National Whistleblower Center
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Chairman, Board on Health Promotion and Disease Prevention
Institute of Medicine
500 Fifth Street NW
Washington DC 20001

Project Identification Number: HPDP-H-04-08-A

Dear Dr. Curran:

I am writing to you on behalf of the National Whistleblower Center (NWC) to bring to your attention serious concerns about the manner in which the Institute of Medicine (IOM) has chosen to structure and conduct its investigation into the HIVNET 012 Perinatal HIV Prevention Study (Project Identification Number: HPDP-H-04-08-A). The NWC is now pursuing its own inquiry into allegations of gross scientific misconduct in connection with this clinical trial. These results will be shared with the relevant committees of the U.S. Congress.

In reviewing the statement of work posted on the IOM web site, the Center has taken note of some glaring irregularities in the way the investigation is to be carried out. In summary, they include:

1. **Apparent Conflicts of Interest**: Despite the representation that the IOM is charged with conducting an independent investigation into HIVNET 012, the independence of the investigation may be viewed as suspect. The Center is aware that a number of the individuals selected to investigate this study are dependent on funding from the NIH Division of AIDS, the oversight office that whistleblowers have alleged participated in the cover-up of the study's deficiencies. This apparent conflict of interest on the part of panel members will make any conclusions reached by the IOM panel highly suspect, thus discrediting the entire effort. Full disclosure to the public of all ties of panel members to HIVNET 012, DAIDS or NIH sponsored research is warranted and all should be required to complete BI/COI FORM 1, *BACKGROUND INFORMATION AND CONFIDENTIAL CONFLICT OF INTEREST DISCLOSURE For Studies Related to Government Regulation, as required by THE NATIONAL ACADEMIES.*

2. **Lack of Objectivity**: The HIVNET 012 investigation committee is scheduled to meet on September 30, 2004 - October 1, 2004. Yet the published agenda for this meeting includes no testimony from critics of HIVNET 012, namely those individuals both inside and outside of DAIDS who have voiced strong opposition to the manner in which the study was carried out and who have knowledge of the suppression of information bearing on the safety of the drug under investigation. Any conclusions that come from this effort will lack credibility if the critics of the HIVNET 012 study are not heard and taken into account, and if all documentation bearing on the safety of the drug in question is not collected and reviewed. Upon request the NWC will assist the Board in identifying individuals knowledgeable in the conduct of HIVNET 012 who can present evidence bearing on the collection of safety data and regulatory compliance.

3. **Expertise Lacking**: The IOM investigation panel lacks specialists in critical skill and knowledge areas. The reviewing panel appears to lack an expert in Regulatory Affairs, a physician expert in Drug Safety, an expert on monitoring Good Clinical Practice (GCP) at clinical trials sites, and a representative from OHRP, all essential to a credible comprehensive review of HIVNET 012. An AIDS patient advocate should also be represented on the panel.

4. **Insufficient Scope**: In our view the questions forming the scope of the IOM investigation are incomplete and, in our estimation, will not lead to a fair and comprehensive understanding of HIVNET 012 deficiencies. Some of the questions which need to be asked include, but are not limited to:

   i. Was the protocol prescribed by HIVNET-012 followed in all respects?
   ii. Was the remonitoring effort conducted properly and was it sufficiently extensive?
   iii. Did investigator and clinical site practices adequately confer human subjects protections on the study volunteers?
   iv. Were investigator and clinical site practices adequate to assure that the chain of custody of study products was maintained?
   v. Was the remonitoring effort capable of recovering the thousands of unreported adverse events that were not recorded, as the principal investigators admitted to the Westat auditor?
   vi. Are the safety conclusions of the study valid if thousands of unreported adverse events are unaccounted for?
   vii. Since the study physicians evaluated adverse events often on the basis of third hand descriptions from non-physicians and without personally examining all patients, can this safety data and the evaluations of severity and causality be relied upon?

viii. Was the NIAID endorsement (March 2002) of the results of the HIVNET 012 clinical trial and the 1999 Lancet article premature in light of the fact that the remonitoring of the study had not yet been performed?

ix. Did the HIVNET 012 Remonitoring Report (3/30/03) accurately describe the safety findings of the remonitoring effort and the safety data review panel?

x. Was removal and substitution of the safety review panel's report from the Remonitoring Report without the panel's knowledge warranted and constitute scientific misconduct?

xi. Who really authored the safety review section of the Remonitoring Report?

xii. Was DAIDS retraction of the IND Safety Report on the finding of hyperbilirubinemia (4/8/03) appropriate?

5. **Cover-up and reprisal**: The IOM has narrowly construed its mandate to include only the technical questions concerning the HIVNET-012 study. Yet, a key element of the story is the apparent cover-up of the adverse event findings by NIH and the failure of the DAIDS oversight mechanism to preserve and present all pertinent data in an even-handed and unbiased way. These should be investigated as well. Additionally, the committee should consider the intimidation and reprisals exacted against DAIDS employees who dared to speak out about the deficiencies in the HIVNET 012 study. The committee should receive testimony from these individuals who have much to contribute to a full understanding of HIVNET-012. The testimony also will establish whether or not the clinical trial was conducted in accordance with established standards.

6. **Potential Undue Influence**: The mandate of the IOM committee does not include an exploration into whether there was undue political influence brought to bear on the NIH and the HIVNET 012 researchers. It is public knowledge that the White House based at least part of its New Mother and Child HIV Prevention Initiative on the promising results attributed to nevirapine by the misleading NIH report of the HIVNET-012 study (June, 2002), DESPITE revelations only 3 months earlier that the validity of the data was seriously suspect. It is important for the public to be reassured that drug trials sponsored by the NIH are conducted free of political influence and according to the highest scientific standards.

7. **No Audit Focus:** The charge given to the IOM committee does not make any provision for a financial audit of the HIVNET 012 study and its remonitoring. This is necessary to ascertain whether or not there were any improprieties in the expenditure of federal funds.

8. **General Reform Needed**: There is much to be learned from the failures of the HIVNET-012 study since this experience may be reflective of a systemic breakdown in the way DAIDS oversees the management of clinical trials. It is the contention of those with whom the NWC has contact that without a strong clinical trials office responsible for policy and enforcement, the problems associated with HIVNET will only be replicated at a great waste of research dollars and with consequent implications for the public health both here and internationally. It is hoped that the committee will conclude its work with recommendations on how to strengthen the entire DAIDS clinical trials oversight mechanism in light of recent, well-publicized failures.

The National Whistleblower Center trusts that the IOM will review the comments contained in this letter with the goal of correcting the obvious deficiencies in the current investigation protocol. This is essential if the public is to gain a thorough understanding of the HIVNET 012 study and the problems associated with the testing and use of nevirapine.

The public interest demands that there be full accountability for the mistakes made in the HIVNET 012 study and for the alleged attempts by some in the NIH research community to cover-up these deficiencies. Additionally, it is imperative that all of the deliberations and conclusions of the committee be open to the public.

Again, the Center stands ready to assist IOM in its investigation.

Thank you for your time and attention to this letter. I ask that it be distributed to all members of the named panel and retained as part of the public record of the panel's work.

Sincerely,

Kris Kolesnik
Executive Director

Cc: The Honorable Joe Barton, Chairman
U.S. House of Representatives, Committee on Energy and Commerce

Other Committees of Jurisdiction, U.S. Senate and the U.S. House of Representatives

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