



THE NATIONAL CATHOLIC BIOETHICS CENTER

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March 6, 2026

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

RE: 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)

Dear Commissioner:

The Catholic Medical Association, the National Catholic Bioethics Center, the National Association of Catholic Nurses, USA, and the National Catholic Partnership on Disability call on the U.S. Food and Drug Administration (FDA) to:

1. Initiate a thorough safety review of the use of estrogen in males, and,
2. Issue a Black Box Warning of the risks with such use.

This comment is submitted on behalf of: the Catholic Medical Association (CMA), the largest organization of Catholic health care professionals in America; The National Catholic Bioethics Center (NCBC), which is an over 500 member non-profit research and educational institute committed to applying the moral teachings of the Catholic Church to ethical issues arising in health care and the life sciences; The National Association of Catholic Nurses, USA (NACN-USA), a non-profit organization of nurses from different backgrounds and specialties, advocating for human rights of vulnerable populations, including the right to health care which heals, not harms persons; and The National Catholic Partnership on Disability (NCPD), established in 1982 to foster implementation of the *Pastoral Statement of U.S. Catholic Bishops on People with Disabilities*, working with dioceses, parishes, ministers, and laity to promote the full and meaningful participation of persons with disabilities in the life of the Church and society.

CMA, NCBC, NACN-USA, and NCPD are aware of the increasing evidence of the harms and lifelong risks of transgender interventions, which constitute sex-rejecting procedures, in minors. Our organizations have been at the forefront of the debate to protect these children and adolescents. In health care, the best

practices are those established on evidence-based studies and sound ethical principles. The use of estrogen in young males for purported “gender transition” has neither scientific support nor a moral purpose. Data which can be reviewed in the references noted below provide a clear rationale for the FDA to review its oversight of estrogen for this purpose. Such an investigation is necessary, as is the need to issue a Black Box Warning that is particularly important given the clear cardiovascular risks associated with estrogen in this population of patients.

Over the past several years, extensive and systematic reviews of the use of sex hormones in minors has identified “low” or “very low” evidence of certainty for benefits. If estrogen is provided to a young male that may persist in his opposite sex identification for the rest of his life, the risks and harms incurred from years of use are increased dramatically. The absence of scientific literature that provides evidence of benefits is troubling enough. However, of even greater concern is the objective demonstration of estrogen’s harms to young males with gender dysphoria found in the references below.

The data are clear that the dangers to young males are multifocal and potentially life-threatening. These include cardiovascular disease, venous thromboemboli, and infertility, as well as significantly increased risk of cognitive impairment, metabolic anomalies, some cancers, and autoimmune disorders.

The FDA’s long-standing mission to “protect and promote public health by ensuring the safety, efficacy, and security...” of drugs, including estrogen, must be followed with a comprehensive re-evaluation of this use of estrogen, and the issuance of a Black Box Warning. CMA calls on the FDA to follow its established protocol under 21 C.F.R. § 201.80(e) and continue to “protect and promote public health” for young men in America.

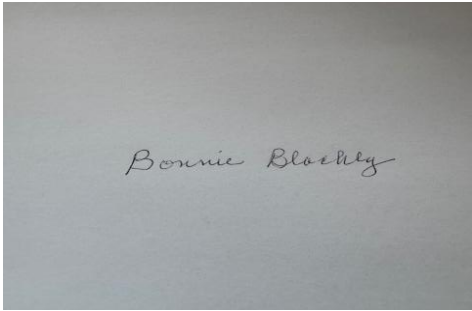
Sincerely yours (submitted under Category – “Association”)



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A handwritten signature in cursive script that reads "Mary O'Callaghan". The signature is written in a fluid, elegant style.

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References

1. Cass H. Independent review of gender identity services for children and young people; 2024. <https://webarchive.nationalarchives.gov.uk/ukgwa/20250310143933/https://cass.independent-review.uk/home/publications/final-report/>.
2. Brignardello-Petersen R, Wiercioch W. Effects of gender affirming therapies in people with gender dysphoria: evaluation of the best available evidence. 2022. https://ahca.myflorida.com/letkidsbekids/docs/AHCA_GAPMS_June_2022_Attachment_C.pdf
3. Ludvigsson JF, Adolfsson J, Höistad M, Rydelius PA, Kriström B, Landén M. A systematic review of hormone treatment for children with gender dysphoria and recommendations for research. *Acta Paediatr.* 2023;112:2279–91. <https://onlinelibrary.wiley.com/doi/10.1111/apa.16791>
4. National Institute for Health and Care Excellence. Evidence review: gender-affirming hormones for children and adolescents with gender dysphoria. NICE; 2020. https://webarchive.nationalarchives.gov.uk/ukgwa/20250310144323mp_/https://cass.independent-review.uk/wp-content/uploads/2022/09/20220726_Evidence-review_Gender-affirming-hormones_For-upload_Final.pdf
5. Zepf FD, König L, Kaiser A, Ligges C, Ligges M, Roessner V, et al. Beyond NICE: AktualisiertesystematischeÜbersichtzurEvidenzlageder Pubertätsblockade und HormongabebeiMinderjährigenmitGeschlechtsdysphorie. *Z Kinder JugendpsychiatrPsychother.* 2024. <https://doi.org/10.1024/1422-4917/a000972>.
6. McDeavitt K. Paediatric gender medicine: longitudinal studies have not consistently shown improvement in depression or suicidality. *Acta Paediatr.* 2024;113:1757–71. <https://onlinelibrary.wiley.com/doi/abs/10.1111/apa.17309>
7. Taylor J, Mitchell A, Hall R, Langton T, Fraser L, Hewitt CE. Masculinising and feminising hormone interventions for adolescents experiencing gender dysphoria or incongruence: a systematic review. *Arch Dis Childhood.* 2024;109:s48–56. <https://adc.bmj.com/content/archdischild/early/2024/04/09/archdischild-2023-326499.full.pdf>
8. Miroshnychenko A, Ibrahim S, Roldan Y, Kulatunga-Moruzi C, Montante S, Couban R, et al. Gender affirming hormone therapy for individuals with gender dysphoria aged <26 years: a systematic review and meta-analysis. *Arch Dis Child.* 2025;110:437–45. <https://adc.bmj.com/content/110/6/437>
9. Treatment for Pediatric Gender Dysphoria. US Department of Health and Human Services; 2025. Available from: <https://opa.hhs.gov/sites/default/files/2025-05/gender-dysphoria-report.pdf>
10. Haupt C, Henke M, Kutschmar A, Hauser B, Baldinger S, Saenz SR, et al. Antiandrogen or estradiol treatment or both during hormone therapy in transitioning transgender women. *Cochrane Database Syst Rev.* 2020. <https://doi.org/10.1002/14651858.CD013138.pub2>.
11. Schwartz L, Lal M, Cohn J, Mendoza CD, MacMillan L. Emerging and accumulating safety signals for the use of estrogen among transgender women. *Discov Ment Health.* 2025 Jun 12;5(1):88. doi: 10.1007/s44192-025-00216-3. PMID: 40506545; PMCID: PMC12162459. <https://link.springer.com/article/10.1007/s44192-025-00216-3>
12. Glintborg D, Christensen LL, Andersen MS. Transgender healthcare: metabolic outcomes and cardiovascular risk. *Diabetologia.* 2024;67(11):2393–403. <https://link.springer.com/article/10.1007/s00125-024-06212-6>
13. Van Zijverden LM, Wiepjes CM, Van Diemen JJK, Thijs A, Den Heijer M. Cardiovascular disease in transgender people: a systematic review and meta-analysis. *Eur J Endocrinol.* 2024;190(2):S13-24. <https://academic.oup.com/ejendo/article/190/2/S13/7596368?login=false>

14. Irwig MS. Cardiovascular health in transgender people. *Rev EndocrMetabDisord*. 2018;19(3):243–51.
<https://link.springer.com/article/10.1007/s11154-018-9454-3>
15. Franco-Moreno A, Ryan P, Muñoz-Rivas N, Valencia J, Torres-Macho J, Bacete-Cebrián S. Riesgo de tromboemboliavenosa en población transgénero en terapia hormonal: una revisión sistemática y metaanálisis. *Med Clin*. 2025;164(12): 106921.
<https://www.sciencedirect.com/science/article/abs/pii/S0025775325001150?via%3Dihub>