Exhibit FF

IN THE UNITED STATES DISTRICT COURT
DISTRICT OF MARYLAND

PFLAG, INC., et al., *Plaintiffs*, v. DONALD J. TRUMP, in his official capacity as President of the United States, et al., *Defendants*.	Civil Action No. 8:25-cv-00337-BAH

REPLY EXPERT DECLARATION OF
ARMAND H. MATHENY ANTOMMARIA, MD, PhD, FAAP, HEC-C

INTRODUCTION

I, Armand H. Matheny Antommaria MD, PhD, hereby declare and state as follows:

1. I have been retained by counsel for Plaintiffs as an expert in connection with the above-captioned litigation. I am over 18 years old, of sound mind, and in all respects competent to testify.

2. I have actual knowledge of the matters stated herein.

3. The bases of my opinions are set forth in paragraph 3 of my initial expert declaration. I provide this reply declaration to respond to the arguments contained in the memorandum filed by the Defendants, the amicus brief filed by the organization Do No Harm, Inc., and the amicus brief filed by the State of Alabama and other states.

OVERVIEW

4. Contrary to Defendants' Memorandum and Alabama's Brief, no European country has prohibited gender-affirming medical care as the Denial of Care Order has. Do No Harm's Brief mischaracterizes the role of systematic reviews and Alabama's Brief the making of discordant recommendations and the management of potential conflicts of interest.

EUROPEAN COUNTRIES

5. Contrary to Defendants' Memorandum's statement that "Other countries have also adopted similar restrictions [on gender-affirming care for minors] (5),"[1] no European country has prohibited gender-affirming medical care as the Denial of Care Order has. The only categorical prohibition of a form of gender-affirming medical care appears to be the Finnish Council for Choices in Health Care's statement, "[s]urgical treatments are not part of the treatment methods for dysphoria caused by gender-related conflicts in minors."[2] (It is not clear whether surgical treatments as used in this statement includes masculinizing chest surgery.) Pubertal suppression and gender affirming hormone treatment are nonetheless permitted for minors in Finland.[3]

6. The United Kingdom's (U.K.'s) regulation of gender-affirming medical care has evolved in several stages. On March 11, 2024, NHS England made gonadotropin-releasing hormone (GnRH) analogs no longer available as "a routine commissioning treatment option" for treating gender dysphoria.[4] GnRH analogs are, however, anticipated to be available through a

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[1] See also Alabama's Brief 2-3.

[2] Palveluvalikoima. Summary: Medical treatment methods for dysphoria associated with variations in gender identity in minors – recommendations. June 16, 2020. Accessed February 26, 2025. Available at https://palveluvalikoima.fi/documents/1237350/22895008/Summary_minors_en+(1).pdf/fa2054c5-8c35-8492-59d6-b3de1c00de49/Summary_minors_en+(1).pdf?t=1631773838474.

[3] Palveluvalikoima. Summary: Medical treatment methods for dysphoria associated with variations in gender identity in minors – recommendations. June 16, 2020. Accessed February 26, 2025. Available at https://palveluvalikoima.fi/documents/1237350/22895008/Summary_minors_en+(1).pdf/fa2054c5-8c35-8492-59d6-b3de1c00de49/Summary_minors_en+(1).pdf?t=1631773838474.

[4] NHS England. Clinical Policy: Puberty suppressing hormones (PSH) for children and young people who have gender incongruence / gender dysphoria [1927]. March 12, 2024. Accessed February 26, 2025. Available at https://www.england.nhs.uk/wp-content/uploads/2024/03/clinical-commissioning-policy-gender-affirming-hormones-v2.pdf.

clinical study that is currently being designed and was initially anticipated to begin enrollment in late 2024.[5] On March 21, 2024, NHS England announced that gender-affirming hormones are available as "a routine commissioning treatment option" around individuals' 16th birthday.[6] The recommendations contained in Dr. Hilary Cass's final report, issued on April 10, 2024,[7] are largely consistent with the NHS clinical policies pertaining to GnRH analogs and gender-affirming hormone treatment. On May 29, 2024, the Secretary of State for Health and Social Care and the Minister for Health made a temporary prohibition on the private prescription of GnRH analogs to minors for the treatment of gender dysphoria to provide consistency between

[5] NHS England. Consultation report for the clinical policy on puberty suppressing hormones for children and adolescents who have gender incongruence / gender dysphoria. March 11, 2024. Accessed February 26, 2025. Available at https://www.england.nhs.uk/publication/clinical-policy-puberty-suppressing-hormones/ under "Puberty suppressing hormones consultation report 11 March 2024."

[6] NHS England. Clinical Commissioning Policy: Prescribing of gender affirming hormones (masculinising and feminising hormones) as part of the Children and Young People's Gender Service. March 21, 2024. Accessed February 26, 2025. Available at https://www.england.nhs.uk/wp-content/uploads/2024/03/clinical-commissioning-policy-prescribing-of-gender-affirming-hormones.pdf.

[7] Cass H. The Cass Review: Independent review of gender identity services for children and young people. April 2024. Accessed February 26, 2025. Available at https://cass.independent-review.uk/home/publications/final-report/.

Following the release of the Cass Review's Final Report, NHS Scotland announced a "pause" in new prescriptions for GnRH analogs and a minimum age of 18 years for new prescriptions of gender affirming hormones. See Sandyford. Gender Service for Young People at Sandyford: Important service update – Young Person's Gender Service. Accessed February 26, 2025. Available at https://www.sandyford.scot/sexual-health-services/gender-service-at-sandyford/gender-young-people-service/. NHS Scottland's Chief Medical Officer Professor Sir Gregor Smith subsequently submitted recommendations to make the services provided by NHS Scottland consistent with those of NHS England and the Cass Review. Scottish Government. Cass Review – implications for Scotland: letter from Chief Medical Officer. July 4, 2024. Accessed February 26, 2025. Available at https://www.gov.scot/publications/cass-review-implications-for-scotland-letter-from-chief-medical-officer-professor-sir-gregor-smith/.

the public and private healthcare systems in the U.K.[8] None of these policies constitute a ban on gender-affirming medical care comparable to the Order's purported goal.

SYSTEMATIC REVIEWS

7. Do No Harm's Brief asserts that systematic reviews represent the highest form of medical evidence and that systematic reviews of gender-affirming medical care demonstrate that there is no reliable evidence for gender-affirming medical care. While the "pyramid of standards of evidence" places systematic reviews and meta-analyses at the top of the pyramid, it is important to note that systematic reviews are "filtered information" in contrast to "unfiltered information" (Do No Harm's Brief 3). This means that systematic reviews are not a type of research study, but rather a summary of research studies. The Grading of Recommendations Assessment, Development and Evaluation (GRADE) system does not rate the quality of systematic reviews, but rather the studies contained in systematic reviews. The tool commonly used to evaluate the quality of systematic reviews is instead the Assessing the Methodological Quality of Systematic Reviews (AMSTAR) checklist.[9]

8. Do No Harm's Brief emphasizes that systematic reviews of the literature report that the level of evidence for gender-affirming medical care is "weak" (5).[10] As I explain in paragraphs 22-27 of my expert declaration, the terms used by the GRADE system to characterize the strength of the evidence are terms of art, the levels are relative to one another, and "low" does not

[8] Legislation.gov.uk. The Medicines (Gonadotrophin-Releasing Hormone Analogues) (Emergency Prohibition) (England, Wales, and Scotland) Order 2024. May 29, 2024. Accessed February 26, 2025. Available at https://www.legislation.gov.uk/uksi/2024/727/made.

[9] Shea BJ, Reeves BC, Wells G, et al. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. *BMJ*. 2017;358:j4008.

[10] See also Alabama's Brief at 3.

necessarily mean poor or inadequate. Do No Harm's Brief trades on the differences between these technical meanings and the colloquial uses of these terms (9).

9. Contrary to Do No Harm's Brief's misleading implications, studies of systematic reviews of the evidence for medical interventions generally have found that the majority of the evidence that they identify is low or very-low quality. Padhraig S. Fleming and colleagues, for example, conducted a review of systematic reviews for medical and health-related interventions published on the Cochrane Database of Systematic Reviews between January 1, 2013 and June 30, 2014. They focused on those that incorporated the GRADE approach and examined the quality of evidence for the first listed primary outcome. Of the 608 reviews, 82 (13.5%) reported high, 197 (30.8%) moderate, 193 (31.7%) low, and 126 (24%) very low-quality evidence.[11] In a subsequent study, a related group of authors found that updated reviews did not consistently demonstrate an improvement in the quality of the evidence.[12] The level of evidence supporting gender-affirming medical care is therefore similar to the level of evidence supporting other types of medical treatment.

10. It should be noted that Do No Harm's Brief provides a narrative, rather than a systematic, review of systematic reviews of gender-affirming medical care. As the Brief notes, "narrative reviews can cherry-pick examples and individual studies—discussing only those that support their conclusions and ignoring those that do not (5)." In fact, a recent systematic review

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[11] Fleming PS, Koletsi D, Ioannidis JP, Pandis N. High quality of the evidence for medical and other health-related interventions was uncommon in Cochrane systematic reviews. *J Clin Epidemiol*. 2016;78:34-42. See also Howick J, Koletsi D, Ioannidis JPA, et al. Most healthcare interventions tested in Cochrane Reviews are not effective according to high quality evidence: A systematic review and meta-analysis. *J Clin Epidemiol*. 2022;148:160-169 that found only 10.1% of interventions (158 of 1,567) had high quality evidence supporting their benefits.

[12] Howick J, Koletsi D, Pandis N, et al. The quality of evidence for medical interventions does not improve or worsen: A metaepidemiological study of Cochrane reviews. *J Clin Epidemiol*. 2020;126:154-159.

of gender-affirming medical care performed by the RAND Corporation states, "these interventions have not shown the serious risks of harm that would suggest the need for policies to restrict the interventions (35)."[13]

CLINICAL PRACTICE GUIDELINES

11. Though Do No Harm's Brief focuses extensively on systematic reviews, systematic reviews do not make treatment recommendations. The Cochrane Collaboration defines systematic reviews as follows: "A systematic review attempts to collate all empirical evidence that fits pre-specified eligibility criteria in order to answer a specific research question. It uses explicit, systematic methods that are selected with a view to minimizing bias, thus providing more reliable findings from which conclusion can be drawn and decisions made."[14] While systematic reviews may provide findings upon which recommendations can be made, they, unlike clinical practice guidelines, do not make treatment recommendations.[15] Citing their conclusions about the quality of the evidence is therefore not sufficient to demonstrate that recommendations for gender-affirming medical care are inappropriate. Clinical practice guidelines consider the benefits and risks of treatments and patients' values and preferences in addition to the quality of evidence in making treatment recommendations.[16]

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[13] Dopp AR, Peipert A, Buss J, et al. Interventions for gender dysphoria and related health problems in transgender and gender-expansive youth: A systematic review of benefits and risks to inform practice, policy, and research. November 26, 2024. Accessed February 26, 2025. Available at https://www.rand.org/pubs/research_reports/RRA3223-1.html.

[14] Cochrane Collaboration. "What is a systematic review?" in *Cochrane Handbook for Systematic Reviews of Interventions.* Version 5.1.0. ed. Higgins JPT, Green S. March 2011. Accessed February 26, 2025. Available at https://handbook-5-1.cochrane.org/chapter_1/1_2_2_what_is_a_systematic_review.htm.

[15] National Heart, Lung, and Blood Institute. About systematic evidence reviews and clinical practice guidelines. Accessed February 26, 2025. Available at https://www.nhlbi.nih.gov/node/80397.

[16] Andrews JC, Schunemann HJ, Oxman AD, et al. GRADE guidelines: 15. Going from

12. Do No Harm's Brief asserts that the risks and benefits of gender-affirming medical care justifies treating it differently from other forms of medical care that is supported by the same level of evidence. For many patients the potential benefits of gender-affirming medical care outweigh its potential risks and this risk benefit ratio is favorable to withholding pharmacological and surgical treatment. Do No Harm's Brief also downplays the risks of inadequately treated gender dysphoria, which are great, as discussed in my expert declaration (53-60). While treatments for different clinical conditions do not have identical benefits and risks, they may nonetheless have similar benefits and risks which permit comparison. The risks of a mastectomy in an adolescent with gender dysphoria are similar in kind to the risks of breast reduction surgery in adolescents who do not have gender dysphoria. On the other hand, Do No Harm's Brief overstates the risks of gender-affirming medical care and mischaracterizes my prior statements (11-12). For example, while one risks being infertile while receiving gender-affirming medical care, treatment with GnRH analogs and sex hormones do not inherently result in sterility—permanent infertility.

13. Alabama's (14) and Do No Harm's (10) Briefs also criticize clinical practice guidelines for making strong recommendations based on low- or very low- quality evidence, as those terms are understood within the GRADE system. Making strong recommendations based on low- or very low-quality evidence is not unique to guidelines about gender-affirming medical care or guidelines produced by the Endocrine Society. For example, 33.9% (121 of 357) of the strong recommendations in all of the Endocrine Society clinical practice guidelines published between 2005 and 2011 and 55.4% (160 of 289) in World Health Organization (WHO) guidelines on a wide variety of topics published between 2007 and 2012 were based on low- or very low-quality

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evidence to recommendation-determinants of a recommendation's direction and strength. *J Clin Epidemiol*. 2013;66(7):726-735.

evidence.[17] The GRADE approach does not preclude this from being done and identifies 5 situations in which it is appropriate.[18] In Gordon H. Guyatt and his colleagues' study of the Endocrine Society's guidelines, they found that 3 of the 8 strong recommendations based on low- or very low-quality evidence in the first version of the gender-affirming medical care guideline fulfilled these conditions, including "we recommend that suppression of pubertal hormones start when girls and boys first exhibit physical changes of puberty …, but no earlier than Tanner stages 2-3" and "we recommend that GnRH analogues be used to achieve suppression of pubertal hormones."[19] Even if one believed that a strong recommendation for an intervention was not justified by the best available evidence, the requisite correction according to the GRADE guidelines[20] would be to make a weak recommendation for the intervention and not a strong

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[17] Brito JP, Domecq JP, Murad MH, Guyatt GH, Montori VM. The Endocrine Society guidelines: When the confidence cart goes before the evidence horse. *J Clin Endocrinol Metab*. 2013;98(8):3246-3252; Alexander PE, Bero L, Montori VM, et al. World Health Organization recommendations are often strong based on low confidence in effect estimates. *J Clin Epidemiol*. 2014;67(6):629-634. Dr. Guyatt and his colleagues also conducted a study of guidelines developed by the American College of Cardiology and the American Heart Association, and the American Society of Clinical Oncology. Although these organizations use alternative methods to characterize the quality of the evidence and the strength of the recommendations, Guyatt et al. found that 32.4% (232 of 715) and 21.7% (122 of 561) of their recommendations respectively were discordant—strong recommendations based on low-quality evidence. Yao L, Ahmed MM, Guyatt GH, et al. Discordant and inappropriate discordant recommendations in consensus and evidence based guidelines: Empirical analysis. *BMJ*. 2021;375:e066045.

[18] Andrews JC, Schunemann HJ, Oxman AD, et al. GRADE guidelines: 15. Going from evidence to recommendation-determinants of a recommendation's direction and strength. *J Clin Epidemiol*. 2013;66(7):726-735. One of these five situations is, for example, when there are two alternatives and, although there is low-quality evidence regarding the relative benefit of the first alternative, there is high-quality evidence of the relative harm of the second alternative.

[19] Brito JP, Domecq JP, Murad MH, Guyatt GH, Montori VM. The Endocrine Society guidelines: When the confidence cart goes before the evidence horse. *J Clin Endocrinol Metab*. 2013;98(8):3246-3252. See Supplemental Table 4.

[20] Andrews J, Guyatt G, Oxman AD, et al. GRADE guidelines: 14. Going from evidence to recommendations: The significance and presentation of recommendations. *J Clin Epidemiol*. 2013;66(7):719-725.

recommendation against it.

CONFLICT OF INTERESTS

14. Contrary to Alabama Brief's general assertions, clinical expertise is necessary for the development of clinical practice guidelines. The Institute of Medicine (IOM) recommends, "The [guideline development group] should be multidisciplinary and balanced, comprising a variety of methodological experts *and clinicians*, and populations expected to be affected by the [clinical practice guideline] (italics added)."[21] The report states that the clinicians should include both generalists and subspecialists involved in clinical practice guideline-related care processes. The exclusions to the management of conflicts of interest acknowledge, "In some circumstances, a [guideline development group] may not be able to perform its work without members who have [conflicts of interests], such as relevant clinical specialists who receive a substantial portion of their incomes from services pertinent to the [clinical practice guideline]."[22] In the United States (U.S.), it is unclear who would produce clinical practice guidelines if not medical professional organizations.

15. Alabama's Brief characterizes WHO's and IOM's standards as bare minimums when they are instead ideal standards that individuals and organizations can seek to achieve but that individuals and organizations in all medical specialties infrequently meet in actual practice. The only organization in the U.S. of which I am aware that potentially meets these expectations is the U.S. Preventive Services Task Force (USPSTF). The USPSTF is convened and supported by the U.S. Department of Health and Human Services' Agency for Healthcare Research and

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[21] Institute of Medicine. *Clinical Practice Guidelines We Can Trust.* The National Academies Press; 2011: 93.

[22] Institute of Medicine. *Clinical Practice Guidelines We Can Trust.* The National Academies Press; 2011: 83.

Quality.[23] It is important to note that the USPSTF does not exclude all potential conflicts of interest but has policies and procedures to manage them.[24] For example, general membership in a professional society need not be disclosed. And while providing public comments, giving expert testimony, and participating in a professional society as an officer must be disclosed, this does not limit the Task Force member's participation in the topic process. The USPSTF is thus able to both recruit members who are highly regarded research, clinicians, and academicians necessary to produce high quality, evidence-based recommendations and maintain public confidence in the integrity of the process.[25] USPSTF's scope is limited to making recommendations about clinical preventive services, like screenings and preventative medications,[26] and recommendations for medical treatments, such as gender-affirming medical care, are outside of its scope. I am unaware of a comparable U.S. organization that develops clinical practice guidelines for medical treatments. The IOM, renamed the National Academy of Medicine, which Alabama's Brief cites, for example, does not produce clinical practice guidelines.

16. Professional medical organizations provide a valuable service to their members and the patients they treat by using their own resources to develop clinical practice guidelines in the absence of a better alternative. These organizations generally have policies and procedures to

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[23] U.S. Preventive Services Task Force. About the USPSTF. Accessed February 26, 2025. Available at https://www.uspreventiveservicestaskforce.org/uspstf/about-uspstf.

[24] U.S. Preventive Services Task Force. Conflict of interest disclosures. July 2024. Accessed February 26, 2025. Available at https://www.uspreventiveservicestaskforce.org/uspstf/about-uspstf/conflict-interest-disclosures.

[25] U.S. Preventive Services Task Force. Procedure Manual Section 1. Overview of U.S. Preventive Services Task Force Structure and Processes. Accessed February 26, 2025. Available at https://www.uspreventiveservicestaskforce.org/uspstf/about-uspstf/methods-and-processes/procedure-manual/procedure-manual-section-1#7.

[26] U.S. Preventive Services Task Force. About the USPSTF. Accessed February 26, 2025. Available at https://www.uspreventiveservicestaskforce.org/uspstf/about-uspstf.

manage conflicts of interest and acknowledge remaining potential conflicts of interest in the published guidelines. The Endocrine Society, for example, requires potential authors to disclose potential conflicts of interest including relationships with non-commercial organizations and paid or unpaid expert testimony.[27] Its clinical practice guideline for the endocrine treatment of gender-dysphoric/gender-incongruent persons includes disclosures of its authors.[28]

CAUSES

17. Contrary to Do No Harm's Brief's implication (13), there are many medical conditions whose cause is not known but that nonetheless have well established treatments. Kawasaki disease, for example, is an acute febrile illness in children which causes inflammation of the blood vessels and, in some cases, ballooning of the blood vessels that supply the heart. The American Heart Association's (AHA's) clinical practice guideline for the diagnosis, treatment, and long-term management of this condition states, "Kawasaki disease (KD) is an acute, self-limited febrile illness of unknown cause that predominantly affects children <5 years of age" and that "[d]espite 4 decades of investigation, the cause of KD remains unknown." The AHA nonetheless recommends individuals with Kawasaki disease be treated with intravenous immunoglobulin (Class 1; Level of Evidence A).[29] The American College of Cardiology

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[27] Endocrine Society. Conflict of interest policy and procedures for Endocrine Society clinical practice guidelines. June 2019. Accessed February 26, 2025. Available at https://www.endocrine.org/-/media/endocrine/files/cpg/methodology-page-refresh/conflict_of_interest_cpg_final.pdf. The policy at the time the guideline on the endocrine treatment of gender-dysphoric/gender-incongruent persons was published, as best as I can discern, was as follows: Endocrine Society. Clinical practice guideline methodology. 2017. Accessed February 26, 2025. Available at https://web.archive.org/web/20170627174844/http://www.endocrine.org/education-and-practice-management/clinical-practice-guidelines/methodology.

[28] Hembree WC, Cohen-Kettenis PT, Gooren L, et al. Endocrine treatment of gender-dysphoric/gender-incongruent persons: An Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab*. 2017;102(11):3895.

[29] McCrindle BW, Rowley AH, Newburger JW, et al. Diagnosis, treatment, and long-term

Foundation and the AHA use different categories for the quality of evidence and the strength of recommendations[30] than the GRADE system. This treatment recommendation can, nonetheless, be interpreted as a strong recommendation based on high quality evidence.

CHANGES IN PREVALENCE

18. The increased number of transgender individuals and those receiving medical treatment, contrary to Do No Harm's Brief's implication (13), does not support the Denial of Care Order. The causes of these changes are likely to be multifactorial including increased social acceptance of transgender individuals and availability of gender-affirming medical care.[31] Changes in demographics are not unique to gender dysphoria and have been seen in other conditions such as autism spectrum disorder and childhood-onset type 1 diabetes.[32] These changes are a justification for further research on gender-affirming medical care rather than prohibiting these treatments and thereby preventing further research on them.

CONCLUSIONS

19. Treating adolescents and adults with gender dysphoria with gender-affirming

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management of Kawasaki disease: A scientific statement for health professionals from the American Heart Association. *Circulation*. 2017;135(17): e927-e999. The quotations appear on pages e928 and e931 respectively.

[30] American College of Cardiology Foundation, American Heart Association. Methodology manual and policies from the ACCF/AHA Task Force on practice guidelines. June 2010. Accessed February 26, 2025. Available at https://www.acc.org/-/media/Non-Clinical/Files-PDFs-Excel-MS-Word-etc/Guidelines/About-Guidelines-and-Clinical-Documents/Methodology/2014/Methodology-Practice-Guidelines.pdf?la=en&hash=157B7835091CF7856B26528717BE14B33BE8226F.

[31] Wiepjes CM, Nota NM, de Blok CJM, et al. The Amsterdam Cohort of Gender Dysphoria Study (1972-2015): Trends in prevalence, treatment, and regrets. *J Sex Med*. 2018;15(4):582-590.

[32] Christensen DL, Maenner MJ, Bilder D, et al. Prevalence and characteristics of autism spectrum disorder among children aged 4 years - Early Autism and Developmental Disabilities Monitoring Network, seven sites, United States, 2010, 2012, and 2014. *MMWR Surveill Summ*. 2019;68(2):1-19; The DIAMOND Project Group. Incidence and trends of childhood type 1 diabetes worldwide 1990-1999. *Diabet Med*. 2006;23(8):857-866.

medical care under clinical practice guidelines, like the Endocrine Society's, is evidence-based; its potential benefits outweigh its potential risks for many patients; and, in the case of adolescents, these risks are well within the range of other medical decisions that adolescents and their parents or guardians have the discretion to make in consultation with their healthcare professionals.

20. Based on my research and experience as a pediatrician and bioethicist, there is no sound medical or ethical basis to prohibit healthcare professionals and entities from providing gender-affirming medical care to individuals with gender dysphoria under 19 years of age. Doing so puts clinicians and healthcare entities in the untenable position of having to harm their patients and violate their integrity and ethical obligations due to the threat of loss of federal funding.

21. The documents that I have reviewed in preparing this reply declaration have not caused me to change my mind on these conclusions.

I declare under penalty of perjury under the laws of the United States of America that the foregoing is true and correct.

Executed on FEB 26, 2025

ARMAND H. MATHENY ANTOMMARIA, MD, PhD