Submitted electronically
The Commissioner of Food and Drugs
c/o Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

RE: Dr. Rodney Story and IFPC Legal Center's Comment on the Citizen Petition Pursuant to 21 C.F.R. § 10.30 Requesting the FDA (A) Open a Docket, (B) Hold a Part 15 Public Hearing Regarding the Off-Label Use of Estrogen in Natal Males for Gender Affirmation, and (C) Consider Regulatory Action Including a Boxed Warning Under 21 C.F.R. § 201.80(e) (Docket FDA-2025-P-7321).

Introduction

The role of medicine is to heal broken bodies not to break healthy bodies. But doctors around the country are progressively willing to dispense estrogen to biological males for off-label use for cases of gender dysphoria, despite many known risks. Those risks are especially dire for children, who lack the capacity to fully process how artificially imbalancing their hormones can permanently affect their bodies. That is why states like Idaho (with research, drafting, and support from Idaho Family Policy Center) have prohibited doctors from giving supraphysiological doses of cross-sex hormones to children.[1]

A cultural whim should not overrun the dictates of medical ethics and sound data. As a hobbyist approach to the endocrine system is increasingly proven to be scientifically untenable, the FDA should take the first step in implementing basic controls. The IFPC Legal Center and Dr. Rodney Story support the petition to open a public docket, convene a Part 15 hearing, and take further actions like requiring warning labels, mandating adverse event reporting, and initiating further study into the safety issues with off-label estrogen use.[2]

---

[1] Idaho Code § 18-1506C(3).

[2] Dr. Rodney Story is a highly trained physician who has spent more than 20 years in family medicine. He has provided medical care in many settings—emergency rooms, hospitals, hospice, and nursing homes. He now runs his own practice, Story Family Medicine, in Moscow, Idaho. Dr. Story completed his medical education at the University of Washington School of Medicine in Seattle, and afterwards completed his residency at LaCrosse Mayo Family Practice Residency in Wisconsin. He is certified by the American Board of Family Medicine in Family Medicine, Hospital Medicine, and Hospice and Palliative Medicine.

208.260.5844 | 1116 S. VISTA AVENUE, SUITE 227, BOISE, ID 83705 | IDAHOFAMILY.ORG

I. Increasing scientific data supports extra precautions for off-label estrogen use.

Supraphysiological doses of estrogen have significant, documented health risks—risks too great to ignore. Although many pharmaceuticals have side effects or risks, estrogen stands out as one of the only hormones being prescribed off-label in a manner that is not intended to address a physical malady. Widespread prescription persists despite the breadth and magnitude of adverse effects from feminizing hormones like estrogen. To make matters worse, those risks are often not made clear to those who are taking estrogen.

These risks are increasingly well-documented and include:

- **Blood clots (venous thromboembolism or VTE).** These clots are strikingly more prevalent in biological males taking cross-sex hormones. One study found males taking cross-sex hormones have 42.8 occurrences of VTE per 10,000 patient years versus just 10.8 occurrences for females taking male cross-sex hormones per 10,000 patient years.[3] Another study found that men taking estrogen have 50% more VTE incidents than other men, and after two years VTE incidence can go up 5.1 times.[4] Such clots can be deadly, especially if they occur in a lung or other organ vein.[5]

- **Strokes.** Ischemic stroke risk has been documented to increase by 30% when a male begins taking estrogen and continues climbing up to ten times higher after six years.[6]

- **Infertility.** Recent studies suggest that estrogen and other feminizing hormones deplete Leydig cells and disrupt the biological processes involved in spermatogenesis, impacting fertility.[7] The younger a person begins receiving cross-sex hormones, the more likely the person is to

---

[3] Vasanth S. Kotamarti et al., *Risk for Venous Thromboembolism in Transgender Patients Undergoing Cross-Sex Hormone Treatment: A Systematic Review*, 18 J. Sexual Med. 1280 (2021).

[4] Darios Getahun et al., *Cross-sex Hormones and Acute Cardiovascular Events in Transgender Persons: A Cohort Study*, 169 Annals Internal Med. 205 (2018).

[5] *Venous Thromboembolism*, Cleveland Clinic (Feb. 22, 2022), https://my.clevelandclinic.org/health/diseases/22614-venous-thromboembolism.

[6] Lauren Schwartz et al., *Emerging and Accumulating Safety Signals for the Use of Estrogen Transgender Women*, Springer Nature: Link (June 12, 2025), https://link.springer.com/content/pdf/10.1007/s44192-025-00216-3.pdf.

[7] Anna Chiara Conflitti et al., *Gender-affirming Hormone Therapy: Effect on Semen Quality and Use of Fertility Preservation*, 14 Andrology 322, 323–24 (2026).

become permanently infertile—especially if the hormones are first administered to a prepubescent child.[8]

- **Cancer.** Some research suggests that risks for breast, testicular, and thyroid cancer increases with the use of cross-sex hormones.[9]

These studies suggest that off-label estrogen use is not just life-altering—it is life-threatening. Bafflingly, physicians are increasingly prioritizing a patient's sense of identity over their physical, bodily well-being. The Citizen Petition appropriately encourages the Agency, and by extension the entire medical profession, to take this more seriously. The proposed warning labeling requirements would be a good first step to alert people that taking estrogen when it is not clinically indicated has the potential to cause serious harm or death.

II. The Citizen Petition supports a cautious approach to improvised hormone prescriptions, in line with medical ethics.

Off-label drug prescriptions are a time-honored medical tradition for treating the nuances of patient conditions, but such prescriptions must occur within the bounds of medical ethics. The most basic principle of medical ethics, nonmaleficence—"Do No Harm"—ought to be at the forefront of practitioners' minds when prescribing pharmaceuticals in ways that have not been rigorously tested. The FDA should mandate warning labels and take further action to discourage physicians from prescribing estrogen in an unethical manner.

Even the earliest statements on medical ethics are in line with a cautious approach to prescribing drugs or procedures with the potential to harm. The Hippocratic Oath—one of the best-known and earliest creeds on medical ethics—stated: "I will do no harm or injustice to [my patients]."[10] Thomas Percival's

---

[8] *Feminizing Hormone Therapy*, Mayo Clinic (July 12, 2024), https://www.mayoclinic.org/tests-procedures/feminizing-hormone-therapy/about/pac-20385096

[9] Elayna M. Shanker et al., *Exploring the Incidence of Testicular Neoplasms in the Transgender Population: A Case Series*, 149 Archive Pathology & Lab'y Med. 668, 671 (2025) ("The higher incidence rate of testicular cancer among [men identifying as females] in our series may be due in part to maturation arrest from pretreatment with hormones or blockers, a known risk factor for testicular cancer."); John David Christensen et al., *Thyroid Cancer Prevalence, Risk Exposure, and Clinical Features Among Transgender Female Veterans*, J. Endocrine Soc'y at 3 (Mar. 27, 2024) (thyroid cancer higher among males taking estrogen than other males), https://pmc.ncbi.nlm.nih.gov/articles/PMC11023629/; Mayo Clinic, *supra* note 8 ("Evidence suggests that people who take feminizing hormone therapy may have a higher risk of breast cancer when compared to cisgender men—men whose gender identity aligns with their sex assigned at birth.").

[10] *Ancient Greek Medicine*, Nat'l Lib. Medicine, https://www.nlm.nih.gov/hmd/topics/greek-medicine/index.html#case1.

Medical Ethics noted that even when patients insist on quack medicines and other treatments they have seen advertised, doctors ought to advise the patient of any dangers and the ill-advised nature of the product.[11]

The ethical concerns are even stronger when the risks are known and well documented, as described above. The risks of supposed gender transition procedures and cross-sex hormone prescriptions are painted in technicolor by the rise of detransitioner medical malpractice cases. These cases involve patients who regret surgeries and pharmaceutical regimens intended to align with a patient's gender dysphoria—especially from those who received such interventions as children. Even worse, many of these individuals were pressured by their own doctors to transition.[12]

The most well-publicized case involves a recent two-million dollar jury award to a biological woman who had transitioned.[13] This trend has continued to biological men prescribed estrogen off-label.

For example, Christopher Miller recently settled his lawsuit with Identity Hormones LLC after he alleged that he suffered harm from the off-label estrogen he was prescribed.[14] Similarly, Miles Yardley—formerly a famed fashion model—recently filed a lawsuit after he claimed the off-label estrogen usage caused him extensive bodily problems, including a brain tumor and thyroid and other organ malfunction.[15] Yardley alleges the medical interventions significantly upended his life and caused him extensive permanent physical damage.

These malpractice suits are gaining momentum as science demonstrates the harms caused by the prescription of estrogen to males for hormone alteration.

---

[11] THOMAS PERCIVAL, MEDICAL ETHICS 44–45 (1803).

[12] Lisa Littman, *Individuals Treated for Gender Dysphoria with Medical and/or Surgical Transition Who Subsequently Detransitioned: A Survey of 100 Detransitioners*, J. ARCHIVES SEXUAL BEHAVIOR at 3360 (noting survey responses including ""My gender therapist acted like it [transition] was a panacea for everything" and "[My] [d]octor pushed drugs and surgery at every visit" (alterations in original)) (Oct. 19, 2021), https://doi.org/10.1007/s10508-021-02163-w.

[13] Bryan Chai, *Detransitioner Fox Varian Awarded $2 Million in Historic Lawsuit*, All. Defending Freedom (Feb. 13, 2026), https://adflegal.org/article/detransitioner-fox-varian-awarded-2-million-in-historic-lawsuit/.

[14] Benjamin Ryan, *Detransitioner Settles Malpractice Lawsuit Days Before Trial In Oregon*, Hazard Ratio: Benjamin Ryan (April 29, 2026), https://benryan.substack.com/p/detransitioner-lawsuit-settles-on.

[15] Chadwick Moore, *Fashion Model Learning to be a Man after being Pushed to Transition at Age 15: "I was Really Crazy on the Hormones,"* N.Y. Post (July 26, 2025), https://nypost.com/2025/07/26/us-news/fashion-model-learning-to-be-a-man-after-being-pushed-to-transition/.

Prescription of a hormone with such high risks for harm without at least informed consent through proper labeling presents serious ethical concerns for physicians. The FDA should at a minimum require warning labels for these use cases.

CONCLUSION

No person should be taking estrogen for off-label use without a full knowledge of the consequences. Basic safeguards like warning labels and adverse event reporting are a step towards encouraging physicians to resist cultural pressure to prescribe pharmaceuticals that will greatly harm their patients. The citizen petition advances the laudable outcome of encouraging physicians to discuss all the harms with patients, as well as giving patients the means (through box labeling) to acquaint themselves with the risks before deciding to take supraphysiological doses of cross-sex hormones. The FDA should open a public docket and convene a Part 15 hearing.

Respectfully submitted,

Rodney R. Story, MD
Diplomate, ABFM, Hospital Medicine, Hospice and Palliative Medicine
Story Family Medicine

A. Caleb Pirc
Director | IFPC Legal Center

Isaac N. Helland
Litigation Counsel | IFPC Legal Center

Lili M. Pirc
Attorney | IFPC Legal Center

---

* Special thanks to IFPC Legal Center interns Breana Proffer, Nathan McOwen, Mason Plattner, and Zach Atwood for their assistance with this comment.