THE NATIONAL CATHOLIC BIOETHICS CENTER
600 REED ROAD, SUITE 102, BROOMALL, PA 19008 (215) 877-2660 (215) 877-2688 FAX NCBCENTER.ORG

January 29, 2024

Division of Reproductive Health
National Center for Chronic Disease Prevention and Health Promotion
Centers for Disease Control and Prevention
4770 Buford Highway NE, Mailstop S107–2
Atlanta, Georgia 30341

Attention: Assisted Reproductive Technology Surveillance and Research Team/Tiffany Brown.

Re: Docket No. CDC-2023-0093 – 0001 to obtain comment on and review of proposed modifications to data collection fields for reporting of pregnancy success rates from assisted reproductive technology (ART) programs and proposed modifications to data validation procedures. [Document Citation: 88 FR 83131]

Division of Reproductive Health:

On behalf of The National Catholic Bioethics Center (NCBC), the Catholic Medical Association (CMA), and the National Association of Catholic Nurses, USA (NACN-USA) we would like to respond to the following provisions in the "proposed modifications to data collection fields for reporting of pregnancy success rates from assisted reproductive technology (ART[1]) programs and proposed modifications to data validation procedures."

The National Catholic Bioethics Center (NCBC) was established in 1972 to address the ethical issues arising in health care and the life sciences, as technological advances, including assisted reproductive technologies (ART), were outpacing the ethical analysis needed to assure the protection of vulnerable populations. Its educational programing, leading to two graduate degrees, publications, and most importantly its consultation services attest to the fact that persons have struggled with the consequences of certain methods of ART. Fertility Awareness

[1] Assisted Reproductive Technology: Anytime eggs or embryos are handled outside a woman's womb. See https://cbc-network.org/issues/making-life/making-life-2/.

Based Methods (FABM) avoid the risks and side effects, not only to women but also to the children engendered, especially by *in vitro* fertilization (IVF).[2]

The Catholic Medical Association (CMA) and the National Association of Catholic Nurses, USA (NACN-USA) represent thousands of health care providers, who are committed to serving the best interest of the hundreds of thousands of persons for whom they provide care, including the children who are engendered, regardless of how those sacred lives come into existence. As such they share the concerns summarized above, by NCBC.

NCBC, CMA, and NACN-USA are very concerned about the evidenced-based consequences of certain methods of assisted reproductive technologies, including the risks and side effects, not only to women but also to the children engendered, especially by *in vitro* fertilization (IVF). While we oppose methods that separate the sacred unity of a husband and wife in achieving procreation, we wish to comment on the need for rigorous record keeping and reporting when such manipulation of human reproduction is occurring. We are grateful to you for the opportunity to express our concerns, as follows:

CDC proposal to remove the requirement for clinics to report dosage information for fertility medications including Clomiphene, Letrozole, and long-acting FSH.

Some may argue that this proposed change in data collection is not problematic, particularly due to the infrequent use of long-acting follicle-stimulating hormone (FSH). However, long-acting FSH is available for three-month trials in the United States,[3] and is considered to be more desirable by some oocyte (egg) donors. A Brazilian study of corifollitropin alfa combined with GnRH agonist in triggering in oocyte donation cycles found:

> Regarding corifollitropin alfa, a single injection of this long-acting FSH on the first day of stimulation can replace the first seven daily injections of rFSH, simplifying treatment and making assisted reproduction more acceptable of patients; which for donors can be of particular importance, especially during a first treatment when they may be nervous or afraid as they have had no previous experience of the procedure. In fact, when donors were asked to choose which treatment they preferred, the results clearly showed a positive trend favoring corifollitropin alfa, suggesting that this new protocol may reduce the treatment burden and increase donor adherence.[4]

Thus, there is a desire for the use of long-acting FSH by donors. However, FSH, regardless of protocol has documented risks. Side effects of ovarian stimulation include ovarian

---

[2] Facts about Fertility (FACTS, Re-vitalizing Women's Health Care Together). Last viewed January 25, 2024. https://www.factsaboutfertility.org/.

[3] "The FDA allows the importation of up to three months supply for personal use," *IVF Pharmacy*. Accessed January 26, 2024. https://www.ivfpharmacy.com/drug/Elonva.aspx#:~:text=The%20FDA%20allows%20the%20importation,required%20to%20buy%20Elonva%20online.

[4] Ioannis Tsakiridis, et al., "Evaluation of the safety and efficacy of corifollitropin alfa combined with GnRH agonist triggering in oocyte donation cycles. A prospective longitudinal study," *JBRA Assist Reprod*. (2020 Oct-Dec; 24(4)): 436–441. https://www.ncbi.nlm.nih.gov/pmc/journals/3116/.

hyperstimulation syndrome (swollen and painful ovaries); and the risks of *in vitro* fertilization include: ectopic pregnancy; multiple births; a slightly higher risk of a baby being born with heart issues, digestive problems, or other conditions; and the risk that the baby will be born early or with a low birth weight.[5] And while earlier studies found a link to a specific type of ovarian tumor, more recent studies do not support these findings. However, some studies have found that the use of clomiphene citrate (Clomid) for at least a year may increase risk for ovarian tumors. The risk was highest among women who did not get pregnant, so it remains unclear if the risk is due to infertility or the drug.[6] This is significant since ovarian cancer grows quickly and can progress from early stages to advanced stages within a year.[7] Thus, collecting data on dosing of any of these drugs, including frequency of dosing, is critical, especially since the dose of some such medicines will be different for different patients.[8]

These reports indicate the need for the gathering of as much data as possible, including data on the variable doses that may be used. The long-term impact on such women needs to be identified, and that can only be done by reporting. This need is compounded by the fact that while the U.S. Centers for Disease Control and Prevention do regulate the safety of the tissue (sperm/eggs) of donors, they do not track long term effects on the donors of eggs (oocytes):

> The Centers for Disease Control and Prevention (CDC) collects and publishes data on ART procedures. The Food and Drug Administration (FDA) controls approval and use of drugs, biological products, and medical devices and has jurisdiction over screening and testing of reproductive tissues, such as donor eggs and sperm. The Centers for Medicare and Medicaid Services (CMS) is responsible for implementation of the Clinical Laboratory Improvement Act to ensure the quality of laboratory testing.[9]
>
> The FDA also has jurisdiction over screening and testing of reproductive tissues, such as the eggs and sperm that will be implanted in human recipients. Regulations issued by the agency contain strict requirements for egg and sperm donors, including thorough medical histories, identification controls, freedom from infectious diseases, and rigorous inspection of the facilities in which these tissues are handled. Inspectors can order the recall or destruction of tissue that is infected with a communicable disease. The agency

---

[5] Mayo Clinic, "In vitro Fertilization: Risks" (Sept. 1, 2023). https://www.mayoclinic.org/tests-procedures/in-vitro-fertilization/about/pac-20384716.

[6] Roswell Park Comprehensive Cancer Center, *Ovarian Cancer Risk Factors.* Accessed January 25, 2024. https://www.roswellpark.org/cancer/ovarian/what-ovarian-cancer/risk-factors#:~:text=Some%20studies%20found%20that%20women,to%20infertility%20or%20the%20drug..

[7] The University of Kansas Cancer Center, *What Is Ovarian Cancer: Symptoms, Detection and Treatment.* Accessed January 25, 2024. https://www.kucancercenter.org/news-room/blog/2020/08/what-is-ovarian-cancer-symptoms-treatment#:~:text=Ovarian%20cancer%20grows%20quickly%20and,spread%20in%20weeks%20or%20months.

[8] Mayo Clinic, "Drugs and Supplements: Follitropin Beta (Subcutaneous Route)" (Last updated May 1, 2023). https://www.mayoclinic.org/drugs-supplements/follitropin-beta-subcutaneous-route/side-effects/drg-20063913?p=1.

[9] American Society for Reproductive Medicine, "Oversight of Assisted Reproductive Technology," *ASRM*. Accessed Jan. 27, 2024. https://www.asrm.org/advocacy-and-policy/media-and-public-affairs/oversite-of-art/#:~:text=The%20Centers%20for%20Disease%20Control%20and%20Prevention%20(CDC)%20collects%20and,as%20donor%20eggs%20and%20sperm.

has established good tissue practices that are codified in 21 CFR 1271 (https://www.ecfr.gov/current/title-21/chapter-I/subchapter-L/part-1271).[10]

Furthermore, other than laboratory regulation, and contracts related to surrogacy and donation, there is little regulation at the state level. Clearly, the long-term follow up of donors and those women who are egg/embryo recipients, including surrogates, should be mandated. Furthermore, as addressed, below, the requirement of reporting information of research cycle study type should be retained.

CDC proposal to remove the requirement for clinics to report information on research cycle study type.

This deletion will apply to all data fields for research study types: Device study, Protocol study, Pharmaceutical study, Laboratory technique, and other research. Currently cycle-specific data for the following patients must be reported: (1) All patients undergoing assisted reproductive technology (ART), (2) all patients undergoing ovarian stimulation or monitoring with the intent of undergoing ART but who did not proceed to oocyte retrieval or transfer of embryos for any reason, including patients whose cycles were canceled for any reason, (3) all patients providing donor oocytes, and (4) all patients undergoing monitoring and/or embryo (or oocyte) thawing with the intention of transferring cryopreserved embryos. However, this proposal states: "This deletion will apply to all data fields for research study types."[11] Even if only a small number of research cycles are performed each year, each cycle involves human subjects who need the protections associated with such reporting. Furthermore, there must be the protections of an independent Institutional Review Board, especially in for-profit fertility practices in which there can be a disincentive to document less-than-favorable data. This is especially problematic since there is a fine line between fertility treatments and research. Patient safety requires that this differentiation between practice and research be clearly identified. This is especially of concern since the definition of assisted reproductive technology involves gametes and embryos outside of a women's' body. Herein raises the questions of the long-term wellbeing of surrogates, sometimes termed "gestational carriers," as well as the unborn, and subsequently the child who is born.

There needs to be strong regulation to prevent the abuse of women as "gestational carriers," which is an afront to the women and the children who are considered a commodity by these very procedures. This is especially true if the ART involves research. If a clinic study type is not reported, significant abuses can occur. The same is true for research involving recent technologies such as "three person embryos" by mitochondrial donation.[12] And although the implantation of such engendered embryos is not permitted in the United States, they are

[10] *Ibid.*
[11] 88 FR 83131.
[12] Hana Carolina Moreira Farnezi, "Three-parent babies: Mitochondrial replacement therapies," *JBRA Assist Reprod.* (2020 Apr-Jun; 24(2)): 189–196. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7169912/.

engendered in the U.S. and implanted in a foreign country.[13] Thus, such research processes need to be well regulated. There are significant risks to the embryos engendered, and potentially to the egg or embryo donor, and the potential negative effects to the gene pool.[14] Furthermore, the whole area of uterus transplants raises ethical questions concerning the wellbeing of the mother and the risks to which the embryo/fetus is subjected. The transplant is regulated by the Organ Procurement and Transplantation Network, which addresses issues of transplantation, but not assisted reproductive technology.[15] Again, there is a fine line between fertility treatments and research, and there is a need for the reporting on these specific issues, specifically of research cycle study type.

CDC proposal to add the requirement for clinics to report date of cryopreservation for fresh embryos.

This proposal indicates that this new requirement will allow for the classification of embryo stage of development before embryo freezing, and the dates of freezing and implantation into the uterus. Monitoring of such factors could impact assisted reproductive technology success rates. While this is a violation of the dignity of the human person, who is the embryo, and who is treated as a commodity to be frozen for an uncertain fate, the more data that are reported on ART, the more regulatory oversight there can be of a field subject to for-profit incentives. However, there is the reality that such dating may be used to label these young human beings as "unworthy" of implantation, and thus relegate them for research and/or destruction. Already the embryo is subject to procedures that commodify the embryo through preimplantation genetic diagnosis and other manipulations that are dangerous to the embryo. The results often relegate the embryo to research and/or destruction, which would be an unethical fate, violating the very purposes of reproductive technology. However, the reporting of such data and procedures could identify incentives for successes which could put the embryos at risk of never being allowed the protection of a mother's womb.

CDC proposal to not pursue targeted validation of clinics and identification of major data discrepancies.

Although identifying major data discrepancies would require review of a large number of clinic records at select clinics, perhaps creating a data collection burden on clinics, there remain significant reasons for patient safety to pursue major data discrepancies. Declining to participate in annual assisted reproductive technology data validation should raise the concern

[13] Emily Mullin, "U.S. researcher says he's ready to start four pregnancies with 'three-parent' embryos," *STAT* (April 18, 2019). https://www.statnews.com/2019/04/18/new-york-researcher-ready-to-start-pregnancies-with-three-parent-embryos/.

[14] Vicente Javier Clemente-Suárez, et al., "Mitochondrial Transfer as a Novel Therapeutic Approach in Disease Diagnosis and Treatment," *Int J Mol Sci.* (2023 May; 24(10)): 8848. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10218908/#:~:text=Mitochondrial%20transfer%20involves%20the%20exchange,types%20%5B1%2C13%5D.

[15] Health Resources and Services Administration, *Guidance on Optimizing VCA Recovery (2023 Version)*. (Dec. 4, 2023). 2023dec_vca_guidance_language PDF (optn.transplant.hrsa.gov).

for pursuing these same discrepancies, especially in a for-profit industry. We recommend data gathering and regulatory follow-up on discrepancies, especially requiring data on:

> Oocyte yield per procedure;
> Methods of fertilization: e.g., Intracytoplasmic sperm injection (ICSI);
> Number of attempts and successes in implantation per cycle;
> Number of embryos implanted in each woman, and number resulting in a successful birth or selectively reduced through abortion;
> Birth weights;
> Number of ectopic pregnancies;
> Status of embryos not implanted, number donated for research;
> Number of genetic defects/chromosomal abnormalities, e.g., cleft lip or palate, neural tube defect, cardiac defects, limb defects, other defects;
> Number of cycles from donors, as well as gestational carriers;
> Long term follow-up of the health and wellbeing of the children engendered, and the women who have undergone ovarian hyperstimulation/donors/gestational carriers (a live birth does not necessarily guarantee the long-term health of the baby.).

Furthermore, the Organ Procurement and Transplantation Network (OPTN) prohibits monetary inducements for tissue donation for transplant.[16] Reproductive tissue is included in the regulation of vascular composite allographs for transplantation. However, the donation of egg and sperm for ART purposes has no such regulatory provisions. There appears to be a reliance on self and peer regulation through professional organizations which are voluntary mechanisms. In the *Fertility Clinic Success Rate and Certification Act* of 1992 and subsequent regulations, clinics were required to report data, including pregnancy success rates.[17] This proposal will allow clinics to avoid addressing discrepancies in reported data. Some clinics do rely on verification from the Centers for Disease Control and Prevention (CDC) to demonstrate that they are in good standing with the CDC. More importantly, consumers rely on the CDC to provide them with accurate information when selecting a fertility clinic. Omitting a follow-up to data discrepancies by the CDC adds further to the self-regulation mentality, allowing fertility clinics to market themselves as in full regulatory compliance without the requisite oversight. It is deceptive to the public. This proposed provision will potentially do more harm to women and their babies. There is potential for placing women and embryos at risk, through profit incentives. There must be rigorous enforcement mechanisms for rectifying major data discrepancies as well as non-reporting of required data.

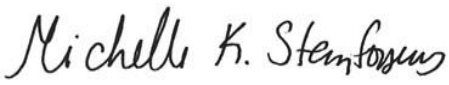
[16] Organ Procurement and Transplantation Network, "Financial Incentives for Organ Donation: A Report of the Payment Subcommittee of the Ethics Committee" (June 1993). https://optn.transplant.hrsa.gov/professionals/by-topic/ethical-considerations/financial-incentives-for-organ-donation/#:~:text=Based%20on%20the%20Uniform%20Anatomical,the%20rate%20of%20organ%20donation.

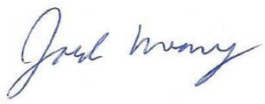
[17] *Fertility Clinic Success Rate and Certification Act* of 1992, Public Law 493, U.S. Statutes at Large 106 (1992): 3146-3152. https://www.govinfo.gov/app/details/STATUTE-106/STATUTE-106-Pg3146.

Conclusion

While the assisted reproductive technology policies addressed here are not consistent with our understanding of the sacred nature of human reproduction between a husband and a wife, in partnership with the Author of Life, our Creator, the National Catholic Bioethics Center, the Catholic Medical Association, and the National Association of Catholic Nurses, USA are grateful to the Centers for Disease Control and Prevention for allowing us this opportunity for public comment. By so doing, we hope to at least provide for the protection of all the women involved in these technologies, and to plead for methods that respect the life and dignity of the embryos and fetuses who are subject to risks, and sometimes to destruction, by such technologies.

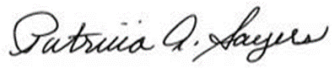
Sincerely yours,





Michelle K. Stanford, MD
President
The Catholic Medical Association
550 Pinetown Road Suite 205
Fort Washington, PA 19034
484-270-8002

Joseph Meaney, PhD
President
The National Catholic Bioethics Center
600 Reed Road, Suite 102
Broomall, PA, 19008
215-877-2660



Patricia Sayers, DNP, RN
President
The National Association of Catholic Nurses, USA
P.O. Box 4556
Wheaton, IL 60189
630-909-9012