

CASE STUDIES

Case Study 3

Background

Obligations to Third Parties in the Face of Possible Harm

There has been much discussion in recent years about the need for a woman-controlled technology to prevent the transmission of HIV and other sexually transmitted diseases (STDs). Vaginal microbicides are one such product, and function by potentially providing a chemical barrier to HIV and STDs. An effective microbicide would provide a woman with the means to protect herself from disease without encountering the resistance and even violence that might occur should she suggest to her male partner that he use a condom. This issue is particularly troublesome in settings where women trade sex for money or where they are traditionally expected to be unquestioningly subservient and obedient to the needs of the man.

Until recently, the major candidates being investigated were microbicides that contain nonoxynol-9 (N-9) as the active ingredient. N-9 products are licensed for use in the United States as spermicides, and are effective as a contraceptive, particularly when used with a diaphragm. At the 13th International AIDS Conference held in Durban, South Africa in July, 2000, results were presented from a UNAIDS study conducted in four African countries that sought to determine whether low doses of an N-9-containing microbicide in commercial sex workers could prevent HIV infection.

Almost 1,000 HIV-negative women were enrolled in the study, which was conducted from 1996 through May 2000. The effectiveness of an N-9 containing gel called COL-1492 was compared with an inactive placebo gel, a vaginal moisturizer named Replens, in a double-blind design, so neither the researchers nor the participants knew who was using which product. All of the women were informed of the possible risks, benefits, and unknowns involved in the study.

They were also counseled on how to use condoms, urged to use them consistently, and provided with a free supply.

The disappointment was tremendous, therefore, when the results were announced that the "women who used the N-9 gel had become infected at about ~50% higher rate than the women who used the placebo gel. Further, the more frequently women used only N-9 gel (without a condom) to protect themselves, the higher their risk of becoming infected. Simply stated, N-9 did not protect against HIV infections and may have caused more transmission. Women who used N-9 also had more vaginal lesions, which might have facilitated transmission" (CDC, August 4, 2000).

Questions

You are the Chair of the Institutional Review Board (research ethics review committee) at the large U.S. University that is home to the principal investigator of the study. You have recently received a letter from the principal investigator that accompanies the final report about the N.9 study. In the letter the investigator explains that although the risks to the women were properly disclosed in the consent process, the unexpectedly poor effectiveness of the N-9 has resulted in understandable anger and frustration among the women who participated in the study and has left the investigator wondering how she should respond. As well, the increased incidence of vaginal lesions has raised concerns for the investigator about the potential toxicity of N-9 and has also raised the question in her mind about what obligation, if any, she might have to the male partners of the women, who were exposed unknowingly to a potentially toxic agent and who may now be at an increased risk, although the precise nature or the magnitude of that risk is not

known.

Specifically, the investigator poses 3 questions to you as the Chair of the IRB as she seeks direction on what her obligations are in light of the results of the trial:

1. Under the circumstances, what are my obligations to the women who seroconverted during the study?
2. Do the results give rise to new obligations to the women who did not seroconvert? What should I do, if anything, for these women?
3. In light of the potential harm to the male partners of the women in the study, I am concerned about my real or potential obligation to them. What obligations do investigators have to third parties in research and specifically, what steps should I take, if any, to notify these particular men?

Bibliography

1. Botkin JK. Protecting the privacy of family members in survey and pedigree research. *JAMA* 2001; 285: 207-211.
2. Van Damme L, Chandeying V, Ramjee G, Rees H, Sirivongrangson P , / Laga M, Perriens J. Safety of multiple daily applications of COL-1492, a nonoxynol-9 vaginal gel, among female sex workers. COL-1492 Phase II Study Group. *AIDS* 2000 Jan 7;14(1):85-8.
3. Coggins C, Elias C. Safety of three formulations of nonoxynol-9 containing vaginal spermicides. N-9 Formulation Preferences Study Group Committee. *Int J Gynaecol Obstet* 2000; 68(3):267-8.
4. Ramjee G, Morar NS, Alary M, Mukenge- Tshibaka L, Vuylsteke B, Ettiegne- Traore V, Chandeying V, Karim SA, Van Damme L. Challenges in the conduct of vaginal microbicide effectiveness trials in the developing world. *AIDS* 2000;14(16):2553-7.
5. Stafford MK, Ward H, Flanagan A, Rosenstein IJ, Taylor-Robinson D, Smith JR, Weber J, Kitchen VS. Safety study of nonoxynol-9 as a vaginal microbicide: evidence of adverse effects. *J Acquir Immune Defic Syndr Hum Retrovirol.* 1998;17(4):327-31.

ADAPTED FROM JOHNS HOPKINS CASE STUDY PROVIDED BY DR NANCY KASS