binding, and the FDA continues to approve drugs that were not tested in a diverse participant population, drug developers have no real incentive to follow the FDA's guidance.

The FDA should promulgate an administrative rule requiring drug developers to increase diversity in their clinical trials before they approve drugs for general use. This rule would place a procedural requirement on the drug approval process and put the burden on drug developers to prove that they have made a "good faith effort" to recruit diverse trial participants. This rule would be similar to the NIH policy that requires minority populations to be included in NIH-funded clinical research unless no significant distinguishable racial or ethnic safety or efficacy concerns exist. Increasing inclusion of minority populations is an important step towards reducing health disparities and rebuilding trust between minority populations and the medical community—goals with critical importance which cannot be ignored during the COVID-19 pandemic and moving forward.