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Joan Claybrook, President

October 17, 1996

Harold Varmus, MD
Director
National Institutes of Health
Building 1, Room 126
9000 Rockville Pike
Bethesda, Maryland 20892

Dear Dr. Varmus:

We are writing to urge you to immediately cancel the National Institutes of Health (NIH) funding of a research project in Anchorage, Alaska that would randomize people who are injection drug users (IDUs) to receive or not receive syringes from needle exchange programs (NEPs). Half of the people in the study will be actively prevented from using the NEP, even though almost all scientists who have conducted research in this area believe that NEPs can reduce the transmission of HIV and do not lead to increases in drug use. It is simply unconscionable for the NIH, the nation's leading health research institution, to fund a project that so clearly violates basic research ethics in a manner that the researchers themselves admit in their grant proposal "represents the withholding of a potentially life-saving service."

The research project, which is entitled "Interventions to Reduce HBV (hepatitis B virus), HCV (hepatitis C virus) and HIV in IDUs," is led by Dr. Dennis Fisher of the Psychology Department of the University of Alaska Anchorage. The study was recently funded by the National Institute on Drug Abuse, one of the NIH institutes, and is now in its early stages. The protocol has been approved by both the Institutional Review Board of the University of Alaska Anchorage and NIH's Office for Protection from Research Risks. The project was proposed to run for three years at a cost of $2.7 million to the NIH.

Dr. Fisher is proposing to establish a NEP in Anchorage for the purpose of

Ralph Nader, Founder

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conducting research on the effectiveness of the programs. NEPs, while a standard component of HIV prevention efforts throughout the industrialized world, are severely limited in the U.S. because of a ban on the use of federal funding for providing syringes even though the government can fund studies such as this one as long as needles and syringes are not paid for. There are now six reviews[1,2,3,4,5,6] (covering hundreds of studies) that have been funded by the federal government and all, including one conducted by a group led by one of us (Peter Lurie) in 1992-93,[3] concluded that NEPs can reduce the rate of HIV infection without increasing drug use rates. (These are the criteria that, according to federal legislation, must be met for the ban to be lifted.) We are enclosing a letter from 32 leading NEP researchers from around the world to Health and Human Services Secretary Donna Shalala protesting her comments on needle exchange which includes a table describing the six reviews. (See Appendix 1.) As you can see, all the signatories assert that NEPs can reduce HIV transmission rates without increasing drug use rates. In addition, many major medical organizations, including the government's own Centers for Disease Control and Prevention, have endorsed NEPs as components of a comprehensive strategy to prevent HIV among IDUs. (See Appendix 2.)[4] No such group has come out against the programs. Indeed, in an effort to justify the study, the Alaska researchers were forced to cite a widely discredited 1992 report from former Drug Czar Bob Martinez, a non-scientist with transparently political motivations for opposing NEPs.

It is a fundamental tenet of research ethics that when the community of experts has concluded that an intervention is effective in improving health outcomes,

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[1] National Commission on Acquired Immune Deficiency Syndrome. The twin epidemics of substance use and HIV. Washington DC, 1991.

[2] General Accounting Office. Needle exchange programs: research suggests promise as an AIDS prevention strategy. (GAO/HRD-93-60). U.S. Government Printing Office, Washington, DC, 1993.

[3] Lurie P, Reingold AL, eds. The public health impact of needle exchange programs in the United States and abroad, Volume I. University of California, 1993.

[4] Satcher D. Note to Jo Ivey Boufford. December 10, 1993. Available from the Drug Policy Foundation, 4455 Connecticut Avenue, NW, Suite B-500, Washington, DC, 20008.

[5] Normand J, Vlahov D, Moses LE, eds. Preventing HIV transmission: the role of sterile needles and bleach. National Research Council/Institute of Medicine. National Academy Press, Washington, DC, 1995.

[6] Office of Technology Assessment. The effectiveness AIDS prevention efforts. Washington, DC, 1995.

randomized trials that exclude many people from the benefits of the intervention are no longer ethical. Despite the consensus described above, the NIH-funded researchers propose to randomize 600 IDUs to NEPs or a comparison condition. If one agrees to participate in the study, one stands a 50% chance of being permitted to attend the NEP. The remaining 50% of study subjects (300 people) will be turned away from the NEP (subjects will be issued a bar-coded identification card which can generate an image on the research project's computer) and will instead be given information about purchasing syringes from pharmacies, information many or most will already have.

The study examines whether those assigned to attend the NEP develop hepatitis B at a rate greater or less than those assigned to the comparison condition. (Hepatitis B is used instead of HIV infection as a marker of program effectiveness because HIV infection levels among IDUs in Anchorage are too low to be able to demonstrate program effectiveness statistically. Thus a decrease in new hepatitis B infections due to an intervention is thought to represent a decrease in risk for HIV infection as well.) In fact, there was already evidence that NEPs decrease the risk of acquiring hepatitis by the time Dr. Fisher submitted his grant proposal to the NIH in December 1995. An article in the *American Journal of Public Health* in November 1995 describes a case-control study that demonstrated a six-fold reduction in the odds of acquiring hepatitis B and a seven-fold reduction in the odds of acquiring hepatitis C among IDUs who had ever attended an NEP in comparison to IDUs who had never attended a NEP.[7]

The researchers somehow believe that referrals for the pharmacy purchase of syringes represent an ethical alternative to the NEP condition for those not randomized to the NEP. Abundant data suggests otherwise. First, all the non-randomized controlled studies on the effect of NEPs on IDUs' risk behaviors implicitly compare syringe availability through NEPs with syringe availability through pharmacies and diverted sources. In all studies, the reduction in the rate of syringe sharing, the behavior that transmits HIV infection, was as great or greater in the NEP group.[3] Thus, the control group proposed by the researchers has already been demonstrated to be inferior. Second, the researchers argue that the study is ethical because Alaska has no requirement for a medical prescription in order to purchase a syringe. Again the data, conveniently excluded from their research proposal, do not support them. For example, in St. Louis, Missouri (a state without a syringe prescription law), an African American and a white research assistant each requested ten syringes from 33 pharmacies. Eighteen percent of the pharmacies stated that small quantities of syringes were not available (IDUs tend to purchase small numbers of syringes at a

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[7] Hagan H, Des Jarlais DC, Friedman SR, Purchase D, Alter MJ. Reduced risk of hepatitis B and hepatitis C among injection drug users in the Tacoma syringe exchange program. *American Journal of Public Health* 1995; 85:1531-1537.

time), an additional 12% refused to sell to either research assistant and an additional 12% refused to sell to the African American only.[8] Thus, African Americans were prevented from purchasing syringes in 42% of pharmacies. In New Orleans, Louisiana, also a state without a prescription law, only 14.5% of pharmacists said they sold syringes to anyone, and many required a prescription.[9] All of this assumes that the IDU has the money to purchase the syringe.

From a public health perspective, it would be ideal for IDUs to have access to both NEPs and pharmacies. Individual IDUs prefer different sources of syringes and maximizing the IDUs' choices is likely to be the most effective HIV prevention strategy. For the researchers, however, this creates the problem of "crossover": IDUs assigned to the NEP may want to attend the pharmacy or vice versa. Thus, the researchers go out of their way to prevent "crossover," going so far as to have the NEP open only when the pharmacy that accounts for most sales of syringes to IDUs is also open. This stands public health common sense on its head and places people who are IDUs at risk for fatal infections. NEPs should complement alternative syringe sources, not compete with them. In this sense, the study is not even a reasonable test of the public health question it should be investigating.

The research is, therefore, unethical for at least three reasons:

1. If an IDU does not enroll in the study, he or she cannot use the NEP at all, thus coercing subjects to enroll;[10]

2. For IDUs who enroll in the study, only 50% will be permitted to attend the NEP; the others will be turned away; and

3. It is highly inappropriate to stand by and watch IDUs in both research groups contracting potentially fatal hepatitis B infections when an extremely effective vaccine

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[8] Compton W, Cottler L, Decker S, Mager D, Stringfellow R. Legal needle buying in St. Louis. *American Journal of Public Health* 1992; 82:595-596.

[9] Lawrence D, Lawrence M, Atkinson W, Risi G, Lauro A. Needle-sharing among intravenous drug users in New Orleans. *Journal of the Louisiana State Medical Society* 1991; 143:18-21.

[10] The researchers' grant proposal appears to imply that the NEP is only for IDUs in the research study; this seems most likely, as IDUs would otherwise have no incentive to enroll. However, if the NEP is available to IDUs not in the study, this is even more unethical because the study then results in the forcible denial to some study subjects of services available to everyone else in the community.

for hepatitis B exists. It is difficult for us to imagine an analogous study in which babies were monitored for the occurrence of tetanus, while not being provided with the existing vaccine.

Remarkably, the researchers themselves acknowledge the ethical problems presented by the study when they admit on page 75 of their proposal to the National Institute on Drug Abuse "the fact that (the non-needle exchange) condition represents the withholding of a potentially life-saving service." In our view, this ethical concern applies equally to the withholding of hepatitis B vaccine. The parallels here to the Tuskegee Syphilis Study, in which African-American men were denied penicillin treatment for syphilis for about three decades, are clear. Although in the Tuskegee, study known effective treatment for a life-threatening disease was withheld, in this human experiment, two known effective means of prevention–hepatitis B vaccine and the provision at no cost of sterile needles and syringes–are being withheld.

In summary, this study should not be funded unless:

1. All IDUs in the study are provided with hepatitis B vaccine; and

2. All IDUs are permitted to attend the NEP; and

3. The research project design is overhauled so that no IDUs are denied access to needle exchange services.[11]

In their successful grant application for NIH funding, the Alaskan researchers appealed for support on the grounds that such a randomized, controlled study of the benefits of needle exchange programs has never been done and, later in the application, admitted to "much agonizing over the ethics of this project." There are excellent reasons, discussed above, why such a study has never been done and why one should never be done.

The study represents a classic conflict between the alleged needs of researchers and the clear demands of public health. By funding this project, the NIH has allowed research to take precedence over public health prerogatives, with potentially catastrophic results for some IDUs in the study who may contract HIV or

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[11] Such a study could, for example, involve opening an NEP and following a group of IDUs over time to see if those who attend the program most often are more or less likely to change behavior or develop HIV infection. While this would not have the benefits of the randomized design, it would be ethical as all IDUs would be able to attend the NEP. Such a study would also vaccinate all IDUs who are still susceptible to hepatitis B with the hepatitis B vaccine.

hepatitis after being turned away from the NEP. If the NIH wishes to maintain its credibility as the nation's "watchdog" for unethical scientific practices, you will ensure that this dangerous, unethical and exploitative study is halted immediately and will launch an investigation into how this study passed the NIH's ethical review.

Sincerely,

Peter Lurie, MD, MPH
Research Associate

Sidney M. Wolfe, MD
Director
Public Citizen's Health Research Group

cc: Congressman Henry Waxman
Senator Edward Kennedy

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Wednesday, January 17, 1996

Appendix 1

Secretary Donna Shalala
Department of Health and Human Services
200 Independence Ave, SW
Washington, DC 20201
Fax: (202)690-7203

Dear Secretary Shalala:

As needle exchange program (NEP) researchers from four continents, we write to protest your recent public comments regarding the efficacy of NEPs in preventing HIV infection among injection drug users, their sex partners and their children. To assert, as you did in the New York Times on December 7, 1995, that there is "controversy over research" or that "different experts disagree," as you told CNN on December 5, is to grossly mischaracterize the enormous body of research on NEPs, much of it generated by the signatories to this letter. As you must know, multiple studies have shown that NEPs can decrease HIV transmission rates without increasing community levels of drug use. We therefore call on you to immediately lift the federal ban on NEP services. These programs have the ability to significantly reduce HIV infections related to injection drug use, now estimated by HHS to be occurring at a rate of over 20,000 per year in the United States.

What is most notable about research in needle exchange is the astonishing unanimity among researchers who have looked at this issue in detail. The attached Table summarizes the results of six federally funded reviews of NEP efficacy conducted between 1991 and 1995. All six of the reviews concluded that NEPs reduce HIV transmission rates and do not increase the amount of drug use. Four of the six reviews recommended lifting the ban on federal funding for NEPs and revoking or modifying the state prescription and paraphernalia laws that limit injection drug users' access to sterile syringes. The only two institutions that did not make these recommendations, the General Accounting Office and the Office of Technology Assessment, simply reviewed the data and did not make any policy recommendations, although their conclusions clearly support a recommendation to lift the ban.

Ironically, your statements to the press were made almost two years to the day that scientists in your own department recommended that the federal ban on NEPs be lifted (the fourth study in the Table). On December 10, 1993, after reviewing the data on NEP efficacy in detail and consulting with the four HHS agencies with jurisdiction over substance abuse (National Institutes for Health, Food and Drug Administration, Substance Abuse Mental Health Services Administration, Health Resources and Services Administration), the Centers for

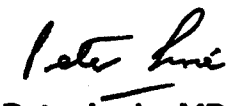
Disease Control and Prevention reached the following conclusions and made the following recommendations:

> " ... these observations indicate that NEPs are likely to reduce HIV transmission ..."
>
> "No data exists indicating increases related to NEPs in either drug use or in the number of discarded syringes."
>
> "We conclude that the ban on Federal funding of NEPs should be lifted ..."
>
> "... we also recommend that States consider the repeal of laws requiring a physician's prescription to buy needles and syringes and the removal of criminal penalities [sic] for the possession of needles and syringes ..."

Moreover, the data demonstrating NEP efficacy have become even more convincing since your advisors recommended lifting the ban on federal NEP funding in December 1993. The September 1995 National Academy of Sciences (NAS) review (the fifth study in the Table) examined three unpublished studies previously mentioned by HHS in justifying its inaction on NEP funding. The NAS found the (still unpublished) studies either seriously wanting or inconclusive and went on to recommend that the federal government fund NEPs.

Injection drug use is now the number one cause of new HIV infections in this country, and NEPs are therefore a critical component of any comprehensive HIV prevention strategy. Basing your opposition on purported scientific concerns can no longer be justified, particularly when there are six federally funded studies, including one by your own staff, that endorse federal NEP funding. Such a mischaracterization of scientific information is particularly regrettable when coming from the Secretary of HHS, who has responsibility for the vast majority of medical research funded by the federal government. Even if the research had not reached the consensus that it has, your own thoughtful comments to Dateline NBC on December 13, 1995 regarding the potential of HHS' Public Service Announcements to induce more sexual activity among teenagers provide a more appropriate guideline for federal action. "But we can't wait for a scientific breakthrough," you said, "or we're going to lose another generation of Americans. It's not worth it. I'd rather take all the criticism and save lives."

Sincerely,



Peter Lurie, MD, MPH
Assistant Professor

Please see attached page for additional signatories

Conclusions and Recommendations of U.S. Government-funded Reports on the Efficacy of Needle Exchange Programs (NEPs)

Report, year	NEPs Reduce HIV transmission	NEPs do not increase drug use	Revoke Federal funding ban	Revoke state prescription and paraphernalia laws
NCOA, 1991	Yes[1]	Yes	Yes	Yes
GAO, 1993	Yes[2]	Yes	N/A[3]	N/A[3]
UC, 1993	Yes	Yes	Yes	Yes
CDC, 1993	Yes	Yes	Yes	Yes
NAS, 1995	Yes	Yes	Yes	Yes
OTA, 1995	Yes	Yes	N/A[3]	N/A[3]

[1]Legal barriers precluding needle exchange lead to increased HIV transmission
[2]"Research suggests promise as an AIDS prevention strategy"
[3]The OTA and GAO reviewed the data without making policy recommendations

NCOA=National Commission on AIDS
GAO=General Accounting Office
UC=University of California
CDC=Centers for Disease Control and Prevention
NAS=National Academy of Sciences
OTA=Office of Technology Assessment

Appendix 2

Organizations that have Endorsed Needle Exchange Programs (partial listing)

American Medical Association
American Academy of Pediatrics
American Psychiatric Association
American Public Health Association
American Society of Addiction Medicine
Association of State and Territorial Health Officers
Centers for Disease Control and Prevention
National Association of Social Workers
National Association of State Alcohol and Drug Abuse Directors
World Health Organization

Needle exchange researchers signing the letter to Secretary Shalala (signatures on file)*

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