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Joan Claybrook, President

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

Dear Dr. Varmus:

Thank you for the opportunity to respond to the report of the panel (hereafter referred to as the Panel Report) that reviewed Dr. Dennis Fisher's proposal to conduct a randomized, controlled trial of needle exchange programs (NEPs) in Anchorage, Alaska. Unfortunately, the panel's report omits critical information, is naive to the realities of IDU syringe purchase in pharmacies, and continues to deny those injection drug users (IDUs) who so desire optimal access to sterile syringes in an NEP even though, as the panel acknowledges, "studies support the hypothesis that needle exchange lowers the incidence of blood-borne infections [such as hepatitis B and HIV] in injecting drug users" (Panel Report, page 5). In addition, the mechanisms now identified by Dr. Fisher (but not mentioned in his protocol) for offering hepatitis B vaccine are inadequate, a concern you voiced in two questions to the panel.

Several federally funded reports have recommended the combination of NEPs and pharmacy sales (not one or the other) as the optimal approach to preventing HIV transmission among IDUs (see, for example, reports by the University of California, Centers for Disease Control and Prevention, and Institute of Medicine). In most western countries and some cities in the U.S., this dual option is available. Yet, if Dr. Fisher's study is conducted according to plan, most IDUs will not receive this standard of care. Those randomized to the pharmacy condition will be turned away from the NEP, those randomized to the NEP may purchase syringes at the pharmacy and those excluded from the study (many IDUs in Anchorage simply because of

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the size of the study) or not choosing to participate will get neither access to the NEP nor the misnamed "enhanced" pharmacy option.

The panel seems to have bought in to the naive notion that providing a bus map, pharmacy opening hours, syringe prices and information on how to dress and act in order to convince pharmacists that one is not an IDU will significantly increase syringe availability through pharmacies. Is it really possible that people who have been injecting drugs for years do not already have access to this information? It was under precisely these conditions that Anchorage had the second highest syringe sharing rate of the 22 NIDA-funded Cooperative Agreement sites. The panel has completely ignored the only available data on syringe availability through Anchorage pharmacies (Dr. Fisher provides only anecdotes and unsupported assertions): our study from last month (see our Nov. 18 letter to you) found that only 14% of pharmacies consistently sell syringes to IDUs without encumbrance. The panel has also ignored the ethnic bias evident from our study: an African American woman was refused syringe sales at all five pharmacies she visited, including two that had sold syringes to non-African Americans the day before. Even Dr. Fisher stated at the meeting that at present 50% of Anchorage IDUs currently do not purchase syringes from pharmacies. Under these conditions, how can pharmacy sales be considered an ethical alternative to free syringes at NEPs?

The panel also seems not to have considered a crucial fact excluded by Dr. Fisher from the main section of his protocol, and which we could discern only from close inspection of the sheets planned to be used by study staff to educate IDUs participating in the study. Although Alaska has no paraphernalia law precluding the sale and possession of syringes unless for a legitimate medical purpose, city of Anchorage has such an ordinance. This probably, in part, explains the difficulty in purchasing syringes demonstrated in our study. Dr. Fisher has continued to mislead the NIH and the ad hoc panel by neglecting to mention this critical point.

The panel puts great emphasis on the virtues of the randomized design, particularly the issue of avoiding self-selection into the trial. However, in the real world, IDUs will select the syringe procurement strategy that best fits their needs. The information provided by this artificial experiment will therefore have little relevance to the real world in which IDUs live.

The panel asserts that "By permitting persons in the needle exchange part of the trial to still purchase sterile syringes at pharmacies, this project can help describe the characteristics of people who strongly prefer one mechanism of distribution over another." This effectively acknowledges

that the randomization claimed as the benefit of this study is likely to be substantially violated. (The panel failed to acknowledge, as Dr. Fisher does in his November 12, 1996 letter to you, that NEP syringes will also cross-over to the pharmacy group, and vice versa, further undermining the randomization.) If one were really interested in the question of which IDUs would use particular syringe sources, one would provide unrestricted access to all syringe sources and see what IDUs choose. In any event, the study provides no information on which of the IDUs assigned to the pharmacy would prefer to attend the NEP, as those individuals will simply be turned away.

There is an ethical alternative to the proposed research design. IDUs could be recruited and provided with full information about the study (not the incomplete and deceptive informed consent form that we criticized in our letter to you on December 12). Those who choose to enroll in the randomized study could be randomized to the NEP or pharmacy option. Others recruited to the study would be provided access to whichever interventions they prefer, with all of the follow-up, vaccination, counseling and testing which will occur in the group which chooses to be randomized. Thus, any IDU in Anchorage who wished to attend an NEP could do so. This would remove the coercive aspects of Dr. Fisher's trial and provide those IDUs who so choose with access to the standard of care: sterile syringe access through both pharmacies and NEPs.

The coercion in Dr. Fisher's trial is a clear violation of the first principle of the Nuremberg Code which requires truly voluntary informed consent. It belies the concept of voluntary informed consent to withhold access to needle exchange---proven, unlike the enhanced pharmacy option, to decrease the spread of infection---unless people volunteer for an experiment in which they have a 50% chance of being denied access. In a study cited in the Panel Report the superiority of NEPs to pharmacy purchase is demonstrated. IDUs in Tacoma, Washington--a city with state restrictions on pharmacy purchase similar to the municipal restrictions in Anchorage--who had hepatitis B were six times more likely to have never used an NEP than carefully matched IDUs who had not contracted hepatitis B. (Am J Public Health, November, 1995).

It is, of course, possible that many IDUs would decline enrollment in the randomized portion of such a study. But that would only confirm our central assertion: that the present study denies IDUs access to the syringe procurement option of their choice, with potentially fatal results for those randomized to the pharmacy option.

Incredibly, the Panel Report completely ignores the obvious failings of Dr. Fisher's informed consent form which we obtained through the Freedom of Information Act. These include: 1. If you are assigned to the pharmacy condition you cannot attend the NEP. 2. If you are assigned to the pharmacy condition and attempt to exchange needles at the NEP you will by turned away. 3. If you do not sign up for the study you cannot attend the NEP. 4. The syringes at the NEP are free. 5. The NEP will provide other free services such as condoms, bleach, alcohol wipes, sterile water and HIV protection literature. 6. The researchers will be monitoring to see if you develop potentially fatal hepatitis B infection, even though they have a vaccine that could prevent it. (In fact, there is no mention of hepatitis B vaccine at all in the informed consent form.)

The mechanisms for providing hepatitis B vaccine remain inadequate. The panel seems willing to accept Dr. Fisher's claim that various referrals and vouchers will result in adequate access to the vaccine. If Dr. Fisher is so devoted to the provision of the vaccine, why was there no mention of this in his protocol or in the informed consent form? A prospective trial is an excellent opportunity for delivering hepatitis B vaccine at the study site as it requires multiple injections and the study would have ongoing contact with subjects. Previous studies have demonstrated that researchers who really put their minds to providing hepatitis B vaccine have had significant success (Lugoboni F, Mezzelani P, Venturini L, Fibbia GC, Des Jarlais DC. An HBV vaccination program from street injecting drug users: implications for testing an HIV vaccine. Presented at VIIIth International Conference on AIDS, Amsterdam, 1992 (PoC 4796)). The unpleasant fact is that, to the extent that vaccination is provided, the study's statistical power could be dramatically reduced. Given the conflict of interest inherent in this research project, and Dr. Fisher's failure to mention the vaccination efforts that he now claims after the fact, we do not feel confident that vaccination levels with the voucher-go-somewhere-else-system will be significant; preventable hepatitis B infections will be the result.

We stand by our assertion that is unethical to determine that someone with whom you will have ongoing contact is at risk for a potentially fatal infection, and then to monitor them to see if they develop that infection without adequately providing for vaccination. The statement by the panel that the Institute of Medicine Report recommended that "NEPs not be burdened with a requirement to provide such intensive preventive health efforts [as providing hepatitis B vaccine]" is irrelevant to the question at hand. The question is whether the research project should be required to provide such vaccinations. We believe, as you suggested at the Thursday

meeting, that studies funded by the NIH, especially a prospective intervention study such as this, should meet a higher ethical standard. This means providing on-site hepatitis B vaccination.

Aside from the crucial issues of serious breeches in ethics and violations of both the first and fifth principles of the Nuremberg Code, there is another very important question not adequately addressed in the panel report. What is the importance, relevance, or projected future usefulness of this study? Inevitably, not too long from now, the United States will join the rest of the civilized world and offer, with the help of Federal funding, to most if not all IDUs who wish to decrease their likelihood of getting blood-borne infection, the choice of either unrestricted purchase in pharmacies or access through NEPs. It is close to impossible that, since as the report acknowledges some people prefer one alternative, some the other, any finding of this study will have any influence on progress in this direction. No randomized trial was thought necessary or useful to start extensive NEPs in many countries and at 100 sites in this country. This project merely squanders $2.4 million in scarce NIH funds.

You have one last chance to avoid a serious ethical blow to NIH's reputation as the nation's and probably the world's leader in biomedical research. Rather than accepting the recommendations of a panel that excluded IDUs or their representatives, included several individuals who are NIH grant recipients and thus may be reluctant to criticize the agency, and relied on often misleading and after-the-fact pronouncements by Dr. Fisher, we urge you to put the lives of IDUs first by putting an abrupt end to this exploitative and unnecessary study, as it is currently designed.

Since your panel's report confirms the findings of previous Federally-funded reviews that the two criteria necessary for lifting the Federal-funding ban---that NEPs be shown to reduce HIV transmission and not increase drug use--have been met, we strongly urge you to demand that Secretary Shalala immediately lift the ban.

Yours sincerely,

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Research Associate

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Director