
HIV VACCINES AND THE COMMUNITY

The Community Advisory Board Bulletin

Volume 1, Issue 4 November 2000

BIOMEDICAL ETHICS 101

A very brief discussion of a very dense topic

By Siobhan Malone

Although a brief discussion of ethical standards is nearly impossible, we will try in this and the next issue of the CAB Bulletin to highlight some of the current “hot topics” in ethics as they relate to HIV vaccine research. Two of the “hot topics” that we’ll touch on in this issue include standards of care and trial location in developing versus developed countries as it pertains to funding and development of HIV vaccines.

To begin with, it is important to understand that a number of internationally recognized codes of ethics have been developed since World War II to ensure the protection of human subjects in biomedical research. They include:

- ◆ *The Nuremberg Code, 1947*
- ◆ *Declaration of Helsinki 1964, (last amended in October 2000)*
- ◆ *The Belmont Report, 1979*
- ◆ *The CIOMS Guidelines, 1982, (last amended in 1992)*
- ◆ *Ethical considerations in HIV Preventive vaccine research: UNAIDS Guidance Document, 2000*

These Codes of Ethics form an important body of work meant to guide human behavior. Controversies and debates often arise from guidelines that seem too restrictive or too general because of their broad international scope. In order to understand why a brief ethics discussion is very difficult, it is also important to realize the process involved in creating and amending these documents. For example, the UNAIDS Guidance document was developed over a three year span from 1997 to 1999 with meetings convened in Geneva, Brazil, Thailand, Uganda and Washington. The meetings included lawyers, activists, social scientists, ethicists, vaccine scientists, epidemiologists, representatives of NGOs, people living with HIV/AIDS, and people working in health policy. The entire process involved people from a total of 33 countries.

We, in the HVTN community education program, encourage local CABs to seek out ethicists or other knowledgeable people in the field and invite them to a local meeting so that broader topics and ethical concerns can be explored in more depth.

All ethical guidelines for the protection of humans in research have at their core these three main principles:

AUTONOMY- respect for persons

“The voluntary consent of the human subject is absolutely essential. This means that the person involved should have legal capacity to give consent; should be so situated so as to be able to exercise free power of choice, without the intervention of any element of force, fraud, deceit, duress, over-reaching or other ulterior form of constraint or coercion; and should have sufficient knowledge and comprehension of the elements of the subject matter involved as to enable him [or her] to make an understanding and enlightened decision” – Nuremberg Code

BENEFICENCE- benefits outweigh risks

“Biomedical research involving human subjects must conform to generally accepted scientific principles and should be based on adequately performed laboratory and animal experimentation and on a thorough knowledge of scientific literature” – Declaration of Helsinki

“Any experiment should be such as to yield fruitful results for the good of society, unprocurable by other methods or means of study, and not random and unnecessary by nature”- Nuremberg Code

JUSTICE- selection of subjects is equitable

“The selection of research subjects needs to be scrutinized in order to determine whether some classes (e.g. welfare patients, particular racial and ethnic minorities, or groups confined to institutions) are being systematically selected simply because of their easy availability, their compromised position, or their manipulability, rather than for reasons directly related to the problem being studied” – Belmont Report



A typical ethics debate!

An example of a current hotly-debated ethical issue

One of the current “hot topics” centers around the issue of care provided to participants in HIV vaccine trials who become HIV infected during the trial. There are those who believe that all participants in all countries, rich and poor, should receive the best proven therapy, meaning that if life-long antiretroviral treatment is available to a participant in the US or France, then life-long antiretroviral treatment should be available to a participant in Uganda or Brazil. And in the other camp are those who believe that demanding that best proven therapy (life-long antiretroviral treatment) be given to a participant in a developing country might be considered an inducement to enter the trial if that therapy is not available otherwise. Can a country be forced to provide HIV vaccine trial participants with therapies that it can't afford to provide to the general public? Why should a trial participant in a poorer country be denied what his counterpart is receiving in another country? These are important questions and concerns that have no easy answer. After years of discussion and deliberation, the UNAIDS Guidance document struck this compromise:

Guidance Point 16: Care and treatment

Care and treatment for HIV/AIDS and its associated complications should be provided to participants in HIV preventive vaccine trials, with the ideal being to provide the best proven therapy, and the minimum to provide the highest level of care attainable in the host country in light of the circumstances listed below. A comprehensive care package should be agreed upon through a host/community/sponsor dialogue which reaches consensus prior to initiation of a trial, taking into consideration the following:

- level of care and treatment available in the sponsor country
- highest level of care available in the host country
- highest level of treatment available in the host country, including the availability of antiretroviral therapy outside the research context in the host country
- availability of infrastructure to provide care and treatment in the context of research
- potential duration and sustainability of care and treatment for the trial participant.

In the next issue we will explore the implications, if any, of the newly revised Declaration of Helsinki for HIV vaccines. To view the document, please visit the World Medical Association's web site at www.wma.net



The following piece from the HVTN Protocol 040 gives a concrete example of how ethical guidelines can become outdated and need to be amended to reflect our current global situation.

Ethical Considerations related to the locus of a Phase I trial involving developed and developing countries

From HVTN Protocol 040

The 1993 CIOMS guidelines specifically address the issue of a drug or vaccine from a developed country being tested in a developing country. In the CIOMS guidelines, the issue is examined in the discussion of Externally Sponsored Research "Guideline 8: Research Involving Subjects in Underdeveloped Communities" (pp. 25-26). Designed to protect the especially vulnerable from exploitation, the commentary on this guideline states, "Phase I drug studies and Phase I and II vaccine studies should be conducted only in developed communities of the country of the sponsor. In general, Phase III vaccine trials and Phase II and III drug trials should be conducted simultaneously in the host community and the sponsoring country; they *may be omitted* in the sponsoring country on condition only that the drug or vaccine is designed to treat or prevent a disease or other condition that rarely or never occurs in the sponsoring country." Since the Helsinki Declaration and the Nuremberg Code were developed in specific contexts of abuse of patients and subjects by researchers, they do not address the broader issue of international research.

The driving force behind the CIOMS guideline was the prevention of exploitation; where potentially harmful drugs and vaccines may be tested in developing countries when they would not be acceptable in a developed country. It is also assumed in this guideline that the capacity to monitor safety and immunogenicity and to respond to life threatening events does not exist in developing countries.

While well-intentioned, the rapidly changing situation in international research has resulted in this guideline being interpreted as paternalistic and too restrictive. It was not until the international collaborative effort that resulted in the UNAIDS Guidance Document, which was published in the year 2000, that a full discussion of the CIOMS perspective was given and that very perspective was subject to important modification. Guidance point 8 asserts that "generally" early research on candidate vaccines should be conducted in communities "less vulnerable to harm." But no longer is it assumed that the less developed country is vulnerable in morally relevant ways. Hence, the guidance states, "Countries may choose for valid scientific and public health reasons to conduct any phase within the populations if they are able to ensure sufficient scientific infrastructure and sufficient ethical safeguards."

(Continued on page 4)

Our Story at the University of Rochester HVTU

by Patrick Fisher

On behalf of our HVTU, I'd like to thank Steve and Siobhan for their talents and leadership and for allowing us this opportunity to introduce our unit to the rest of the HVTN. I'd also like to acknowledge our department's administrative staff and our CAB members who work diligently with our unit toward the overall success of the HIV vaccine program. Together, we hope you enjoy meeting with us for this short while. May we also take a moment to add our best wishes for safe and memorable holidays.

OUR COMMUNITY...

The metropolitan area of the *City of Rochester* provides for a population of over a million people and is situated on the south shore of Lake Ontario in Western New York State. Rochester is a city with cultural diversity and historically has been the headquarters location for Fortune 100 companies such as Eastman Kodak Company, IBM and Xerox. As well, Rochester is home to many schools of higher learning. Among them, University of Rochester, Eastman School of Music, Rochester Institute of Technology, and the National Technical Institute for the Deaf. Like many urban American communities, we are still learning to balance the benefits of being culturally diverse while acknowledging the needs of various other human groups including gay, lesbian, bisexual, transsexual and transgender.

OUR UNIT...

One of the original 5 AVEG sites, our HIV vaccine unit was established over 12 years ago, in 1988. Since that time, we have welcomed a base of almost 600 volunteer participants into our program.

Our HVTU team includes our Principal Investigator, researchers, lab directors, lab technicians, a pharmacist and a data manager as well as clinical and administrative staff. We feel we are as diverse as our volunteers.

MICHAEL C. KEEFER, M.D. Title: *PRINCIPAL INVESTIGATOR*
SHIRLEY ERB, R.N., C.C.R.C. Title: *STUDY COORDINATOR*
CAROL GOMBORONE, R.N., C.A.S.A.C. Title: *RESEARCH NURSE*
JENNIFER ST. AMOUR, R.N. Title: *RESEARCH NURSE*
CATHERINE BUNCE, R.N., B.S.N. Title: *RESEARCH NURSE*
PATRICK A. FISHER Title: *COMMUNITY EDUCATION COORDINATOR*

OUR MISSION...

To stimulate and enhance community-based dialogue concerning HIV-preventive vaccines thereby creating a supportive environment for present and future vaccine studies necessary to identifying a safe and effective HIV vaccine.

OUR VISION...

To promote HIV-preventive vaccine awareness and education, fostering community support for vaccine studies, while creating partnerships with local groups, businesses and other organizations, that they may be effectively and efficiently informed about HIV vaccine research in order to respond to their constituency inquiries.

OUR OBJECTIVES...

- To facilitate local recruitment efforts by creating interactive partnerships with local groups, business, news media and other organizations.
- To collaborate with other HVTU Community Education Coordinators towards a global supportive environment that fosters creative solutions to common needs and goals.
- To provide informed commentary to the Division of AIDS (DAIDS) in an on-going effort to support HVTN clinical sites.

OUR COMMITMENT...

Make heroes and heroines of our willing volunteers,
Establish pride in being a volunteer,
Leverage existing community, national, international and electronic resources to the benefit of our unit,
Involve community leaders as active CAB participants,
Obligate us to provide on-going education to all those involved in our success,
Recognize and reduce the fear of vaccines across all ethnic groups in our community,
Acknowledge history and always place the well-being of our volunteers as priority #1.

MELIORA is the University of Rochester logo. It is Latin and is interpreted to mean "Always better".

OUR NEWEST POSTER...

Participate now in a study of a research HIV vaccine.
Vaccines do not cause AIDS. (Payment is provided.)

Don't just
Do It,
Do It Proud ...



We Did.

Do It for you, or
Do It for someone you love.
But, please, DO IT NOW.

CALL TODAY
University of Rochester Medical Center
273 - AIDS (2437)

VOLUNTEERS NEEDED NOW
You may qualify if you are:
- Healthy
- HIV negative
- 18-60 years of age

"If not you, who?"

(Continued from page 2)

Among the reasons given for permitting early trials in host nations are that the vaccine may be directed at a viral clade prevalent in the host nation but absent from the sponsoring nation. As a consequence, it may be the only way to determine "whether safety and immunogenicity are acceptable in the virally vulnerable population." Second, a nation confronting an especially explosive epidemiological situation might be willing to test a vaccine concept not being examined in other countries. Finally, early trials may provide the basis for capacity building for Phase III trials.

Striking in this formulation is the recognition that some less developed countries may choose to undertake early trials and that such choices were not the equivalents of impositions. Hence, the protective posture of the CIOMS guidelines are implicitly rejected as overly paternalistic, as reflecting an assumption that all less developed countries are in need of protection from choices they might make. In that way the move from the 1993 CIOMS guidelines to the UNAIDS guidance parallels the shift that occurred within developed countries during the 1980s—a shift away from what came to be viewed as the overly protective posture of the ethics of research, especially with regard to vaccine trials. That shift was driven by AIDS activists who saw in research not primarily a threat but also promise of a better future. It is now almost certain that the 1993 CIOMS guidelines' position on Phase I/II trials will be absent from the new CIOMS guidelines when they are issued.

Applying the revised guidelines to this protocol, specific consideration of the following is required:

- The candidate vaccine was developed through a joint venture between Alphavax, US scientists and South African scientists.
- The candidate vaccine contains a gag gene from a South African clade C virus.
- Clade C predominates in South Africa while it is only occasionally found in the USA.
- The rationale for doing the Phase I study in South Africa is the urgent need for a vaccine in South Africa and that this candidate vaccine has been designed specifically for South Africa.

Hence the issue of exploitation where South Africa may be abused for benefit of developed countries is not pertinent in this instance. Based on the UNAIDS guidelines, this protocol's proposal to initiate these Phase I vaccine trials simultaneously in the USA and in South Africa are well within the current ethical approach and guidelines.

From the Canadian HIV/AIDS Legal Network

The major challenges to developing a safe, effective and accessible vaccine can be divided into three principle areas. The first area concerns the rights and protection of research subjects and communities in which the research takes place. For example, trial participants and their communities may face discrimination, or participation in a vaccine trial may have a negative impact on preventive behavior. It will also be crucial to insure that participants understand they may receive a placebo, or that the vaccine may not be effective. The impact of trials on women and girls must be considered, and concerns about the participation of children must be addressed. Finally, arrangements must be made for people who test HIV positive either during volunteer screening, or while the trial is taking place.

A second area of concern is the issue of equity in research, and access to the benefits of vaccine research. There are major challenges in ensuring that a successful vaccine, once developed, will be made available as quickly as possible to vulnerable communities. Other, more immediate, benefits should also accrue to communities participating in research, such as the strengthening of local technical expertise and research facilities.

Finally, competent local ethical review mechanisms must be established to review ethical research protocols, and to monitor the research as it takes place.

*By David Patterson, in his Durban conference paper
"Resolving legal, ethical and human rights challenges in HIV vaccine research."*

<http://www.aidslaw.ca/durban2000/e-durban-vacc.htm>

CALENDAR OF EVENTS

CAB PROTOCOL WORKING GROUP CONFERENCE CALL:

December 5, 2000 7 p.m. EST, 4 p.m. PST. (non-staff)

GLOBAL CAB CONFERENCE CALL:

December 14, 2000 7 p.m. EST, 4 p.m. PST (non-staff)

COMMUNITY EDUCATION/RECRUITMENT COORDINATION CALL:

December 19, 2000 2:30 p.m. EST, 11:30 p.m. PST (staff)

HAPPY HOLIDAYS!



HIV VACCINE
TRIALS NETWORK



*Please send suggestion, questions and article submissions to:
Stobhan Malone- Community Project Coordinator
HVTN/FHCRC, 1100 Fairview Avenue North
PO Box 19024, M/S: MW 832
Seattle WA 98109-1024
Stobhan@scharp.org
Tel: 206-667-6350 Fax: 206-667-6366*
