

December 23, 1999

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Dockets Management Branch(HFA-305)
Food and Drug Administration
5360 Fishers Lane Room 1061
Rockville, Md 20852

RE: Docket #97N-484S; Suitability Determination for Donors of Human Cellular and Tissue-based products.

Dear Committee:

I am a board certified reproductive endocrinologist in private practice in Arizona. I am responding to the proposed recommendations and the impact these will have on my practice and the outcomes. At the current time, the recommendations from SART have been followed by all colleagues with whom I have spoken. Screening labs for egg donors are applied, and there is question as to the practicality of certain practices. Your recommendations extend things further and will create greater efforts with little to no observable benefit. Theoretical risk is often too small to measure and hence has to be juxtaposed against the benefit of the proposed options/processes.

The current proposals for egg donors would have them tested for HIV types 1 and 2, hepatitis B, hepatitis C, syphilis, and transmissible spongiform encephalopathies. Additionally, there is proposed testing for HTLV I and II and CMV. Screening for chlamydia and gonococcus within 48 hours of recovery. All this and then six months of cryo-quarantine for the embryos/eggs and retesting negative prior to using the tissues.

There is no evidence that the oocytes, embryos or isolated sperm cells used with IVF-ET are vectors of the disease listed in the FDA proposal. HIV or other infectious diseases are not passed by IVF-ET. No specific papers claiming this have been found. No HIV has been contracted from IVF in 21 years as far as anyone knows. To better understand this risk, I recommend you refer to the literature regarding transmission of HIV with single acts of intercourse, then with simple washed semen, and then with density gradient washed semen. The trend is astounding. Semprini et al have been showing us for years no transmission of HIV to mother or offspring in couples inseminated with semen from HIV positive/infected males. Since the density gradient process removes almost all the white blood cells, the viral load is radically diminished. Even so, Semprini has shown that viral fragments remain on the sperm, but this has not demonstrated viral transmission. As we have been taught, the chance of infection is partly a function of infectious load, and with ART, the opportunity to minimize transfer of any agent is radically reduced, and may be more safe. It seems in the proposed rules, there seems to be no understanding by the FDA that using semen carries with it a much different risk for transmission of disease that the hypothetical risk(so far no risk demonstrated) associated with the use of isolated and washed sperm cell, oocytes and embryos.

97N 484S

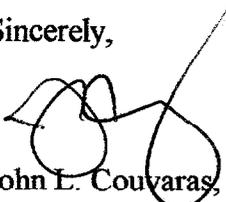
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The past scare for transmission of TSE from potentially tainted biological media, albeit real, has not been given any magnitude because no cases have surfaced that we are privy to after almost 3 years. The incubation time may be longer than this time frame, but we should look at the general population for an assessment of risks versus benefits. My neurology colleagues tell me there is not a good test for such prion presence. Again, I would argue that the proposed protections are for theoretical risks that are incalculable, but the negative impact on the couples using donor eggs or embryos would be profound.

The greatest public health risk at large is still the blood supply and there is no recommendation to freeze the components and quarantine them. This area has the largest impact on the population and yet we are not subjecting them to similar criteria. Are we now facing these new criteria for Assisted Reproduction because there is pressure to appear to take action in the face of the recent infectious disease issues? If so, this discourse should be done, but then a prudent, scientific approach would prevail and cost/benefit and risk/benefit analysis would suggest against the current proposed recommendations. There is risk in everything in this world. Our infertility patients know this more than most and if they are counseled as to the theoretical risks of the presumed infections versus the enhanced outcomes with fresh eggs/embryos, I am confident they would go with the fresh embryos. The option to quarantine has always been available to any person who desires it, but none have sought this option for obvious cost and success issues.

I ardently desire this committee to reconsider their proposed recommendations in the context of the public health arena. Will they really prevent any HIV or TSE transmission in our population to justify setting back the success for thousands of pregnancies. In doing so, the recommendations to cryopreserve and quarantine eggs/embryos should be considered a bad public health opinion.

Sincerely,



John L. Couvaras, M.D.



VF PHOENIX

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