Lambda
LEGAL

August 23, 2004

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, Maryland 20852

Re: *Docket No. 2004D-0193, Draft Guidance for Industry: Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products*

To Whom It May Concern:

We write to you on behalf of Lambda Legal Defense and Education Fund, the Gay and Lesbian Medical Association, the Human Rights Campaign and the National Center for Lesbian Rights regarding the Food and Drug Administration's proposed Guidance for Industry regarding Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products ("the draft Guidance"). In a letter dated December 22, 2003, the organizations on whose behalf we now write submitted a letter regarding the proposed regulations on "Suitability Determination for Donors of Human Cellular and Tissue-Based Products," which the FDA later published as the "Donor Eligibility Rule." That letter raised several concerns regarding the FDA's anticipated but then-unpublished draft Guidance regarding donor eligibility determinations. Some of the concerns and suggestions discussed in the following pages reiterate the comments in our December 2003 letter. In light of the formal publication of the draft Guidance for Industry and the FDA's call for comments in May 2004, we write today to reinforce and supplement some of our earlier suggestions and specifically to address the substance and reach of the draft Guidance.

As organizations dedicated to advancing the civil rights of people with HIV, we strongly support efforts to prevent the spread of HIV and other contagious diseases through science-based policies and programs. We share the FDA's laudable goals of protecting the public health and preventing the transmission of communicable diseases through cell and tissue donation. However, we do not believe that either public health or broader public policy objectives are served by the draft Guidance's exclusion from anonymous reproductive tissue donation of every man who has had

2004D-0193 C17

sex with another man within the five years prior to donation. For the reasons detailed below, we believe that the exclusion of men who have sex with men ("MSMs") is unnecessary and ill-conceived. While we understand that the FDA's final Guidance document will be non-binding, we urge you to remove the MSM exclusion from the Guidance's recommendations. In the place of the broad exclusion of MSMs, we suggest an individualized risk-based assessment that more accurately predicts a donor's actual risk of HIV or hepatitis exposure.

1. The Proposed Guidance's Recommendation that Men Who Have Had Sex with Other Men Be Prohibited from Donating Sperm Lacks a Foundation in Sound Science.

We find no legitimate scientific rationale for the suggestion in the draft Guidance that MSMs should not be permitted to serve as anonymous donors of reproductive tissue. As you know, recently published 21 C.F.R. § 1271.50(b) provides that all anonymous sperm donors must pass mandatory "donor screening" and testing in order to be considered eligible for donation. Men who wish to donate sperm anonymously may do so only if they are "free from risk factors for, and clinical evidence of, infection due to relevant communicable disease agents and diseases," including HIV, hepatitis B virus and hepatitis C virus. 21 C.F.R. § 1271.50(b)(1). The FDA's draft Guidance lists all "conditions and behaviors [that] increase the donor's relevant communicable disease risk," and recommends that any anonymous donor exhibiting any of the listed behaviors should be considered "ineligible." *See* Draft Guidance for Industry, § III.E. Among other exclusions, the draft Guidance notes that tissue should not be accepted from "men who have had sex with another man within the preceding 5 years." *See* draft Guidance for Industry, § III.E.1.

We do not believe that this broad exclusion of men who have had sex with men is necessary or appropriate to minimize the risk of HIV or hepatitis transmission to sperm donation recipients. In the preamble to the final Donor Eligibility Rule, the FDA suggested that the draft Guidance's proposed five-year exclusion of MSMs serves two purposes. First, the FDA has suggested that the exclusion will prevent donations by men who recently have been exposed to HIV or hepatitis, but who do not yet test positive on standard assays, noting that "even [nucleic acid amplification] testing may fail to detect early stage HIV and other infection." *See* 69 Fed. Reg. 29786, 29806 (May 25, 2004). Second, the FDA has proposed excluding MSMs in order to provide additional insurance in case of laboratory error during screening for relevant diseases because "even the best test may fail to provide an accurate test result due to human error in running the test or in linking the test result to the correct donor." *See id.* However, in light of the mandatory six-month quarantine and double testing of all donors' blood for relevant contagious diseases, neither of these rationales actually justifies the five-year exclusion in the draft Guidance. In short, the five-year exclusion of MSMs is excessive and does not serve the goals proposed by the FDA.

a. The FDA's concerns about donations during the "window period" do not support the five-year exclusion of MSMs.

First, to the extent that the FDA bases its suggested five-year exclusion on concerns about sperm donations during the "window period" in which a donor may transmit HIV or hepatitis without testing positive in standard assays, the exclusion is vastly out of proportion to the actual period of risk. A person exposed to HIV or hepatitis C ("HCV") typically develops detectable antibodies within the first two to three months after infection, if not earlier, and the overwhelming majority seroconvert within the first six months.[1] People with hepatitis B ("HBV") similarly test positive for the HBV surface antigen shortly after exposure.[2] Moreover, advances in testing technology are effectively shrinking these "window periods" even further.[3] The five-year exclusion in the draft Guidance far exceeds the actual period during which an HIV- or hepatitis-infected donor might test negative for these viruses.

The FDA's purported concerns about the "window period" are even less well-founded in light of the availability of nucleic acid amplification testing ("NAT"). While an individual often may experience a one- or two-month window between initial exposure to HIV, HCV or HBV and a positive test result on a standard antibody assay, NAT testing reduces the window between exposure and detection to a matter of days

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[1] L. R. Petersen et al., Duration of Time from Onset of Human Immunodeficiency Virus Type 1 Infectiousness to Development of Detectable Antibody, *Transfusion* 1994; 34: 283; C. A. Ciesielski et al., Duration of Time Between Exposure and Seroconversion in Healthcare Workers with Occupationally Acquired Infection with Human Immunodeficiency Virus, *American Journal of Medicine* 1997; 102(5B):115; S. Lindbäck et al., Diagnosis of Primary HIV-1 Infection and Duration of Follow-up After HIV Exposure, *AIDS* 2000; 14:2337; Centers for Disease Control and Prevention, Recommendations for Preventing Transmission of Infections Among Chronic Hemodialysis Patients, *Morbidity and Mortality Weekly Report* 2001; 50 (No. RR-5):11-12.

[2] Centers for Disease Control and Prevention, Recommendations for Preventing Transmission of Infections Among Chronic Hemodialysis Patients, *Morbidity and Mortality Weekly Report* 2001; 50 (No. RR-5): 2-9.

[3] *See* B. Weber et al., Reduction of Diagnostic Window by New Fourth-Generation Human Immunodeficiency Virus Screening Assays, *Journal of Clinical Microbiology* 1998; 36(8): 2235-2239; D. P. Kolk et al., Significant Closure of the Human Immunodeficiency Virus Type 1 and Hepatitis C Virus Preseroconversion Detection Windows with a Transcription-Mediated-Amplification-Driven Assay, *Journal of Clinical Microbiology* 2002; 40(5): 1761-1766.

or weeks.[4] In fact, the FDA's draft Guidance specifically recommends that sperm donors "be tested with FDA-licensed NAT blood donor screening tests for HIV and HCV." *See* Draft Guidance for Industry, § V.A. In light of the extremely small "window period" allowed by NAT testing, the FDA's five-year exclusion for all MSMs lacks validity.

Moreover, as currently drafted, the proposed Donor Suitability Rule already addresses any "window period" concerns by requiring the quarantine of all anonymous donations for at least six months to allow for retesting of donors. Indeed, the commentary preceding the final Donor Eligibility Rule noted that the purpose of the six-month quarantine was to address precisely this issue. *See* 69 Fed. Reg. at 29800 ("The requirement to retest the donor was intended to provide an important added measure of protection by addressing the 'window period' between the time of infection and the presence of detectable levels of antigens and/or antibodies to communicable diseases and agents such as HIV."); *see also* 64 Fed. Reg. 52696, 52706 (September 30, 1999). This six-month quarantine eliminates any concern about false-negative testing during the "window period," rendering the draft Guidance's additional five-year deferral for MSMs unnecessary.

b. In light of the rarity of testing error and the double-testing of all anonymous donations, the FDA's concerns about testing error cannot justify the exclusion of MSMs.

Second, to the extent that the FDA's suggested five-year MSM exclusion reflects a concern about testing error, the danger is similarly overstated and similarly overbroad. While rates of testing error vary depending on the quality of particular testing programs, lab error in HIV and HCV testing is extraordinarily rare. For instance, a 2000 study of false-negative testing errors in routine blood donor screening found that the rate of procedural errors in the testing process was .05 percent.[5] Applying this error rate to the donor pool as a whole, the authors estimated a false-

[4] *See* S. Stramer et al., Detection of HIV-1 and HCV Infections among Antibody-Negative Blood Donors by Nucleic Acid-Amplification Testing, *N. Eng. J. Med.* 2004, 351(8): 760-768; S. Zou et al., Probability of Viremia with HBV, HCV, HIV, and HTLV among Tissue Donors in the United States, *N. Eng. J. Med.* 2004, 351(8): 757. *See generally* Human Cells, Tissues and Cellular and Tissue-Based Products: Risk Factors for Semen Donation, Blood Products Advisory Committee (BPAC) Meeting, Hilton Silver Spring Hotel, December 14, 2001, testimony of George Schreiber.

[5] M.P. Busch et al., False-Negative Testing Errors in Routine Viral Marker Screening of Blood Donors, *Transfusion* 2000, 40:585-589.

negative HIV test error rate of approximately four per 10 million. An earlier review of 5.4 million HIV-1 antibody tests conducted by the U.S. Army between 1985 and 1992 reached a similar conclusion, finding an error rate of .000588 percent.[6]

Moreover, these error estimates were based on the assumption that each donor will be tested once, not twice, as the FDA's Donor Eligibility Rule requires for anonymous sperm donors. The FDA's requirement that each anonymous donor submit to two separate rounds of testing reduces the risk to nearly zero that any donor infected with HIV or hepatitis will unwittingly pass the donor screening process as a result of laboratory error. As Roy, et al noted in the *Journal of the American Medical Association*, testing error, while exceedingly uncommon, "can be best controlled by repeating all procedures twice."[7]

2. The Proposed Guidance Arbitrarily Subjects Men Who Have Sex with Men to a Five-Year Exclusion from Donation While Permitting Other Individuals at Risk for HIV to Donate Only One Year After Possible Exposure.

The five-year exclusion for men who have had sex with men is particularly questionable when compared to some of the other exclusionary risk factors listed in the draft Guidance. For instance, the draft Guidance suggests the exclusion of any donor who, in the preceding twelve months, has had sex with someone he knows or suspects to be infected with HIV, HBV or HCV. *See* Draft Guidance for Industry, § III.E.5. Similarly, the draft Guidance suggests the exclusion for one year of a donor who has undergone tattooing or piercing with instruments that are known to have been shared with others. *See* Draft Guidance for Industry, § III.E.10. It is not clear why high-risk activities such as these warrant exclusion from sperm donation for twelve months while sex with another man warrants exclusion for five times as long. If you maintain this distinction in the final Guidance, we request that you explain the rationale behind it.

3. The Guidance Should Suggest Donor Deferral Criteria That Are Based on Individualized Risk Assessments Rather Than Sexual Orientation.

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[6] M.J. Roy et al., Absence of True Seroreversion of HIV-1 in Seroreactive Individuals, *JAMA* 1993; 269(22): 2876-2879.

[7] *Id.* at 2878. *See also* Human Cells, Tissues and Cellular and Tissue-Based Products: Risk Factors for Semen Donation, BPAC Meeting, Hilton Silver Spring Hotel, December 14, 2001, testimony of George Schreiber ("Testing error is very small, and with the quarantine, . . . it's reduced almost to zero.").

The screening protocol recommended in the draft Guidance will effectively prohibit most gay and bisexual men from providing anonymous sperm donation, regardless of their individual risk of HIV or hepatitis infection. The draft Guidance does not reflect the reality that an individual's likelihood of exposure to HIV and hepatitis corresponds to the specific high-risk activities in which he engages, not to the sex of the person with whom he has intercourse. Indeed, different sexual practices pose drastically different risks to the participants. For instance, receptive anal sex poses roughly one hundred times as much risk of HIV transmission as insertive fellatio.[8] Additionally, the transmission risk of any sexual act increases approximately twenty-fold if the participants do not use condoms.[9] The FDA's current guidance document does not recognize these distinctions, instead treating protected oral sex between two men in the context of a monogamous relationship the same as unprotected anal intercourse between male strangers. Merely asking whether a donor has had sex with another man within the preceding five years tends to screen donors on the basis of sexual orientation rather than on the basis of actual risk.

To remedy this problem, the final Guidance should suggest more specific screening criteria that measure a potential donor's high-risk activities rather than his sexual orientation. We believe that there are many possible behavioral screening devices that would determine HIV risk more accurately than the criteria proposed in the draft Guidance. For example, the HIV Medicine Association of the Infectious Diseases Society of America has adopted a set of criteria that the Association suggests should be used to screen potential blood donors, but that we suggest can be applied equally in the context of reproductive tissue donation as well. The purpose of the Association's criteria is to screen for HIV risk while ensuring "that individuals are excluded based on risk factors and not solely based on sexual orientation or country of origin." The Association recommends that the FDA should prohibit donation by any individual from the United States[10] who:

1. has tested positive for HIV;
2. has used illicit drugs within the previous 12 months;

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[8]Centers for Disease Control and Prevention, Incorporating HIV Prevention into the Medical Care of Persons Living with HIV: Recommendations of CDC, the Health Resources and Services Administration, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America, *Morbidity and Mortality Weekly Report* 2003; 52 (No. RR-12): 9.

[9] *Id.*

[10]The Association's suggested criteria for donors from other countries is slightly different.

3. has had a needle stick exposure to someone else's blood within the previous 12 months; or
4. in the previous 12 months, has had unprotected oral, vaginal, or anal sexual intercourse with:
    - An individual with HIV,
    - An individual known to use illicit drugs, or
    - An individual of unknown HIV status *outside of a monogamous* relationship

We urge you to consider recommending a screening protocol like this one that screens potential donors on the basis of individual risk without subjecting them to stereotypes based on sexual orientation.

4. The Medical Director or Responsible Individual Should Have Discretion to Follow the FDA's Guidance or to Adopt Alternative Screening Criteria.

Finally, we commend you for acknowledging that the FDA's Guidance, whatever its final content, represents only one of many possible legitimate approaches to donor screening. While any screening protocol naturally should screen donors who exhibit risk factors for HIV, HBV and HCV, there may be a range of different ways to meet that important end. The draft Guidance presents just one possibility. The HIV Medicine Association's suggested blood donor deferral criteria is another legitimate option. Individual sperm banks or state regulators may adopt or suggest other possibilities. As the Federal Register commentary accompanying the draft Guidance indicates, "[a]n alternative approach may be used if such approach satisfies the requirements of the applicable statutes and regulations." *See* 69 Fed. Reg. 29835 (May 25, 2004).

To avoid any confusion in the industry or among potential sperm donors, we request that you explain in plain terms at the beginning of the final Guidance that the document's recommendations are not binding and that the Medical Director or other responsible individual at each sperm bank or clinic has the authority and discretion to adopt alternative screening protocols. We further request that you explicitly mention some alternative screening protocols, such as the HIV Medicine Association criteria described above, that banks and clinics might choose to adopt.

Conclusion

In conclusion, we object to the draft Guidance's exclusion from sperm donation of all men who have sex with other men within the preceding five years. Simply, this screening tool is not tailored to health goals and it unfortunately reinforces anti-gay stigma and suggests falsehoods about the nature of testing and transmission risks. We urge you to remove this criterion from the final Guidance. Thank you for the opportunity to submit these comments. If you have any questions or need additional information, please feel free to contact Jonathan Givner, Lambda Legal, 120 Wall Street, Suite 1500, New York, New York, 10005, telephone (212) 809-8585, email jgivner@lambdalegal.org.

Sincerely,

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