

FDA Regulation Must Uphold Women's Health

GENEVIEVE GRABMAN & CARA TENENBAUM*

ABSTRACT

Progress in U.S. medical product regulation is not due to a greater understanding of women, their biology, their needs, or their capabilities. Instead, public health tragedy is the historical catalyst for major U.S. legislative and policy changes, and these tragedies unnecessarily harmed women. Congress and the Food and Drug Administration (FDA) have made multiple, often belated, attempts to make medical products safe and effective for women, but more work remains.

FDA created the Office of Women's Health (OWH) in 1994, but despite OWH's efforts over the intervening thirty years since its creation, repeated regulatory failures of drugs and devices continue to imperil women's health. Women remain underrepresented in clinical trials. In addition, labeling of medicines women use is confusing and incomplete. Tests, especially laboratory developed tests (LDTs) for gynecologic cancers and other conditions, have escaped regulation to women's detriment. Device regulation remains very problematic, with multiple loopholes for contraceptive devices, morcellators, and breast implants and no clear regulatory path for new, digital devices.

To respond to women's needs, FDA must build and leverage OWH's expertise to evaluate appropriately the data from pre- and post-market reviews of drugs and devices. These data will inform meaningful and correct sex-specific recommendations and labeling, which will permit consumers of all sex and gender expressions to make informed decisions about their own health. OWH also must step forward to lead on women's health, anticipating future challenges and using its existing authorities to convene actors across the government to develop strategic responses.

I. INTRODUCTION

Food, device, and drug law has evolved over the United States' history, but this evolution is not due to a greater understanding of women, their biology, their needs, or their capabilities. Instead, public health tragedy is the historical catalyst for major U.S. legislative and policy changes, and these tragedies unnecessarily harmed women.

* Genevieve Grabman is the author of *Challenging Pregnancy: A Journey through the Politics and Science of Healthcare in America* (Univ. Iowa Press, 2022). She has a JD from Georgetown and an MPH from Johns Hopkins. She is an attorney at the Pan American Health Organization on secondment to the UN High Commissioner for Refugees. The views in this Article do not represent those of the author's employers or their member states. Cara Tenenbaum is a principal at Strathmore Health Strategy, advising patient advocacy organizations, consumer groups, and industry on health policy issues. Prior to founding Strathmore Health Strategy, Cara spent six years at FDA working on laboratory developed tests, digital health, and personalized medicine, among other issues. She spent seven years at a patient advocacy organization representing the needs of people with ovarian cancer and their families. Cara has a JD and MBA from Case Western Reserve University and a BA in Economics from the University of Maryland, College Park.

Many FDA and congressionally led programs have helped address public health research disparities between women and men, but women remain “other” when it comes to FDA regulations. To respond to women’s needs, FDA must improve the process by which it drafts, reviews evidence for, authorizes, and enforces regulations of drugs and medical devices.

The public health needs of women are different from those of men. Those whose biological sex is female have different hormones, different fat to muscle ratios, and differing average body size than people who are biologically male.¹ Women appear to metabolize drugs differently, and, therefore, suffer from adverse events due to that metabolism.² However, there is a paucity of data on these issues; and where there are data, they are not always correct.³ Distinctions based on sex as a biological variable demand a different response to public health for men and for women. In addition, people who are biologically female may become pregnant and lactate, requiring drugs and devices during that time frame. Gender bias pervades medical care,⁴ having a measurable effect on health.⁵ For example, more women experience chronic pain than men,⁶ but male mice and rats are far more often studied in neuroscience and pharmacology studies.⁷

Despite the biological differences between women and men, drug and device regulation did not require sex disaggregation of study data or subjects or targeted information for women and men until relatively recently. When FDA was given authority to regulate medical devices in 1976, for example, gender was not mentioned in the congressional committee report describing the proposed law—only “patients.”⁸ In the 1990s, FDA published a guidance regarding inclusion of women in drug development, analysis of data by gender and information about the conduct of clinical

¹ See, e.g., the section on “volume distribution” in David R. Rubinow & Molly Moore, *Sex-Dependent Modulation of Treatment Response*, 6 DIALOGUES CLINICAL NEUROSCIENCE 39 (2004).

² See Irving Zucker & Brian J. Pendergast, *Sex Differences in Pharmacokinetics Predict Adverse Drug Reactions in Women*, 11 BIOL. SEX DIFFERENCES 32 (2020).

³ For example, a commonly prescribed sleep drug, Ambien®, was shown to be metabolized more slowly by women. In 2013, FDA, based on these data, recommended that women take a lower dose of the drug than men. Later data shows that the lower dosing is not supported by the available data and, rather, could be leading to underrating insomnia. See David J. Greenblatt, Jerold S. Harmatz & Thomas Roth, *Zolpidem and Gender: Are Women Really at Risk?*, 39 J. CLINICAL PSYCHOPHARMACOLOGY 189 (2019).

⁴ *Id.*

⁵ See Geordan Shannon, Melanie Jansen, Kate Williams, Carlos Cáceres, Angelica Motta, Aloyce Odhiambo, Alie Eleveld & Jenevieve Mannell, *Gender Equality in Science, Medicine and Global Health: Where Are We at and Why Does It Matter?*, 393 LANCET 560 (2019), [https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(18\)33135-0/fulltext?rss%3Dyes](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(18)33135-0/fulltext?rss%3Dyes).

⁶ See Kathryn E. Mansfield, Julius Sim, Joanne L. Jordan & Kelvin P. Jordan, *A Systematic Review and Meta-Analysis of the Prevalence of Chronic Widespread Pain in the General Population*, 157 PAIN 55 (2016), <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4711387/>.

⁷ See Annaliese K. Beery & Irving Zucker, *Sex Bias in Neuroscience and Biomedical Research*, 35 NEUROSCIENCE & BIOBEHAVIORAL REVS. 565 (2011), <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3008499/>.

⁸ See, e.g., U.S. DEP’T OF HEALTH, EDUCATION & WELFARE, STUDY GROUPS ON MEDICAL DEVICES, MEDICAL DEVICES: A LEGISLATIVE PLAN § 502 (1970).

trials on women,⁹ and one that recommended analysis of data by sex, among other demographic factors, in a drug application.¹⁰

With no requirement to study the effects of drugs and devices on pregnant women, “shockingly”¹¹ few medicines provide female consumers information about the effects on women, their pregnancies, or developing fetuses.¹² Even as subsequent regulations have expanded requirements to protect women’s health, there continues to be a paucity of research and information about the effects of common drugs and devices, including tests, on women. Particularly sparse is information about medicine and medical devices’ effects on the health and safety of pregnant women and of their fetuses.¹³

To maintain their own health, women deserve improved information about the effects of drugs and devices specifically in women. FDA has lauded its progress in complying with requirements to gather and share more sex-specific information.¹⁴ We agree that much has been done, but there is more to do.

For almost three decades, FDA’s OWH has been charged with advising “the commissioner and other FDA officials on scientific, ethical, and policy issues relating to women’s health.”¹⁵ This office has, historically, provided millions of dollars in research funding and communicated publicly on women’s issues. But reviews of specific medical products are conducted by FDA’s Center for Drug Evaluation and Research (CDER), Center for Devices and Radiological Health (CDRH), and Center for Biologics Evaluation and Research (CBER). OWH has no consulting role with the Centers in evaluating data or making approval decisions. Despite the existence of this office, there remains a dearth of information about how most medical products affect women, at least until there is clear harm.

In this Article, we lay out some of the sex-based historical events that affected FDA’s evolving regulation of drugs and devices to address the health of men and of women. We recommend that FDA develop and leverage its own Office of Women’s Health to ensure that sex-based differences in medical products are studied, evaluated, and disclosed so the whole of the public’s health will be protected. We also suggest priorities for OWH to help the office achieve its mandate.

⁹ See U.S. FOOD & DRUG ADMIN., GUIDELINE FOR THE STUDY AND EVALUATION OF GENDER DIFFERENCES IN THE CLINICAL EVALUATION OF DRUGS (1993), <https://www.fda.gov/media/71107/download>.

¹⁰ See U.S. FOOD & DRUG ADMIN., GUIDELINE FOR THE FORMAT AND CONTENT OF THE CLINICAL AND STATISTICAL SECTIONS OF AN APPLICATION (1988), <https://www.fda.gov/media/75629/download>.

¹¹ *When Pregnant Women Need Medicine, They Encounter a Void*, NPR MORNING EDITION (Aug. 8 2016), <http://www.npr.org/sections/health-shots/2016/08/08/486907088/when-pregnant-women-need-medicine-they-encounter-a-void>.

¹² See *Medications During Pregnancy*, PREGMED, <https://www.pregmed.org/medications-during-pregnancy.htm> (last visited Oct. 1, 2022).

¹³ See *When Pregnant Women Need Medicine*, *supra* note 11.

¹⁴ See Ameeta Parekh, Emmanuel O. Fadiran, Kathleen Uhl & Douglas C. Throckmorton, *Adverse Effects in Women: Implications for Drug Development and Regulatory Policies*, 4 EXPERT REV. CLINICAL PHARMACOLOGY 453 (2011), <https://pubmed.ncbi.nlm.nih.gov/22114855/>.

¹⁵ U.S. FOOD & DRUG ADMIN., OFFICE OF WOMEN’S HEALTH, PROTECTING AND ADVANCING WOMEN’S HEALTH, <https://www.fda.gov/files/science%20&%20research/published/10--Years-and-Beyond--FDA-Office-of-Women's-Health.pdf> (last visited Oct. 1, 2022).

II. HISTORICAL FAILURE TO REGULATE HARMED HEALTH

FDA is more than 100 years old, founded in 1906. At FDA's inception, food adulteration and contamination were widespread problems. Meatpacking was so famously unsanitary that its description in literature caused mass revulsion.¹⁶ Even children's candy¹⁷ was dyed with ingredients such as lead, arsenic, or mercury.¹⁸

Medications were no safer or better. In 1937,¹⁹ a drug to treat strep throat was made into a liquid form by dissolving the approved, active ingredient in diethylene glycol, a toxic substance.²⁰ Approximately 100 people died from taking the newly formulated antibiotic in a short time,²¹ one-third of them children.²² The Pure Food and Drugs Act of 1906²³ contained no provision against dangerous drugs.²⁴

This tragedy led to the enactment of the 1938 Food, Drug, and Cosmetic Act, which was meant to prohibit adulterated and misbranded food, drugs, devices, and cosmetics.²⁵ The bill required disclosure of the ingredients of a new drug or device and that the sponsor provide "adequate testing" to show that the drug or device is safe.²⁶

FDA vigilance kept the dangerous drug thalidomide from being approved to treat nausea during pregnancy. But the agency's rejection of thalidomide was a near miss, with only the persistent advocacy of FDA medical officer Frances Kelsey preventing

¹⁶ See UPTON SINCLAIR, *THE JUNGLE* (1906).

¹⁷ These candies were often colored with copper or lead:

Candy – which would later warrant its own subsection in the Federal Food and Drugs Act of 1906 – was also a problem. A February 18, 1888 article entitled "Poison in Candy" warned that some candy flavorings contained prussic acid and fusel oil, both extremely dangerous, as well as less dangerous but still harmful elements like rancid butter, wood alcohol, and oil of vitriol. The author warned readers: "Beware of the very cheap candies. Goods can be so cheap that the suspicion is warranted that something is wrong about them." Similarly, a short 1886 piece explained how consumers could distinguish pure and adulterated chocolate.

Jenny Ann Diamond, *Who Shall Meet the Foe If Not She? Women's Participation in the Movement Leading Up to the Federal Food and Drug Act of 1906, As Seen Through the Pages of Good Housekeeping* (2002), <https://dash.harvard.edu/bitstream/handle/1/8889492/Diamond.html?sequence=2>.

¹⁸ See *Color Additives History*, U.S. FOOD & DRUG ADMIN., <https://www.fda.gov/forindustry/coloradditives/regulatoryprocesshistoricalperspectives/> (last visited Oct. 1, 2022); BEE WILSON, *SWINDLED: THE DARK HISTORY OF FOOD FRAUD, FROM POISONED CANDY TO COUNTERFEIT COFFEE* (2009), <http://press.princeton.edu/chapters/s8723.pdf>.

¹⁹ See *A Brief History of the Center for Drug Evaluation and Research*, U.S. FOOD & DRUG ADMIN., <https://www.fda.gov/about-fda/fda-history-exhibits/brief-history-center-drug-evaluation-and-research> (last visited Oct. 1, 2022).

²⁰ Carol Ballentine, *Sulfanilamide Disaster*, U.S. FOOD & DRUG ADMIN., <https://www.fda.gov/about-fda/histories-product-regulation/sulfanilamide-disaster> (last visited Oct. 1, 2022).

²¹ Jef Akst, *The Elixir Tragedy, 1937*, *THE SCIENTIST* (2013), <http://www.the-scientist.com/?article/view/articleNo/35714/title/The-Elixir-Tragedy--1937/> (last visited Oct. 1, 2022).

²² See Barbara Martin, *Elixir Sulfanilamide: Deaths of 1937*, *PATHOPHILIA*, <http://bmar.tinmd.com/elixir-sulfanilamide-deaths/> (last visited Oct. 1, 2022).

²³ See *The Pure Food and Drug Act of 1906*, Pub. L. No. 59-384, 34 Stat. 768 (1906).

²⁴ U.S. Sec'y of Agric., Report, *ELIXIR SULFANILAMIDE—MASSENGILL*, 48 CAL. & W. MED. 68 (1938), <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1705805/?page=1>.

²⁵ See *Federal Food, Drug, and Cosmetic Act*, Pub. L. No. 75-717, 52 Stat. 1040 (1938).

²⁶ *Id.* at § 505.

the drug's approval in the United States.²⁷ The close call led to the enactment of the Kefauver-Harris Amendments to the Food, Drug, and Cosmetic Act. These amendments, also called the Drug Amendments of 1962,²⁸ strengthened the rules for drug safety and required manufacturers also to prove their drugs' effectiveness.²⁹

A. Labeling

Drug-induced harm in the 1970s led FDA to require product labeling and advertising language addressed to consumers. The first patient-facing drug label was proposed in 1970, when FDA published a Federal Register notice regarding oral contraceptive labeling for "laymen."³⁰ In 1976, FDA made a major change in how the oral contraceptive pill was marketed. Through the issuance of a Federal Register notice,³¹ FDA proposed a statement of policy that required lay language regarding the risks and possible side effects of oral contraceptives.³² At the time, it was the only drug for which patient labeling was required.

Later, the Drug Regulation Reform Act of 1978 was introduced but was not enacted.³³ It would have, among other things, created requirements and guidelines for drug labeling.³⁴ FDA continued pushing for patient labeling for all medications, proposing a program that would "provide patients with additional information about their prescription drugs, including a description of the drug's uses, risks, and side effects."³⁵ The bill was never enacted.

Stymied on developing patient-centered labeling, FDA continued to move forward with *physician* labeling, with a final rule published in 1979. At that time, per the preamble of the final rule, FDA had "initiated a prescription drug labeling project to consider the appropriateness of patient labeling for other drugs."³⁶ In the absence of patient labeling, FDA reminded "that the distribution to patients of physician labeling

²⁷ See Robert McFadden, *Frances Oldham Kelsey, Who Saved U.S. Babies from Thalidomide, Dies at 101*, N.Y. TIMES (Aug. 7, 2015), <https://www.nytimes.com/2015/08/08/science/frances-oldham-kelsey-fda-doctor-who-exposed-danger-of-thalidomide-dies-at-101.html>.

²⁸ See Drug Amendments Act of 1962, Pub. L. No. 87-781, 76 Stat. 780 (1962).

²⁹ See U.S. FOOD & DRUG ADMIN., KEFAUVER-HARRIS AMENDMENTS REVOLUTIONIZED DRUG DEVELOPMENT (Oct. 2012), https://www.gvsu.edu/cms4/asset/F51281F0-00AF-E25A-5BF632E8D4A243C7/kefauver-harris_amendments.fda.thalidomide.pdf.

³⁰ Yes, a regulation about oral contraceptives used the term "laymen." See New Drugs; Proposed Statement of Policy Concerning Oral Contraceptive Labeling Directed to Laymen, 35 Fed. Reg. 5962 (Apr. 10, 1970), <http://cdn.loc.gov/service/ll/fedreg/fr035/fr035070/fr035070.pdf>.

³¹ See *Oral Contraceptive Drug Products, Notice and Proposal of Revised Physician and Patient Labeling*, 41 Fed. Reg. 53461 (Dec. 7, 1976), <https://tile.loc.gov/storage-services/service/ll/fedreg/fr041/fr041236/fr041236.pdf>.

³² The rule was withdrawn in 2003. See *Withdrawal of Certain Proposed Rules and Other Proposed Actions; Notice of Intent*, 68 Fed. Reg. 19766 (Apr. 22, 2003), <https://www.federalregister.gov/documents/2003/04/22/03-9865/withdrawal-of-certain-proposed-rules-and-other-proposed-actions-notice-of-intent>.

³³ See Drug Regulation Reform Act, H.R. 12980, 95th Cong. (1978).

³⁴ See Congressional Research Service, *H.R. 12980 (95th) Drug Regulation Reform Act* (June 5, 1978), <https://www.govtrack.us/congress/bills/95/hr12980/summary>.

³⁵ See WILSON, *supra* note 18.

³⁶ Labeling and Prescription Drug Advertising; Content and Format for Labeling for Human Prescription Drugs, Final Rule, 44 Fed. Reg. 124 (June 26, 1979).

for prescription drugs is not prohibited by either the act or FDA regulations, and the Commissioner encourages its distribution to patients who desire it.”³⁷

B. Devices

While U.S. law in the 1960s required drugs to be safe and effective, devices were required only to be safe. Nonetheless, unsafe devices came to market, including the now infamous Dalkon Shield—an intrauterine device (IUD). This intrauterine device to prevent pregnancy was dangerous, causing numerous miscarriages, and its multifilament string led to thousands of women getting serious uterine infections.³⁸ It also was less effective than claimed, resulting in conception,³⁹ septic abortions, and birth defects.⁴⁰ The Dalkon Shield escaped FDA's scrutiny because it was a device. The deaths and infections attributed to Dalkon Shield led to the 1976 Medical Device Amendments Act.⁴¹ The law⁴² created three classes of device, based on the level of data needed to “provide reasonable assurance of safety and effectiveness.”⁴³ These classes are still used today to determine the appropriate pathway for device approval and the data required.

C. Testing

Tests for women's health issues, too, have been problematic, leading to additional FDA, and other regulatory, authorities. In the 1960s, many women received false negative results of their Papanicolaou smear—a then-annual test for cervical cancer—now often referred to as a Pap test or Pap smear.⁴⁴ False negatives could spell a death sentence for women. Lulled into believing they were not at risk, women did not find or treat their cervical cancer until it was too late. Forty years ago, cervical cancer was one of the most fatal cancers, although, when detected early, it is one of the most preventable and treatable cancers.⁴⁵

³⁷ *Id.*

³⁸ See Robin Marantz Henig, *The Dalkon Shield Disaster*, WASH. POST: BOOK REV. (Nov. 17, 1985).

³⁹ See *id.*

⁴⁰ See Henig, *supra* note 38.

⁴¹ “Over the next few years, several high-profile public-health problems that involved medical devices were observed. Among the most publicized was the Dalkon Shield, an intrauterine contraceptive device (IUD) that was introduced into the market in late 1970. By 1975, at least 16 deaths, 25 miscarriages, numerous cases of pelvic perforation and pelvic infection, removal of the IUD for medical reasons, and pregnancies due to IUD failure had been reported. Marketing of the device ceased by 1976. . . . In 1974 and 1975, the Senate passed comprehensive legislation for the regulation of medical devices. The House of Representatives, however, did not move with its own bill until March 1976. A conference committee reconciled the differences between the two bills. The Medical Device Amendments of 1976 (MDA) passed both houses of Congress and were signed into law by President Ford on May 28.” NAT'L ACADS. SCI., ENG'G & MATH, *MEDICAL DEVICES AND THE PUBLIC'S HEALTH: THE FDA 510(K) CLEARANCE PROCESS AT 35 YEARS* 213–14 (2011), <http://www.nap.edu/read/13150/chapter/10#213>. See Tracy Schaaf, *In MedTech History: The Medical Regulation Act*, MEDTECH STRATEGIST COMTY. BLOG (Apr. 19, 2020), https://www.mystrategist.com/blog/article/in_medtech_history_the_medical_regulation_act.html (last visited Oct. 1, 2022).

⁴² See Medical Device Amendments of 1976, Pub. L. No. 94-295, 90 Stat. 541 (1976).

⁴³ See *id.*

⁴⁴ See Marguerite Vigliani, *Whatever Happened to the Annual Pap Smear?*, R.I. MED. J. (Jan. 2013), <http://www.rimed.org/rimedicaljournal/2013/01/2013-01-36.pdf>.

⁴⁵ “Cervical cancer used to be the leading cause of cancer death for women in the United States. However, in the past 40 years, the number of cases of cervical cancer and the number of deaths from cervical

In response to the obvious failure, Congress created the Clinical Laboratory Improvement Amendments (CLIA) of 1967 to regulate hospitals and independent laboratories and the tests these labs analyze.⁴⁶ Continued concerns regarding the accuracy of Pap tests, as well as other laboratory test results,⁴⁷ led to CLIA's further amendment in 1988, expanding regulation to all laboratories, including those in doctors' offices.⁴⁸ The laboratory certification process is regulated by the Department of Health and Human Services' Centers for Medicare and Medicaid Services (CMS), because the government could tie reimbursement to certification.⁴⁹ But regulation extends to tests performed on non-CMS beneficiaries, as well. FDA is involved in classifying lab tests to determine if they need to be performed in a CLIA-certified lab.⁵⁰

D. Unregulated Mammography Was a Harmful Test for Women

Mammography has been used as a screening tool for breast cancer for approximately 100 years, but it was not until the 1960s that its tools and methods started to be standardized.⁵¹ Women seeking breast cancer screening were faced with "a wide range of image quality and patient radiation dose level."⁵² In the 1970s, mammography exposed women to varying doses of radiation—"some facilities were using X-ray doses too low to obtain diagnostic images, whereas others were delivering excessive radiation." Due to the widespread fears of radiation exposure from mammograms, FDA began a voluntary program to reduce the amount of unnecessary radiation from the devices. By the end of the decade, pilot studies showed "a 46 percent reduction in the amount of exposure to the breast from the X-ray units tested."⁵³ Properly used, mammograms give only minimal doses of radiation and provide clearer pictures of tumors.⁵⁴

Correct interpretation of mammogram results too was problematic; however, interpretation is outside of FDA's purview. False negative results were widespread,

cancer have decreased significantly." *Cervical Cancer Statistics*, CTRS. FOR DISEASE CONTROL & PREVENTION, <https://www.cdc.gov/cancer/cervical/statistics/index.htm> (last visited Oct. 1, 2022).

⁴⁶ See N.M. DEP'T OF HEALTH, CLINICAL LABORATORY IMPROVEMENT ACT (CLIA), <https://www.nmhealth.org/publication/view/general/2222/> (last visited Oct. 1, 2022); See CTRS. FOR MEDICARE & MEDICAID SERVS., CMS INITIATIVES TO IMPROVE QUALITY OF LABORATORY TESTING UNDER THE CLIA PROGRAM (July 2006), <https://www.cms.gov/Regulations-and-Guidance/Legislation/CLIA/Downloads/060630BackgrounderrlEG.pdf>.

⁴⁷ See Walt Bogdanich, *False Negative, Medical Labs, Trusted as Largely Error-Free, Are Far from Infallible*, WALL ST. J. (Feb. 6, 1987).

⁴⁸ See *id.*

⁴⁹ See *Clinical Laboratory Improvement Amendments (CLIA)*, CTRS. FOR MEDICARE & MEDICAID SERVS., <https://www.cms.gov/Regulations-and-Guidance/Legislation/CLIA> (last visited Oct. 1, 2022).

⁵⁰ The Centers for Disease Control and Prevention maintain a database of CLIA-certified labs, using CMS data, at *CLIA Laboratory Search*, available at <https://www.cdc.gov/clia/LabSearch.html>.

⁵¹ See José Michel Kalaf, *Mammography: A History of Success and Scientific Enthusiasm*, 47 *RADIOLOGIA BRASILEIRA* VII (2014), <https://dx.doi.org/10.1590/0100-3984.2014.47.4e2>.

⁵² JUDITH JOHNSON, CONGR. RSCH. SERV., CRS REPORT FOR CONGRESS, 98-809 STM, MAMMOGRAPHY QUALITY STANDARDS ACT: BACKGROUND AND ISSUES (1998), https://www.everycrsreport.com/files/19981022_98-809_9499d14d57b53ce8c79198fa7b5e19e2028df4ca.pdf.

⁵³ Lawrence Altman, *Rising Medical Use of X-Rays Stirs Concern Over Long Range Hazard*, N.Y. TIMES (July 4, 1979).

⁵⁴ See Gina Kolata, *Mammograms: Safer and More Accurate*, N.Y. TIMES (Oct. 17, 1987).

damaging to women, and expensive.⁵⁵ Congress enacted, and FDA was assigned to implement, the Mammography Quality Standards Act (MQSA) in 1992 to ensure a standard level of mammography, including in staff training, radiation levels, and patient consent practices.⁵⁶ Facilities performing mammograms must be federally certified as achieving these standards, including in capturing and reviewing mammograms.⁵⁷ MQSA was shown, even relatively early after its implementation, to have a positive effect on the quality of mammograms.⁵⁸ Yet again, a law was enacted to regulate medical products only after scores of women were harmed.

III. CREATION OF OFFICE OF WOMEN'S HEALTH AND SUBSEQUENT PROBLEMS WITH WOMEN'S HEALTH PRODUCTS

Congress and FDA's piecemeal and reactive approach to resolving, one-by-one, failures of drugs and devices is an ineffective approach to protecting women's health. Slowly, over 100 years, FDA expanded its regulatory authority in response to problems from discrete drugs or devices. When it comes to ensuring the whole public's health, though, Congress still has not provided FDA with the necessary jurisdiction to regulate drugs or devices that affect women's health. Neither has FDA used to its fullest the jurisdiction it does have.

A. *Office of Women's Health*

After almost a century of scandal and suffering because of inadequate inclusion of women in all aspects of public health, including drug and device regulation, the U.S. government finally moved forward on women's health in the early 1990s. In 1991, Senator Barbara Mikulski and Congresswoman Patricia Schroeder proposed establishing an Office of Research on Women's Health at the National Institutes of Health (NIH).⁵⁹ This proposal died in committee, but it was resurrected in the 1993 NIH Revitalization Act, which funded and secured the Office of Research on Women's Health and gave it the authority to monitor women's inclusion in NIH clinical research.⁶⁰ In 1994, Representative Olympia Snowe introduced legislation to amend the Federal Food, Drug, and Cosmetic Act to establish an Office of Women's Health within the Office of the Commissioner of the Food and Drug Administration.⁶¹ At the same time, congressional hearings on the Clinton Administration's health

⁵⁵ See JOHNSON, *supra* note 52.

⁵⁶ See *Mammography Quality Standards Act (MQSA): Hearing of the Comm. on Health, Education, Labor, and Pensions, First Session on Examining the Mammography Standards Act of 1992, to Amend the Public Health Service Act to Establish the Authority for the Regulation of Mammography Services and Radiological Equipment*, 108th Cong. (Apr. 8, 2003), <https://catalog.hathitrust.org/Record/003889658>.

⁵⁷ See *Mammography Quality Standards Act of 1992*, Pub. L. No. 102-539, 106 Stat. 3547 (1992), <https://www.gpo.gov/fdsys/pkg/STATUTE-106/pdf/STATUTE-106-Pg3547.pdf>.

⁵⁸ See U.S. GEN. ACCT. OFF., GAO/HEHS-96-17, *MAMMOGRAPHY SERVICES: INITIAL IMPACT OF NEW FEDERAL LAW HAS BEEN POSITIVE* (Oct. 27, 1995), <https://www.gao.gov/assets/hehs-96-17.pdf>.

⁵⁹ See *Women's Health Equity Act of 1991*, S. 514 and H.R. 1161, 102nd Cong. (1991).

⁶⁰ See *National Institutes of Health Revitalization Act of 1993*, Pub. L. No. 103-43, 107 Stat. 122 (1993).

⁶¹ See *Women's Health Office Act of 1994*, H.R. 3874, 103rd Cong. (1994).

reform plan emphasized women's health,⁶² as did congressional appropriations to the Office of Women's Health at the Public Health Service and to the Centers for Disease Control and Prevention.⁶³ Also in 1994, Senator Edward Kennedy and Congressman Henry Waxman collaborated on legislation, which passed both chambers of Congress but never became law, that would have established an Office of Women's Health within the Office of the Assistant Secretary of Health.⁶⁴ Viewing Congress' directives to other Department of Health and Human Services entities as a "mandate" to the FDA,⁶⁵ the Commissioner of Food and Drugs established the FDA Office of Women's Health (OWH) on July 28, 1994.⁶⁶ The Office was codified in the "Obamacare" health reform law in 2010.⁶⁷

B. FDA Office of Women's Health Mandate

OWH facilitates FDA's coordination and communication of women's health issues and initiatives.⁶⁸ The office has five purposes:

- (1) To serve as "the principal advisor to the Commissioner and other key officials on scientific, ethical, and policy issues relating to women's health";
- (2) To provide "leadership and policy direction for the Agency regarding issues of women's health" and to coordinate "efforts to establish and advance a women's health agenda for the Agency";
- (3) To monitor "the inclusion of women in clinical trials . . . and the completion of gender analysis";
- (4) To identify and monitor "new challenges to the health of women as they relate to FDA's mission"; and
- (5) To serve as FDA's liaison with regard to the health of women.⁶⁹

OWH's initial actions showed great promise in fomenting change consistent with its mandate. For its first public meeting on November 7, 1994, OWH gathered consumers and representatives from academia, industry, and government to discuss the scientific, legal, and ethical issues associated with testing FDA-regulated products in pregnant women.⁷⁰ Likely reflecting on the lacuna in drug and device safety,

⁶² See 140-2 Cong. Rec. H.D. (daily ed. Jan. 26, 1994) (Committee on Energy and Commerce: Subcommittee on Health and the Environment hearings on the Clinton Administration's Health Care Reform Plan).

⁶³ See 140-84 Cong. Rec. H.H. (daily ed. Jun. 28, 1994) (report for the Departments of Labor, Health and Human Services, and Education, and Related Agencies Appropriations Act, 1995).

⁶⁴ See Disadvantaged Minority Health Improvement Act of 1994, S. 1569, 103rd Cong. (1993) and Minority Health Improvement Act of 1994, H.R. 3869, 103rd Congress (1994).

⁶⁵ *Office of Women's Health*, U.S. FOOD & DRUG ADMIN., (Dec. 2, 2019), <https://www.fda.gov/about-fda/office-commissioner/office-womens-health> (last visited Oct. 1, 2022).

⁶⁶ Dep't of Health & Hum. Svcs., Statement of Organization, Functions, and Delegations of Authority, 59 Fed. Reg. 38482 (July 28, 1994).

⁶⁷ See Patient Protection and Affordable Care Act, 21 U.S.C. 352 § 3509 (2010).

⁶⁸ *Id.*

⁶⁹ *Id.*

⁷⁰ Conference on FDA-Regulated Products and Pregnant Women; Notice of Public Meeting, 59 Fed. Reg. 51988 (Oct. 13, 1994).

efficacy, and toxicity data for pregnant women, the first OWH public meeting intended to devise “strategies to promote research and collection of information on the use of drugs, biologics, and devices in pregnant women and their effects on the fetus.”⁷¹

OWH also had some early success in monitoring “the inclusion of women in clinical trials . . . and the completion of gender analysis.”⁷² Women have 1.5 to 1.7 times as many adverse drug reactions as men, making their inclusion in trials of great importance to understanding how drugs might work in the real world.⁷³ In 1992, the U.S. Government Accountability Office (GAO) found that women were underrepresented in more than half of clinical drug trials used to support FDA approvals.⁷⁴ The GAO reported, “Even when enough women are included in drug testing, often trial data are not analyzed to determine if women’s responses to a drug differed from those of men.”⁷⁵

Per GAO recommendations, FDA issued guidance with explicit language to help sponsors determine when there is “adequate information about the effects of drugs in women.”⁷⁶ In 1998, FDA enacted further requirements that those applying for a drug’s approval must include “effectiveness data . . . presented by gender, age, and racial subgroups.”⁷⁷ OWH spearheaded the implementation of a requirement that FDA make public information who, men or women, participated in clinical trials for drugs and devices.⁷⁸

But over the intervening thirty years since OWH’s creation, and on OWH’s watch, repeated regulatory failures of drugs and devices continue to imperil women’s health. Despite OWH efforts, women remain underrepresented in clinical trials. A 2011 paper reported that women make up half of the population in late phase trials; however, women are less than one-third of early phase trials.⁷⁹ In addition, drug labeling remains confusing and incomplete for women. Tests, especially laboratory developed tests for gynecologic cancers and other conditions, have escaped regulation to women’s detriment. Device regulation remains very problematic, with multiple regulatory loopholes for contraceptive devices, morcellators, and breast implants and no regulatory plan for new, digital devices. We examine each of these challenges in turn.

⁷¹ *Id.*

⁷² Dep’t of Health & Hum. Svcs., Statement of Organization, Functions, and Delegations of Authority, 59 Fed. Reg. 38482 (July 28, 1994).

⁷³ *Id.*

⁷⁴ U.S. GEN. ACCT. OFF., GAO/HRD-93-17, REPORT TO CONGRESSIONAL REQUESTERS, WOMEN’S HEALTH: FDA NEEDS TO ENSURE MORE STUDY OF GENDER DIFFERENCES IN PRESCRIPTION DRUG TESTING (Oct. 1992), <https://www.gao.gov/assets/220/216966.pdf> (last visited Oct. 1, 2022).

⁷⁵ *Id.*

⁷⁶ *Study and Evaluation of Gender Differences in the Clinical Evaluation of Drugs, Guidance for Industry*, U.S. FOOD & DRUG ADMIN. (1993), <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/study-and-evaluation-gender-differences-clinical-evaluation-drugs> (last visited Oct. 1, 2022).

⁷⁷ Applications for FDA Approval to Market a New Drug, 21 C.F.R. § 314.50 (1998).

⁷⁸ This provision to the Food and Drug Administration Safety Improvement Act of 2012 (FDASIA) is commonly known as “Section 907.” See FDASIA § 907, Pub. L. No. 112-144, 126 Stat. 993 (2012), <https://www.congress.gov/112/plaws/publ144/PLAW-112publ144.pdf>.

⁷⁹ Somnath Pal, *Inclusion of Women in Clinical Trials of New Drugs and Devices*, U.S. PHARMACIST (Oct. 16, 2015), <https://www.uspharmacist.com/article/inclusion-of-women-in-clinical-trials-of-new-drug-s-and-devices> (last visited Oct. 1, 2022).

C. Labeling

To address the specific need for and lack of data on the effect of drugs on pregnant and lactating women, in the 1970s FDA adopted a pregnancy category system that expressed the risk of drugs to a fetus by grading them—A, B, C, and D—and “X” for contraindicated.⁸⁰ In 2014, FDA completely changed course. Through the Pregnancy and Lactation Labeling Final Rule, FDA announced it was removing the categories because providers and patients were over-reliant on them.⁸¹ Instead, FDA wanted providers and patients to discuss the underlying data and determine whether to use a particular medication.⁸² While that is, undeniably, a key part of the doctor–patient relationship,⁸³ one small study showed that the change decreased a provider’s willingness to prescribe a drug formerly categorized as “A” or “B”⁸⁴ and a later joint FDA survey found that the overwhelming majority of doctors preferred the latter category.⁸⁵

Serious gaps remain in data on drug safety for women. For anti-anxiety or depression medications, which more women than men use,⁸⁶ drug labels for tricyclic antidepressants (TCA) and selective serotonin reuptake inhibitors (SSRI) rarely mention sex.⁸⁷ Nor does SSRI drug labeling indicate whether dosage should be the

⁸⁰ The pregnancy category system, promulgated in a 1979 final rule, was repeated in FDA’s 2008 proposed rule proposing to amend the 1979 final rule. *See* Content and Format of Labeling for Human Prescription Drug and Biological Products; Requirements for Pregnancy and Lactation Labeling, 73 Fed. Reg. 30,831 (May 29, 2008).

⁸¹ “Through experience and stakeholder feedback, FDA learned that the pregnancy categories were confusing and did not accurately and consistently communicate differences in degrees of fetal risk. In addition, FDA learned that the pregnancy categories were heavily relied upon by clinicians but were often misinterpreted and misused in that prescribing decisions were being made based on the pregnancy category, rather than an understanding of the underlying information that informed the assignment of the pregnancy category. FDA believes that a narrative structure for pregnancy labeling, rather than a category system, is best able to capture and convey the potential risks of drug exposure based on animal or human data, or both. FDA has determined that retaining the pregnancy categories is inconsistent with the need to accurately and consistently communicate differences in degrees of fetal risk. Therefore, the final rule requires the removal of the pregnancy categories A, B, C, D, and X from all drug product labeling.” Content and Format of Labeling for Human Prescription Drug and Biological Products; Requirements for Pregnancy and Lactation Labeling, 79 Fed. Reg. 72,063, 72,065 (Dec. 4, 2014).

⁸² *Id.*

⁸³ *See* AM. MED. ASS’N, CODE OF MEDICAL ETHICS 1.1.3, <https://www.ama-assn.org/system/files/code-of-medical-ethics-chapter-1.pdf>.

⁸⁴ Molly Walker, *Removal of FDA Pregnancy Drug Categories: More Harm than Good?*, MEDPAGE TODAY (Apr. 28, 2018).

⁸⁵ Jennifer Namazy, Christina Chambers, Leyla Sahin, Tamara Johnson, Miriam Dinatale, Brian Lappin & Michael Schatz, *Clinicians’ Perspective of the New Pregnancy and Lactation Labeling Rule (PLLR): Results from an AAAAI/FDA Survey*, 8 J. ALLERGY & CLINICAL IMMUNOLOGY: IN PRACTICE 6 (2020).

⁸⁶ “During 2015–2018, 13.2% of adults aged 18 and over used antidepressant medications in the past 30 days. Use was higher among women (17.7%) than men (8.4%).” Debra J. Brody & Qiuping Gu, *Antidepressant Use Among Adults: United States, 2015–2018*, CTRS. FOR DISEASE CONTROL & PREVENTION (Sept. 2020), <https://www.cdc.gov/nchs/products/databriefs/db377.htm>.

⁸⁷ *See* FDA’s registry of labels for Elavil, https://www.accessdata.fda.gov/drugsatfda_docs/label/2008/071297Orig1s026lbl.pdf; Tofranil, https://www.accessdata.fda.gov/drugsatfda_docs/label/2014/017090s078lbl.pdf; Vivactril, https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/Vivactril.pdf; Effexor, https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/020699s107lbl.pdf; Celexa, https://www.accessdata.fda.gov/drugsatfda_docs/label/2012/020822s042.021046s019lbl.pdf; Zoloft, https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/019839S74S86S87_20990S35S44S45lbl.pdf; Lexapro,

same for men and for women.⁸⁸ The labels of some drugs in this class indicate that sex-disaggregated analyses have been done, but no label data indicates what results were found.⁸⁹ Even where drug data may exist, female patients and their providers cannot access this information to have meaningful discussion of the benefits and risks of using medications.

D. Testing

Today, FDA has approved, under device regulations, eight tests for the primary cause of cervical cancer, the human papillomavirus (HPV).⁹⁰ However, testing in general is in a liminal state, as FDA has traditionally exercised enforcement discretion over a large swath of tests.⁹¹ These laboratory developed tests are “designed, manufactured and used within a single laboratory.”⁹² A framework to regulate LDTs has been included in the Senate version of a large FDA-related bill.⁹³ FDA generally does not require premarket review for LDTs and can take enforcement measures when and if problems are discovered. Many LDTs that have been found to be problematic affect women. For example, certain tests that are marketed as ovarian cancer screening or diagnostics remain largely unregulated.⁹⁴ Non-invasive pre-natal tests (NIPT) are also of great concern as the results can lead to irreversible medical decisions.⁹⁵ Indeed, NIPT and tests for ovarian cancer were included in an FDA report on the evidence supporting regulation of LDTs.⁹⁶ Of the twenty problematic tests in the report, two are for ovarian cancer, one is a type of breast cancer test, one is a test that claims to predict the risk of developing breast cancer, one is an HPV test, and one is an NIPT. The lack of regulation of these tests has a serious effect on women as the results of these tests

https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/021323s047lbl.pdf; Prozac, which does recommend reducing the dose only if taken with Zyprexa, https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/018936s108lbl.pdf; and Paxil, https://www.accessdata.fda.gov/drugsatfda_docs/label/2009/020031s05920710s023lbl.pdf.

⁸⁸ Heather Whitely & Wesley Lindsey, *Sex-Based Differences in Drug Activity*, 80 AM. FAM. PHYSICIAN 1254 (2009).

⁸⁹ See Walker, *supra* note 84.

⁹⁰ See *Nucleic Acid Based Tests*, U.S. FOOD & DRUG ADMIN., <https://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/InVitroDiagnostics/ucm330711.htm> (last visited Oct. 1, 2022).

⁹¹ See U.S. FOOD & DRUG ADMIN., *IN VITRO DIAGNOSTIC MULTIVARIATE INDEX ASSAYS—DRAFT GUIDANCE FOR INDUSTRY, CLINICAL LABORATORIES, AND FDA STAFF* (July 26, 2007), <https://www.fda.gov/media/71492/download>.

⁹² *Laboratory Developed Tests*, U.S. FOOD & DRUG ADMIN., <https://www.fda.gov/medical-devices/in-vitro-diagnostics/laboratory-developed-tests> (last visited Oct. 1, 2022).

⁹³ Food and Drug Administration Safety and Landmark Advancements Act of 2022, S. 4348, 117th Cong. (2022).

⁹⁴ See *Ovarian Cancer Screening Tests: Safety Communication - FDA Recommends Against Use*, U.S. FOOD & DRUG ADMIN. (Sept. 7, 2016), <https://www.fdanews.com/ext/resources/files/2016/09/09-08-16-FDAsafetynotice.pdf?1473536862> (last visited Oct. 1, 2022).

⁹⁵ See Press Release, U.S. Food & Drug Admin., *FDA Warns of Risks Associated with Non-Invasive Prenatal Screening Tests* (Apr. 19, 2022), <https://www.fda.gov/news-events/press-announcements/fda-warns-risks-associated-non-invasive-prenatal-screening-tests> (last visited Oct. 1, 2022).

⁹⁶ See U.S. FOOD & DRUG ADMIN., *THE PUBLIC HEALTH EVIDENCE FOR FDA OVERSIGHT OF LABORATORY DEVELOPED TESTS: 20 CASE STUDIES* (Nov. 16, 2015), <http://wayback.archive-it.org/7993/20171115144712/https://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Reports/UCM472777.pdf>.

can have serious medical consequences, including the option to remove organs⁹⁷ or terminate pregnancies.⁹⁸ Without FDA's regulation of these tests, users cannot know the true extent of their safety or efficacy.

E. Additional Concerns Regarding Some Devices

Many loopholes remain in FDA's regulatory regime for devices, resulting in numerous examples of harm from devices that ostensibly would improve women's lives. The device surveillance system is passive,⁹⁹ which means anyone can report anything that happens, whether it is related to the device or not.¹⁰⁰ Some problems may be double- or triple-reported, while others may go unreported entirely.¹⁰¹ While FDA defines a reportable event as one that "reasonably suggests that a device has or may have caused or contributed to a death or serious injury,"¹⁰² this is often interpreted as a requirement to report events only when harm is due to a device malfunctioning or breaking.¹⁰³ The data FDA receives regarding device malfunctions is relatively time-bound, limiting documentation of a device's long term effects. Patient advocates spurred FDA's investigation of morcellators,¹⁰⁴ Essure,¹⁰⁵ and breast implants¹⁰⁶ when FDA's device surveillance system had not flagged concerns about them.¹⁰⁷

⁹⁷ See Nadine M. Tung, Judy C. Boughey, Lori J. Pierce, Mark E. Robson, Isabelle Bedrosian, Jill R. Dietz, Anthony Dragun, Judith Balmana Gelpi, Erin W. Hofstatter, Claudine J. Isaacs, Ismail Jatoi, Elaine Kennedy, Jennifer K. Litton, Nina A. Mayr, Rubina D. Qamar, Mark G. Trombetta, Brittany E. Harvey, Mark R. Somerfield & Dana Zakalik, *Management of Hereditary Breast Cancer: American Society of Clinical Oncology, American Society for Radiation Oncology, and Society of Surgical Oncology Guideline*, 38 J. CLINICAL ONCOLOGY (Apr. 3, 2020), <https://ascopubs.org/doi/10.1200/JCO.20.00299>.

⁹⁸ See Meredith Vanstone, Alexandra Cernat, Umair Majid, Forum Trivedi & Chanté De Freitas, *Perspectives of Pregnant People and Clinicians on Noninvasive Prenatal Testing: A Systematic Review and Qualitative Meta-Synthesis*, 19 ONT. HEALTH TECH. ASSESSMENT SERIES 1 (Feb. 19, 2019), <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6398533/>; see Hilary Bowman-Smart, Julian Savulescu, Christopher Gyngell, Cara Mand & Martin B. Delatycki, *Sex Selection and Non-Invasive Prenatal Testing: A review of Current Practices, Evidence, and Ethical Issues*, 40 PRENATAL DIAGNOSIS 398 (Mar. 2020), <https://obgyn.onlinelibrary.wiley.com/doi/full/10.1002/pd.5555>.

⁹⁹ "In addition, although MDRs are a valuable source of information, this passive surveillance system has limitations." *Medical Device Reporting (MDR): How to Report Medical Device Problems*, U.S. Food & Drug Admin. (Feb. 18, 2022), <https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems> (last visited Oct. 1, 2022).

¹⁰⁰ See Tara Haelle, *FDA to Take Another Look at Essure Contraceptive Device After Health Complaints*, NPR: SHOTS (July 14, 2015), <https://www.npr.org/sections/health-shots/2015/07/14/421745255/safety-worries-lead-fda-to-take-another-look-at-essure-contraceptive>.

¹⁰¹ See *id.*

¹⁰² See 21 C.F.R. § 803.3(o).

¹⁰³ See 21 C.F.R. § 803.3(o)(2)(ii).

¹⁰⁴ See *Laparoscopic Power Morcellators*, U.S. FOOD & DRUG ADMIN. (June 17, 2022), <https://www.fda.gov/medical-devices/surgery-devices/laparoscopic-power-morcellators> (last visited Oct. 1, 2022).

¹⁰⁵ See *FDA Activities Related to Essure*, U.S. FOOD & DRUG ADMIN. (Oct. 6, 2022), <https://www.fda.gov/medical-devices/essure-permanent-birth-control/fda-activities-related-essure> (last visited Oct. 1, 2022).

¹⁰⁶ See *Breast Implants*, U.S. FOOD & DRUG ADMIN. (Sept. 8, 2022), <https://www.fda.gov/medical-devices/implants-and-prosthetics/breast-implants> (last visited Oct. 1, 2022).

¹⁰⁷ A discussion of some drugs and devices that have harmed women's health can be found in Jennifer L. Carey, Nathalie Nader, Peter R. Chai, Stephanie Carreiro, Matthew K. Griswold & Katherine L. Boyle, *Drugs and Medical Devices: Adverse Events and the Impact on Women's Health*, 39 CLINICAL THERAPEUTICS 10 (2017).

Morcellators were a device used to assist in laparoscopic, minimally invasive surgery. They were found to spread cancer if used to remove cancerous growths in a woman's abdomen.¹⁰⁸ When two women died from cancers that metastasized after they had morcellator-assisted surgeries, their bereaved families demanded FDA action.¹⁰⁹ In 2016, an FDA investigation found that providers and facilities failed to report these adverse events.¹¹⁰ Providers countered that, because there was nothing wrong with the device itself, they would not have reported any cancer upstaging or fatalities as related to the morcellator.¹¹¹ FDA did not receive an adverse event report for the upstaging of uterine sarcoma until 2013, despite these devices being in use since 1991.¹¹² Based on the information it was gathering, FDA published an Immediately In Effect Guidance recommending Boxed Warnings on power morcellators in 2014.¹¹³ The warning that "uterine tissue may contain unsuspected cancer" and the contraindications for known malignancy and for post-menopausal women received significant attention and changed medical practice.¹¹⁴ Throughout its

¹⁰⁸ See Titilope Oduyebo, Alejandro J. Rauh-Hain, Emily E. Meserve, Michael A. Seidman, Emily Hinchcliff, Suzanne George, Bradley Quade, Marisa R. Nucci, Marcela G. Del Carmen & Michael G. Muto, *The Value of Re-Exploration in Patients with Inadvertently Morcellated Uterine Sarcoma*, 132 GYNECOLOGIC ONCOLOGY 360 (2014), <https://pubmed.ncbi.nlm.nih.gov/24296345/>. See also M. H. Einstein, R. R. Barakat, D.S. Chi, Y. Sonoda, K. M. Alektiar, M. L. Hensley & N. R. Abu-rustum, *Management of Uterine Malignancy Found Incidentally After Supracervical Hysterectomy or Uterine Morcellation for Presumed Benign Disease*, 18 INT'L J. GYNECOLOGICAL CANCER 1065 (2008), <https://pubmed.ncbi.nlm.nih.gov/17986239/>. See also Michael Seidman, Titilope Oduyebo, Michael G. Muto, Christopher P. Crum, Marisa R. Nucci & Bradley J. Quade, *Peritoneal Dissemination Complicating Morcellation of Uterine Mesenchymal Neoplasms*, 7 PLOS ONE e50058 (2012), <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3506532/>.

¹⁰⁹ See Matthew Bin Han Ong, *As FDA Weighs its Options on Morcellation, Debate Erupts Over Harvard Device Study*, CANCER LETTER (Nov. 21, 2014), https://cancerletter.com/articles/20141121_1/.

¹¹⁰ "The device functioned as expected and was used in the way it was intended, although with unintended and tragic consequences," the spokeswoman said in an e-mail." Matthew Bin Han Ong, *FDA Finds Lapses in Reporting of Patient Harm, Deaths Resulting from Medical Devices in Hospitals Nationwide*, CANCER LETTER (Dec. 16, 2016), https://cancerletter.com/articles/20161216_1/.

¹¹¹ "But doctors and hospital officials told investigators with the accountability office that before November 2014, when the F.D.A. explicitly stated that cancer spread after morcellation was an adverse event that had to be reported, they would not have regarded it that way or reported it. Previously, they had thought adverse events from surgical tools were related mainly to failures of the device itself. And in the cancer cases, the morcellators were doing exactly what they were supposed to do — slicing up tissue." Denise Grady, *Weak Reporting System Let Risky Surgical Device Stay in Use*, N.Y. TIMES (Feb. 8, 2017), <https://www.nytimes.com/2017/02/08/health/morcellator-gao-report-fda.html>.

¹¹² See U.S. GOV'T ACCOUNTABILITY OFF., GAO-17-231, CANCER RISK LED FDA TO WARN AGAINST CERTAIN USES OF POWER MORCELLATORS AND RECOMMEND NEW LABELING (Feb. 2017), <https://www.gao.gov/assets/gao-17-231.pdf> [hereinafter GAO, CANCER RISK REPORT].

¹¹³ See Immediately in Effect Guidance Document: Product Labeling for Laparoscopic Power Morcellators; Guidance for Industry and Food and Drug Administration Staff, 79 Fed. Reg. 70193 (Nov. 25, 2014).

¹¹⁴ See, e.g., Nina M. Clark, Michael Schembri & Venessa L. Jacoby, *Change in Surgical Practice for Women with Leiomyomas After the U.S. Food and Drug Administration Morcellator Safety Communication*, 130 OBSTETRICS & GYNECOLOGY 1057 (2017), <https://pubmed.ncbi.nlm.nih.gov/29016511/>. See also Lauren N. Wood, Juzar Jamnagerwalla, Melissa A. Markowitz, D. Joseph Thum, Philip McCarty, Andrew R. Medendorp, Shlomo Raz & Ja-Hong Kim, *Public Awareness of Uterine Power Morcellation Through US Food and Drug Administration Communications: Analysis of Google Trends Search Term Patterns*, JMIR PUB. HEALTH & SURVEILLANCE (2018), <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5945987/>. See also Jason D. Wright, Ling Chen & William M. Burke, *Trends in Use and*

handling of morcellators since 2013, FDA has reacted quickly and transparently. However, it remains that “the agency was aware of the potential for power morcellators to spread tissue”¹¹⁵ and, along with the rest of the scientific community, wholly underestimated that risk.

When Essure, a permanent birth control device, was approved by FDA in 2002, it was based on two studies, “including one with two years of follow-up (Phase II study) and one year of follow up in the other (Pivotal study).”¹¹⁶ Post-market data was required, which, after five years, showed a high level of effectiveness and patient satisfaction.

Over the following years, approximately 1,000 adverse events were reported to the FDA—115 adverse events in 2011; 152 in 2012; and more than 800 in 2013.¹¹⁷ These reports surely were undercounted as the manufacturer required “a doctor to confirm an Essure-related injury before it was considered reportable.”¹¹⁸ Under pressure from patients, FDA added a boxed warning and a patient checklist to the Essure materials and published doctors and patients materials about the risks of Essure. FDA also required the device’s manufacturer to do more post-market studies.¹¹⁹ In 2018, the manufacturer announced it would stop selling the device.

Breast implants were on the market long before FDA began regulating devices. In 1976, FDA considered these devices, breast implants, to be of moderate risk and required little safety data about them.¹²⁰ The 1980s saw lawsuits against breast implant manufacturers by women alleging that ruptured implants caused harm, such as autoimmune diseases.¹²¹ By 1992, FDA had restricted the availability of silicone breast implants, saying that “[t]hirty years after silicone breast implants appeared on the market, the list of unanswered questions about their safety remains long.”¹²² In the

Outcomes of Women Undergoing Hysterectomy with Electric Power Morcellators, 316 JAMA 877 (2016), <https://jamanetwork.com/journals/jama/fullarticle/2545671>.

¹¹⁵ See GAO, CANCER RISK REPORT, *supra* note 112, at 2.

¹¹⁶ U.S. FOOD & DRUG ADMIN., FDA REVIEW DOCUMENT, REVIEW OF THE ESSURE SYSTEM FOR HYSTEROSCOPIC STERILIZATION (Sept. 24, 2015) (prepared for the meeting of the Obstetrics and Gynecology Devices Advisory Panel), <https://www.fdanews.com/ext/resources/files/09-15/092815-FDA-materials.pdf?1442940714>.

¹¹⁷ *Id.*

¹¹⁸ Edvard Pettersson, *Bayer Accused of Underreporting Contraceptive Issues to FDA*, BLOOMBERG (July 9, 2020), <https://www.bloomberg.com/news/articles/2020-07-09/bayer-didn-t-report-essure-issues-to-fda-court-filings-say?leadSource=uverify%20wall> (last visited Oct. 1, 2022).

¹¹⁹ See 522 *Postmarket Surveillance Studies Database*, U.S. FOOD & DRUG ADMIN., https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pss.cfm?t_id=356&c_id=3854.

¹²⁰ “Silicone gel-filled breast implants were introduced to the U.S. in 1962. When the U.S. Congress passed the 1976 Medical Device Amendments to the Federal Food, Drug, and Cosmetic Act, breast implants were considered moderate risk (Class II) devices and required to comply with general controls and performance standards. The FDA reviewed new breast implants through the 510(k) premarket notification process as it did other Class II products.” U.S. FOOD & DRUG ADMIN., FDA UPDATE ON THE SAFETY OF SILICONE GEL-FILLED BREAST IMPLANTS (June 2011), <https://www.fda.gov/media/80685/download>.

¹²¹ See *Breast Implants on Trial: Chronology of Silicone Breast Implants*, PBS: FRONTLINE, <https://www.pbs.org/wgbh/pages/frontline/implants/cron.html> (last visited Oct. 1, 2022).

¹²² David Kessler, *The Basis of the FDA’s Decision on Breast Implants*, 326 NEW ENG. J. MED. 1713, 1715 (1992).

2000s, FDA approved alternatives to silicone implants: saline-filled breast implants¹²³ and silicone gel breast implants.¹²⁴ And in 2011, FDA warned the public about breast implant-associated anaplastic large cell lymphoma (BIA-ALCL), a rare cancer of the immune system that takes years to develop.¹²⁵ Due to the BIA-ALCL risk, FDA now requires manufacturers to provide a checklist and patient consent form to people seeking implants.¹²⁶ FDA also requested that a manufacturer of textured breast implants withdraw its product from the market because of the heightened risks these devices pose.¹²⁷ These known risks notwithstanding, since 2011, FDA has approved at least five breast implants.¹²⁸

F. Digital Devices' Effectiveness and Privacy Protections Are Inadequately Regulated

Wearable, trackable, and insertable health technologies are the device wave of the future. The lack of regulation of computer-based fertility trackers, period trackers, pelvic floor trainers, and similar devices pose a real risk to women's health and lives—and to their privacy. Based on these technologies' assurances of their health status, women are making reproductive and other medical decisions based on faulty evidence.

Fertility is a consequential health parameter for many women. Her ability to become pregnant, when, and with whom she chooses can affect every aspect of her life; and fertility awareness—"knowing and recognizing when the fertile time occurs in the menstrual cycle"¹²⁹—is an increasingly popular method of contraception.¹³⁰ Tech developers have made period tracker and fertility awareness into a high-tech

¹²³ See *FDA Approves Saline Breast Implants*, CNN: HEALTH (May 11, 2000), <http://www.cnn.com/2000/HEALTH/women/05/11/fda.saline.implants/index.html>.

¹²⁴ See Janice Hopkins Tanne, *FDA Approves Silicone Breast Implants 14 Years After Their Withdrawal*, 333 *BMJ* 1139 (2006).

¹²⁵ See Felmont Eaves III & Foad Nahai, *Anaplastic Large Cell Lymphoma and Breast Implants: FDA Report*, 31 *AESTHETIC SURGERY J.* 467 (2011).

¹²⁶ See General and Plastic Surgery Devices Panel of the Medical Devices Advisory Committee; Notice of Meeting, 84 Fed. Reg. 4476 (Feb. 15, 2019), <https://www.federalregister.gov/documents/2019/02/15/2019-02380/general-and-plastic-surgery-devices-panel-of-the-medical-devices-advisory-committee-notice-of>.

¹²⁷ See Press Release, U.S. Food & Drug Admin., *FDA Takes Action To Protect Patients From Risk of Certain Textured Breast Implants; Requests Allergan Voluntarily Recall Certain Breast Implants and Tissue Expanders From Market* (July 24, 2019), <https://www.fda.gov/news-events/press-announcements/fda-takes-action-protect-patients-risk-certain-textured-breast-implants-requests-allergan>.

¹²⁸ See *Premarket Approval (PMA) Database*, U.S. FOOD & DRUG ADMIN. (Dec. 5, 2022), <https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pma.cfm>.

¹²⁹ *Fertility Awareness-Based Methods of Family Planning: Frequently Asked Questions*, The Am. Coll. of Obstetricians & Gynecologists (Aug. 2022), <https://www.acog.org/womens-health/faqs/fertility-awareness-based-methods-of-family-planning>.

¹³⁰ See Chelsea Polis, *An Expert's Look at Fertility Awareness Methods*, MEDIUM (Nov. 1, 2019), <https://elemental.medium.com/an-experts-look-at-fertility-awareness-methods-17e4bdf18006>.

business.¹³¹ Dozens of applications (“apps”) are available for download despite serious questions about their accuracy.¹³²

The FDA has allowed three fertility apps¹³³ to be marketed in the United States: Natural Cycles,¹³⁴ Clue,¹³⁵ and Daysy.¹³⁶ These types of apps, even the ones reviewed by FDA, vary in their accuracy.¹³⁷ Natural Cycles had scientific and regulatory issues with its claims. For example, it was reported to regulators in Sweden for causing thirty-seven unwanted pregnancies,¹³⁸ which, while consistent with marketing claims, still led Swedish regulators to ask for clarifying language about failure rates.¹³⁹ Larger, however, was the call for¹⁴⁰ and subsequent retraction¹⁴¹ of the paper supporting

¹³¹ The femtech device industry could be as large as \$50 billion by 2025. *Femtech—Time for a Digital Revolution in the Women’s Health Market*, FROST & SULLIVAN (Jan. 30, 2018), <https://www.frost.com/frost-perspectives/femtechttime-digital-revolution-womens-health-market/>.

¹³² See Sarah Earle, Hannah R. Marston, Robin Hadley & Duncan Banks, *Use of Menstruation and Fertility App Trackers: A Scoping Review of the Evidence*, 47 *BMJ SEXUAL & REPROD. HEALTH* 90 (Apr. 6, 2020), <https://srh.bmj.com/content/47/2/90>.

¹³³ FDA has not cleared or approved Daysy as a fertility tracker or contraceptive; it is registered as a fertility diagnostic but marketed as a fertility tracker. The manufacturer’s website says:

Daysy: the fertility tracker you can trust. Daysy has been developed as a medical device. Not every fertility tracker on the market meets the standards required of a medical device, which are controlled and regulated by a quality management system. Daysy’s precision and quality are our highest priority. . . . The independently reviewed result shows that Daysy has an overall accuracy of 99.4% in differentiating not fertile days versus fertile days.

Accuracy, DAYSY, <https://usa.daysy.me/accuracy/> (last visited Oct. 1, 2022).

¹³⁴ See U.S. FOOD & DRUG ADMIN., *DENOVO CLASSIFICATION REQUEST FOR NATURAL CYCLES (DEN170052)*, https://www.accessdata.fda.gov/cdrh_docs/reviews/DEN170052.pdf.

¹³⁵ See *510(k) Premarket Notification: Clue Birth Control (K193330)*, U.S. FOOD & DRUG ADMIN., <https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm?ID=K193330>; *510(k) Premarket Notification: Natural Cycles (K202897)*, U.S. FOOD & DRUG ADMIN., <https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm?ID=K202897>.

¹³⁶ Daysy, made by Valley Electronics, is registered as a fertility diagnostic, code LHD, which is a pre-amendments device code under enforcement discretion. See *Establishment Registration & Device Listing Database: Daysy*, U.S. FOOD & DRUG ADMIN., <https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfRL/rl.cfm?lid=426490&lpd=LHD>.

¹³⁷ “Most free smartphone menstrual cycle tracking apps for patient use are inaccurate.” Michelle L. Moglia, Henry V. Nguyen, Kathy Chyjek, Katherine T. Chen & Paula M. Castaño, *Evaluation of Smartphone Menstrual Cycle Tracking Applications Using an Adapted APPLICATIONS Scoring System*, 127 *OBSTETRICS & GYNECOLOGY* 1153 (2016).

¹³⁸ See Julia Carrie Wong, *Birth Control App Reported to Swedish Officials After 37 Unwanted Pregnancies*, *THE GUARDIAN* (Jan. 17, 2018), <https://www.theguardian.com/technology/2018/jan/17/birth-control-app-natural-cycle-pregnancies>.

¹³⁹ See Press Release, Swedish Medical Products Agency, *The Assessment of Natural Cycles is Completed* (Sept. 13, 2018), <https://www.mynewsdesk.com/se/lakemedelsverket/pressreleases/the-assessment-of-natural-cycles-is-completed-2692491>.

¹⁴⁰ See Chelsea B. Polis, *Published Analysis of Contraceptive Effectiveness of Daysy and DaysyView App is Fatally Flawed*, 15 *REPROD. HEALTH* (June 25, 2018), <https://reproductive-health-journal.biomedcentral.com/articles/10.1186/s12978-018-0560-1>.

¹⁴¹ See Martin C. Koch, Johannes Lermann, Niels van de Roemer, Simone K. Renner, Stefanie Burghaus, Janina Hackl, Ralf Dittrich, Sven Kehl, Patricia G. Oppelt, Thomas Hildebrandt, Caroline C. Hack, Uwe G. Pöhls, Stefan P. Renner & Falk C. Thiel, *Retraction Note: Improving Usability and Pregnancy rates of a Fertility Monitor by an Additional Mobile Application: Results of a Retrospective Efficacy Study of Daysy and DaysyView App*, 16 *REPROD. HEALTH* (May 14, 2019), <https://reproductive-health-journal.biomedcentral.com/articles/10.1186/s12978-019-0728-3>.

Daysy's claims that it was 99.4% effective.¹⁴² Efficacy failures in apps used for contraceptive decisions could pose significant health harm to women; even a small percentage of failures can have dire consequences. Pregnancy can be dangerous and life-threatening, especially if the pregnancy is unanticipated, undetected, or unintended.¹⁴³

For other new wave devices that monitor other intimate details, FDA may not even have authority to assure consumers that the device will help them and not harm them. Several devices on the market currently are "pre-amendments devices." This means that they are substantially equivalent to products that were on the market in 1976, when the Medical Device bill was enacted.¹⁴⁴ As for the device's safety and efficacy, with limited exceptions, a determination by FDA that one device is substantially equivalent to another device does not reflect an FDA evaluation of the safety or effectiveness of either device.¹⁴⁵

Pelvic floor trainers, which a woman inserts in her vagina to exercise her lower abdominal muscles, are pre-amendments devices. Newer versions, including those for home use with biofeedback¹⁴⁶ or a smartphone app,¹⁴⁷ can still be considered substantially equivalent to devices invented before the dawn of personal computing.

IV. STRENGTHENING THE OFFICE OF WOMEN'S HEALTH

From its auspicious start, OWH's effectiveness has been limited during its three decades of existence. OWH has, over its history, granted more than \$45 million dollars towards more than 400 research projects, ranging from breast cancer to sexually transmitted infections, to neurological disorders, to psychiatric disorders.¹⁴⁸ Some of this research has led to "safety labeling changes for medical products, new guidance for industry on product development, [and] data standardization for vaccine clinical data."¹⁴⁹ But a grantmaking role inextricably ties OWH's effectiveness to its funding level. Without congressional appropriations and internal FDA reallocations,¹⁵⁰ OWH

¹⁴² See Emma Haslett, "It's a Wild West": The Scientist Who Took on the Multi-Million Femtech Industry, THE NEW STATESMAN (Apr. 25, 2022), <https://www.newstatesman.com/the-business-interviw/2022/04/its-a-wild-west-the-scientist-who-took-on-the-multi-billion-femtech-industry>.

¹⁴³ See Carrie S. Klima, *Unintended Pregnancy. Consequences and Solutions for a Worldwide Problem*, 43 J. NURSE-MIDWIFERY 483 (1998).

¹⁴⁴ See 21 U.S.C. § 360e, 21 C.F.R. § 814.

¹⁴⁵ See NAT'L ACADS. SCI., ENG'G & MATH, *supra* note 41, at 37.

¹⁴⁶ See U.S. FOOD & DRUG ADMIN., 510(K) SUMMARY: PELVITAL SYSTEM (July 10, 2020), https://www.accessdata.fda.gov/cdrh_docs/pdf20/K200409.pdf.

¹⁴⁷ See U.S. FOOD & DRUG ADMIN., 510(K) SUMMARY: IEVA REHABILITATIVE POSITIONAL DEVICE (Oct. 9, 2014), https://www.accessdata.fda.gov/cdrh_docs/pdf13/K133990.pdf.

¹⁴⁸ See *OWH Research and Development Program*, U.S. FOOD & DRUG ADMIN. (Jan. 22, 2020), <https://www.fda.gov/science-research/womens-health-research/owh-research-and-development-program> (last visited Oct. 1, 2022).

¹⁴⁹ *Id.*

¹⁵⁰ See, e.g., U.S. FOOD & DRUG ADMIN., U.S. DEP'T OF HEALTH & HUM. SERVS., FISCAL YEAR 2021 JUSTIFICATION OF ESTIMATES FOR APPROPRIATIONS COMMITTEES 280 (2020), <https://www.fda.gov/media/135078/download> (last visited Oct. 1, 2022) (proposing FDA's priorities for 2021 and requesting from Congress funds to achieve these priorities) [hereinafter FDA, FISCAL YEAR 2021 JUSTIFICATION OF ESTIMATES].

cannot meet its own purposes, especially to identify and monitor “new challenges to the health of women as they relate to FDA’s mission.”¹⁵¹

A. *OWH Coordination and Communication of Women’s Health Issues and Initiatives*

OWH’s challenge can be traced to the milquetoast primary description of the office: “to facilitate the Agency coordination and communication of women’s health issues and initiatives.”¹⁵² OWH has easily been relegated to the role of helper, convenor, and disseminator rather than being positioned as leader, policymaker, and drafter. Within the U.S. Department of Health and Human Services (HHS), OWH’s women’s health communications role is not unique. OWH provides the public information “through social media platforms and [via] disseminating health education materials to external stakeholders.”¹⁵³ OWH’s task is largely indistinguishable from similar efforts from other offices of women’s health at the Centers for Disease Control and Prevention (CDC) or Health Resources and Services Administration (HRSA).¹⁵⁴ Still more confusingly, the FDA OWH has the same name, and the same informational role, as the HHS Office of Women’s Health.

B. *OWH Monitoring of the Inclusion of Women in Clinical Trials*

OWH’s Section 907 Action Plan focused on ways FDA could improve gathering and communicating demographic data and how FDA could help increase women’s enrollment in clinical trials.¹⁵⁵ Out of this 907 Action Plan came “Drug Trials Snapshots,” which are part of an overall FDA effort to make demographic data more available and transparent. Drug Trials Snapshots “provide consumers and healthcare professionals with concise information about who participated in clinical trials that supported the FDA approval of new drugs.”¹⁵⁶ The information in the Snapshots also highlights where the trials were conducted and whether there were any differences in the benefits and side effects among different demographic groups.¹⁵⁷

Demographic subgroup data on devices is not yet available in a format like the Drug Trials Snapshots, although the many challenges with device testing and regulation make manifest its need. In 2017, FDA published a guidance on how device

¹⁵¹ Dep’t of Health & Hum. Svcs., Statement of Organization, Functions, and Delegations of Authority, 59 Fed. Reg. 38482 (July 28, 1994).

¹⁵² *Id.*

¹⁵³ FDA, FISCAL YEAR 2021 JUSTIFICATION OF ESTIMATES, *supra* note 150, at 280.

¹⁵⁴ See *CDC Women’s Health*, CTRS. FOR DISEASE CONTROL & PREVENTION (Sept. 29, 2022), <https://www.cdc.gov/women/index.htm> (last visited Oct. 1, 2022). See also *About the Office of Women’s Health*, HEALTH RES. & SERVS. ADMIN. (June 2022), <https://www.hrsa.gov/about/organization/bureau/owh/index.html> (last visited Oct. 1, 2022).

¹⁵⁵ See U.S. FOOD & DRUG ADMIN., FDA ACTION PLAN TO ENHANCE THE COLLECTION AND AVAILABILITY OF DEMOGRAPHIC SUBGROUP DATA (Aug. 2014), <https://www.fda.gov/media/89307/download> (last visited Oct. 1, 2022).

¹⁵⁶ See *Drug Trials Snapshots*, U.S. FOOD & DRUG ADMIN., <https://www.fda.gov/drugs/drug-approvals-and-databases/drug-trials-snapshots> (last visited Oct. 1, 2022).

¹⁵⁷ *Id.*

manufacturers could gather those data.¹⁵⁸ Compliance with this guidance is voluntary, however.

C. OWH as Advisor on Scientific, Ethical, and Policy Issues Relating to Women's Health

OWH is particularly ill-equipped to serve as “advisor to the Commissioner and other key officials on scientific, ethical, and policy issues relating to women’s health.”¹⁵⁹ The office lacks staff with policy, ethical, or scientific expertise such that they could advise the FDA commissioner. The office’s staff are mostly communications and outreach experts; two are medical doctors and one is a pharmacist.¹⁶⁰ No staff appears to have expertise in medical product evaluation or in research design. The individual FDA Centers and their divisions have filled OWH’s skills gap by creating their own health of women programs focused on drugs, devices, and biologics.¹⁶¹ The Centers’ programs channel women’s views and voices to the specific FDA units and foci of regulation, but they could dilute the effectiveness of OWH’s centralized role. Neither has OWH developed an overarching strategy for the promotion of women’s health throughout all FDA Centers and regulatory actions, effectively permitting each Center to chart its own path.

D. OWH Leading Policy Direction on Women's Health

OWH’s mandate is that it provides “leadership and policy direction for the Agency regarding issues of women’s health.”¹⁶² The argument that OWH lacks effectiveness as a policymaking body is bolstered by the absence of any OWH staff listing in the Plum Book, which enumerates federal employees in leadership positions subject to noncompetitive appointment because of their “confidential or policy-determining duties.”¹⁶³ Such duties may involve advocacy of administration policies and programs, and “the incumbents usually have a close and confidential working relationship with the agency head or other key officials.”¹⁶⁴ Although OWH is supposed to “establish short-range and long-range goals and objectives for adequate inclusion of women in all Commission protocols and policies,”¹⁶⁵ there is no evidence that OWH staff establish FDA goals and objectives.

¹⁵⁸ U.S. FOOD & DRUG ADMIN., EVALUATION AND REPORTING OF AGE-, RACE-, AND ETHNICITY-SPECIFIC DATA IN MEDICAL DEVICE CLINICAL STUDIES (Sept. 12, 2017), <https://www.fda.gov/meda/98686/download> (last visited Oct. 1, 2022).

¹⁵⁹ Dep’t of Health & Hum. Svcs., Statement of Organization, Functions, and Delegations of Authority, 59 Fed. Reg. 38482 (July 28, 1994).

¹⁶⁰ See *The Food and Drug Administration (FDA) Directory*, U.S. DEP’T OF HEALTH & HUM. SERVS. (last visited Oct. 1, 2022), <https://hhs.directory/hhsdir/fda-directory/>.

¹⁶¹ See, e.g., *CDRH Health of Women Program*, U.S. FOOD & DRUG ADMIN. (Jan. 18, 2022), <https://www.fda.gov/about-fda/center-devices-and-radiological-health/cdrh-health-women-program> (describing the women’s health program at the Center for Devices and Radiological Health) (last visited Oct. 1, 2022).

¹⁶² Dep’t of Health & Hum. Svcs., Statement of Organization, Functions, and Delegations of Authority, 59 Fed. Reg. 38482 (July 28, 1994).

¹⁶³ See UNITED STATES GOVERNMENT POLICY AND SUPPORTING POSITIONS (PLUM BOOK) iii (Dec. 2020), <https://www.govinfo.gov/content/pkg/GPO-PLUMBOOK-2020/pdf/GPO-PLUMBOOK-2020.pdf>.

¹⁶⁴ *Id.*

¹⁶⁵ See Women’s Health Office Act of 1994, H.R. 3874, 103d Cong. (1994).

OWH feels less like an FDA policy nerve center and more like an afterthought. In 2009, OWH lost its status as a stand-alone office and was moved inside the Office of the FDA Commissioner. According to the Commissioner, this move was intended to raise OWH's profile, making it the "principal advisor to the Commissioner on scientific, ethical, and policy issues relating to women's health."¹⁶⁶ In fact, the move eliminated OWH's substantive and budgetary independence—the last budget justification for the Department of Health and Human Services devised under President Trump does not mention OWH (or women) at all in the FDA section of the briefing document.¹⁶⁷

E. Improvements for OWH

Advocates and members of Congress long have recognized the need for women's health to be better integrated into the whole of FDA's work, especially on newly developed drugs and devices. It was for this reason that the FDA Office of Women's Health was created. OWH started with a bang, was reduced to a whimper, but could regain its voice and power for women. If OWH could achieve its purpose, it could mitigate or prevent the harms associated with inadequate involvement of, testing on, research in, post-market analysis of, and information for women about drugs and devices.

OWH itself may have come to these same conclusions. In September 2020, the office requested public comments about establishing its strategic priorities.¹⁶⁸ OWH was especially interested in six areas, including the following:

- Efforts to encourage analysis and detection of potential sex and gender differences in the safety, efficacy, and use of FDA-regulated products; and
- Efforts to anticipate, meet, and respond to existing and emerging issues related to women's health and FDA-regulated products.¹⁶⁹

Considering past and more recent failures to regulate drugs and devices appropriately and bearing in mind OWH's challenges to meet its mandate and to achieve its purpose, we suggest a few ways OWH could lead a proactive, science-based agenda on women's health.

First, and most importantly, OWH can ensure itself that it has the right staff with right skills to lead policies and strategies on women's health at FDA. The staff's expertise must go beyond communications to allow for proactivity on developing an agenda to address modern and historic challenges in drug and device regulation and women's health. The office requires scientific, ethical, and policy experts to advise the FDA commissioner. Therefore, OWH staff must be proficient in addressing labeling,

¹⁶⁶ Office of the Commissioner Reorganization; Statement of Organizations, Functions, and Delegations of Authority, 75 Fed. Reg. 7490 (Feb. 19, 2010), <https://www.govinfo.gov/content/pkg/FR-2010-02-19/pdf/2010-3161.pdf>.

¹⁶⁷ U.S. DEP'T OF HEALTH & HUM. SERVS., FISCAL YEAR 2022 BUDGET IN BRIEF, <https://www.hhs.gov/sites/default/files/fy-2022-budget-in-brief.pdf>.

¹⁶⁸ Office of Women's Health Strategic Priorities; Establishment of a Public Docket; Request for Comments, 85 Fed. Reg. 41591 (July 10, 2020), <https://www.regulations.gov/document/FDA-2020-N-1391-0001>.

¹⁶⁹ *Id.*

clinical trial representation, and safety monitoring—especially of devices, where so many current challenges are found.

Next, OWH can advise the FDA commissioner as to an overarching structure for evaluating the performance or safety of medical products used on or by women. Some information, including transparency efforts, has been communicated by OWH, but the analysis has been done by the Center for Drug Evaluation and Research (CDER). The office could bring together the analyses of all FDA Centers and serve as a central point for women's health-related issues at FDA. With staff with the correct expertise, OWH could assist FDA reviewers when evaluating the safety and effectiveness of medical products and provide cross-center support for efforts like gynecologic product registries.

OWH should move expeditiously to address the regulatory failures and ongoing challenges that have occurred during the office's thirty years of work.¹⁷⁰ The office should review its Section 907 Action Plan goals to ensure manufacturers test the efficacy and safety of a new drug or device on women, of course, and on demographic subgroups of sex, race, ethnicity, and age. OWH should press that FDA's Drug Snapshots be expanded to include information for medical devices and for previously approved drugs. The office too should support improved labeling and marketing of compounded medications, especially hormonal therapies that are marketed to women.

The most important step for OWH is to become forward-looking, anticipating, instead of reacting to, drug and device regulatory issues that could affect women. OWH currently has the power to convene stakeholders across the government to defend FDA's authority to regulate and approve drugs and devices marketed to the public. OWH should use this power to hold public meetings examining the safety, efficacy, and data privacy of digital devices that collect intimate information about women. In addition, OWH should move rapidly to develop a strategy to respond to state-led challenges to FDA-approved medications, such as mifepristone and misoprostol, used by millions of American women to maintain their health.¹⁷¹

V. CONCLUSION

Historical failure to regulate drugs and devices harmed the public, especially the 51% of the public that is female. Women were particularly and disproportionately vulnerable to the regulatory process's inability to ensure safe and effective medicines, machines, and medical implements. Tragedies resulted in greater regulation of drugs and devices' effectiveness and general safety, but the normative standard for all drugs and devices continued to be an adult male.¹⁷² Little, if any testing or information was provided for women about safety and efficacy.

Beginning in the 1970s and continuing through the creation of the FDA Office for Women's Health in the 1990s, women-specific safety standards were required for

¹⁷⁰ See, e.g., Sarah Christopherson, *FDA Comments—Office of Women's Health Strategic Priorities*, NAT'L WOMEN'S HEALTH NETWORK (Sept. 8, 2020), <https://nwhn.org/fda-comments-office-of-womens-health-strategic-priorities/>.

¹⁷¹ See Lawrence Hurley, *White House Prepare to Fight States Over Abortion Pill*, REUTERS (June 27, 2022), <https://www.reuters.com/world/us/biden-administration-signals-fight-over-medication-abortion-2022-06-25/>.

¹⁷² See TK Sundari Ravindran, Yot Teerawattananon, Cara Tannenbaum & Lavanya Vijayasingham, *Making Pharmaceutical Research and Regulation Work for Women*, 371 *BMJ* m3808 (2020), <https://www.bmj.com/content/371/bmj.m3808>.

certain—but not all—drugs and devices. Product safety scares for women show that manufacturers continue not to provide information that responds to women’s needs across their lifespans.

OWH’s mission and priorities must be revitalized to protect and promote the entire public’s health. Reversing the tokenism of a “women’s office” would contribute to tearing down silos at FDA, ensuring knowledge about women is not confined to OWH. FDA must leverage OWH’s expertise to evaluate appropriately the data from pre- and post-market reviews of drugs and devices. These data will inform meaningful and correct sex-specific recommendations and labeling, which will permit consumers of all sex and gender expressions to make informed decisions about their own health. OWH also must step forward to lead on women’s health, anticipating future challenges and using its current authorities to convene actors across the government to develop strategic responses.